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A double-blind, placebo-controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

**Clinical Study Report for Study 029060/717
(Development Phase III)**

Document Number: HM2002/00207/00 **Compound Number:** BRL-029060

Investigational Product: Paxil CR **Generic Drug Name:** Paroxetine

Indication Studied: Premenstrual Dysphoric Disorder

Initiation Date: 25 June 2001

Completion Date: 9 October 2002

Date of Report: 20 February 2003

Sponsor Signatory: (and Medical Officer)	Dr [REDACTED] M.D. Vice President and Global Leader, Psychiatry, Clinical Development and Medical Affairs. GlaxoSmithKline

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Sponsor Signatory Signature Page

STUDY TITLE: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

Study: 029060/717

Development Phase: III

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

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Date:

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2/20/03

Table of Contents

	Page
List of Tables	7
List of Figures	11
List of Modular Appendices	12
Synopsis	13
Abbreviations	20
1. ETHICS	22
1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)	22
1.2. Ethical Conduct of the Study	22
1.3. Subject Information and Consent	22
2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE	22
3. INTRODUCTION	22
4. STUDY OBJECTIVES	24
5. INVESTIGATIONAL PLAN	25
5.1. Study Design	25
5.1.1. Overall Study Design - Description	25
5.1.2. Discussion of Study Design, Including the Choice of Control Groups	28
5.2. Protocol Amendments	28
5.2.1. Protocol Amendment 1	28
5.2.2. Protocol Amendment 2	28
5.3. Selection of Study Population	28
5.3.1. Inclusion Criteria	29
5.3.2. Exclusion Criteria	30
5.3.3. Predetermined Criteria for Subject Withdrawal	31
5.4. Investigational Products	32
5.4.1. Description of Investigational Products	32
5.4.2. Dosages and Administration	34
5.4.3. Dose Rationale	35
5.4.4. Blinding	35
5.4.5. Treatment Assignment	36
5.4.6. Assessment of Compliance	36
5.4.7. Treatment of Investigational Product Overdose	36
5.5. Prior and Concomitant Medications and Non-Drug Therapies	37
5.5.1. Permitted Medications	37
5.5.2. Prohibited Medications	37
5.6. Study Assessments and Procedures	37
5.6.1. Rating Scales	37
5.6.2. Demographic and Baseline Assessments	41

5.6.3. Efficacy Assessment	41
5.6.4. Quality of Life and Employment Status	42
5.6.5. Safety Assessments	43
5.7. Data Quality Assurance	46
5.8. Data Analysis Methods	46
5.8.1. Timings of Planned Analyses	46
5.8.2. Sample Size Considerations	47
5.8.3. Analysis Populations	48
5.8.4. Treatment Comparisons	48
5.8.5. General Considerations for Data Analyses	49
5.8.6. Data Handling Conventions	50
5.8.7. Study Population	58
5.8.8. Efficacy Analyses	62
5.8.9. Safety Analyses	64
6. STUDY POPULATION RESULTS	67
6.1. Populations Analyzed	67
6.2. Disposition of Subjects	67
6.2.1. Number and Distribution of Subjects	67
6.2.2. Number of Subjects Present at Each Visit	68
6.2.3. Number of Subjects Withdrawn from the Study	69
6.3. Protocol Violations and Deviations	71
6.4. Demographics and Other Baseline Characteristics	72
6.4.1. Demographic Characteristics	72
6.4.2. Baseline Characteristics	73
6.4.3. History of PMDD	73
6.4.4. Obstetrics and Gynecological History	75
6.4.5. Psychiatric Co-morbidity	77
6.4.6. Other Current Medical Conditions	78
6.5. Previous and Concomitant Medications	79
6.6. Treatment Compliance	81
7. EFFICACY RESULTS	83
7.1. Primary Efficacy Results	83
7.2. Secondary Efficacy Results	88
7.2.1. Change from Baseline in VAS Physical Symptoms Score	88
7.2.2. Change from Baseline in Mean Luteal Phase VAS Total Score (Regulatory Requested Variable)	90
7.2.3. Proportion of Responders Defined by a 50% Reduction from their Baseline Luteal Phase VAS-Mood Score	93
7.2.4. Proportion of Responders Defined by Mean Luteal Phase VAS—Mood Score $\leq$ Baseline Mean Follicular Phase VAS-Mood Score	94
7.2.5. Change from Baseline in AUC for Luteal Phase VAS-Mood Scores	95
7.2.6. Change from Baseline in Individual SDS Item Scores	97
7.2.7. Change from Baseline in Total SDS Item Score	99

7.2.8. Change from Baseline in the Observer Rated PMTS-O Total Score	101
7.2.9. Change from Baseline in CGI Severity of Illness Score	103
7.2.10. Proportion of Responders on the CGI Global Improvement Item Scale	106
7.2.11. Proportion of Responders on the PGE	107
7.3. Other Efficacy Results	108
7.3.1. Change from Baseline in Individual VAS Item Scores	108
7.3.2. PESM	109
7.4. Efficacy Conclusions	109
8. QUALITY OF LIFE AND EMPLOYMENT STATUS	111
8.1. Change from Baseline in EuroQol VAS Score	111
8.2. Change from Baseline in the Weighted EQ-5D Health Profile Score (EQ-5D Utility Score)	113
8.3. EQ-5D Health Profiles at Baseline and Treatment Cycle 3	113
8.4. ISCO-88	115
8.5. Overall Work Productivity Score from the WPAI	115
8.6. Quality of Life and Employment Status Conclusions	116
9. SAFETY RESULTS	118
9.1. Extent of Exposure	118
9.2. Adverse Events	119
9.2.1. Pre-treatment Adverse Events	119
9.2.2. Treatment Emergent Adverse Events	119
9.2.3. Treatment Emergent Adverse Events by Severity	120
9.2.4. Treatment Emergent Adverse Events by Relationship to Treatment	121
9.2.5. Treatment Emergent Adverse Events by Time of First Occurrence	122
9.2.6. Adverse Events by Time of Occurrence Relating to Treatment Periods	123
9.2.7. Follow-up Emergent Adverse Events	126
9.2.8. Follow-up Emergent Adverse Events by Severity	126
9.2.9. Follow-up Emergent Adverse Events by Relationship to Treatment	127
9.3. Serious Adverse Events	128
9.3.1. Fatal Events	128
9.3.2. Non-Fatal Events	128
9.4. Adverse Events Leading to Withdrawal from the Study	129
9.5. Pregnancies	130
9.6. Clinical Laboratory Evaluations	130
9.6.1. Laboratory Values Over Time	130
9.6.2. Laboratory Abnormalities of Potential Clinical Concern	131
9.7. Vital Signs	131
9.7.1. Vital Signs Over Time	131
9.7.2. Vital Signs Abnormalities of Potential Clinical Concern	132

9.8. Drug-Drug Interactions	133
9.9. Drug-Disease Interactions	136
9.10. Comparative AE Summaries	139
9.10.1. Paroxetine CR Intermittent Versus Continuous Dosing in PMDD	139
9.11. Safety Conclusions	141
10. DISCUSSION AND CONCLUSIONS	143
10.1. Discussion	143
10.2. Conclusions	145
11. REFERENCES	147
12. DATA SOURCE TABLES: STUDY POPULATION	150
13. DATA SOURCE TABLES: EFFICACY	332
14. DATA SOURCE TABLES: QUALITY OF LIFE	450
15. DATA SOURCE TABLES: SAFETY RESULTS	468
16. DATA SOURCE FIGURES: EFFICACY AND QUALITY OF LIFE	770
Attachment - Statistical Appendix	838
Modular Appendices	887

List of Tables

	Page
Table 1 Outline of Study Procedures and Assessments	27
Table 2 Subject Eligibility for Inclusion in the Study Based on Reference Cycle VAS Scores	29
Table 3 Appearance, Formulation, Dosage Strength and Batch Numbers of Drugs Used in Study 29060/717	32
Table 4 Normal Range and Criteria of Potential Clinical Concern for Laboratory Parameters	57
Table 5 Criteria for Assessment of Vital Signs Changes of Potential Clinical Concern	58
Table 6 The number of Subjects by Study Status and Population (All Subjects)	68
Table 7 Summary of Number (%) of Subjects Remaining in the Study at Each Visit (ITT Population)	68
Table 8 Number (%) of Subjects Who were Withdrawn Pre-Randomization by Reason for Withdrawal (Screening Only Population)	69
Table 9 Number (%) of Randomized Subjects Who Completed the Study or were Withdrawn by Reason for Withdrawal (ITT Population)	70
Table 10 Cumulative Percentage of Subjects Withdrawn Over Time by Reason for Withdrawal (ITT Population)	70
Table 11 Number (%) of Subjects Excluded from the Per Protocol Analyses by Protocol Violation (ITT Population)	71
Table 12 Demographic Characteristics (ITT Population)	72
Table 13 Baseline Scores in Efficacy Rating Scales by Treatment Group (ITT Population)	73
Table 14 Summary Statistics for Persistency of PMDD, Age at Onset of PMDD Symptoms and Duration of PMDD Symptoms (ITT Population) . .	74
Table 15 Relationship to Onset of PMDD Symptoms by Category. Number (%) of Subjects (ITT Population)	75
Table 16 Number (%) of Subjects by Previous Treatment for PMDD (ITT Population)	75
Table 17 Obstetrics and Gynecological History by Treatment Group. Number (%) of Subjects (ITT Population)	76
Table 18 Number (%) of Subjects with Other Psychiatric Disorders from Full Psychiatric History and MINI Interview (ITT Population)	78
Table 19 Summary of Most Frequently Administered (35% in Any Treatment Group) Prior Medications by Generic Term and Treatment Group. Number (%) of Subjects (ITT Population)	80
Table 20 Summary of Most Frequently Administered (35% in Any Treatment Group) Concomitant Medications During the Treatment Phase and Follow-up Phase by Generic Term and Treatment Group. Number (%) of Subjects (ITT Population)	81
Table 21 Number (%) of Subjects who were Overall Compliant with Study Medication (ITT Population)	82

Table 22 Summary and Analysis of Adjusted Change from Baseline in Mean Luteal Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)	84
Table 23 Summary Statistics for Mean Luteal Phase VAS-Mood Scores (ITT Population)	87
Table 24 Summary and Analysis of Adjusted Change from Baseline in Mean Luteal Phase VAS Physical Symptoms Score Adjusted for Center Group, Baseline Group and Age (ITT Population)	89
Table 25 Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS Total Score Adjusted for Center Group, Baseline Score and Age (ITT Population)	92
Table 26 Summary of the Percentage of Subjects Responding (50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score) (ITT Population)	93
Table 27 Summary of Logistic Regression for Subjects with a 50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)	94
Table 28 Summary of the Percentage of Subjects Responding (Mean Luteal Phase VAS—Mood Score $\leq$ Baseline Mean Follicular Phase VAS-Mood Score) (ITT Population)	94
Table 29 Summary of Logistic Regression for Subjects with a Mean Luteal Phase VAS-Mood Score $\leq$ Baseline Mean Follicular Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)	95
Table 30 Summary of the Analysis of Change from Baseline in AUC Luteal Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)	96
Table 31 Summary and Analysis of Adjusted Change from Baseline in SDS Individual Item Scores Adjusted for Center Group, Baseline Score and Age (ITT Population)	98
Table 32 Summary and Analysis of Adjusted Change from Baseline in SDS Total Score Adjusted for Center Group, Baseline Score and Age (ITT Population)	100
Table 33 Summary and Analysis of Adjusted Change from Baseline in PMTS-O Total Scores Adjusted for Center Group, Baseline Score and Age (ITT Population)	102
Table 34 Summary of Analysis for Change from Baseline in CGI Severity of Illness Scores Adjusted for Center Group, Baseline Score and Age (ITT Population)	105
Table 35 Summary of the Percentage of Subjects Responding on the CGI Global Improvement Item (Score of 1 or 2) (ITT Population)	106
Table 36 Summary of Logistic Regression for Percentage of Subjects Responding on the CGI Global Improvement Item Adjusted for Center Group and Age (ITT Population)	107
Table 37 Summary of the Percentage of Subjects Responding on the PGE Item (Score of 1 or 2) (ITT Population)	107

Table 38 Summary of Logistic Regression for Percentage of Subjects Responding on the PGE Adjusted for Center Group and Age (ITT Population)	108
Table 39 Number (%) of Subjects in Each Category of the PESM Questionnaire (ITT Population)	109
Table 40 Summary Statistics for Baseline and Change from Baseline in EuroQol VAS (ITT Population)	111
Table 41 Summary and Analysis of Adjusted Mean Change from Baseline in EuroQol VAS Adjusted for Center Group, Baseline Score, Age and Employment Status (ITT Population)	112
Table 42 Summary Statistics for Baseline, Treatment Cycle 3 and Change from Baseline for EQ-5D Utility Score (ITT Population)	113
Table 43 Summary of EQ-5D Health Profile at Baseline and End of Treatment Cycle 3 by Treatment Group. Proportions of Subjects with a Problem (ITT Population)	114
Table 44 Number (%) of Subjects in Each Category of the ISCO-88 (ITT Population)	115
Table 45 Proportions of Subjects with Health Problems Affecting Work Productivity and Regular Daily Activities from the WPAI (ITT Population)	116
Table 46 Number (%) of Subjects Exposed to Each Dosage of Paroxetine CR and Placebo by Time Intervals and Mean Treatment Duration (ITT Population)	118
Table 47 Number (%) of Subjects with the most Frequently Reported ($\geq 5\%$ in Any Treatment Group) Treatment Emergent Adverse Events (ITT Population)	120
Table 48 Number (%) of Subjects with the most Frequently Reported ($\geq 2\%$ in Any Treatment Group) Severe Adverse Events Occurring During the Treatment Phase (ITT Population)	121
Table 49 Number (%) of Subjects with the most Frequently Reported ($\geq 5\%$ in Any Treatment Group) Related or Possibly Related Adverse Events Occurring During the Treatment Phase (ITT Population)	122
Table 50 Number of Subjects with the Most Frequently Reported Treatment Emergent Adverse Events by Time of First Occurrence Based on Verbatim Term (ITT Population)	123
Table 51 Number (%) of Subjects with the Most Frequently Reported ($\geq 5\%$ in Any Treatment Group at Any Treatment Period) AEs by Time of Occurrence Based on "On Medication" and "Off Medication" Treatment Periods. All Severities Combined (ITT Population)	125
Table 52 Number (%) of Subjects with the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Adverse Events Occurring During the Follow-up Phase (ITT Population)	126
Table 53 Number (%) of Subjects with the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Severe Adverse Events Occurring During the Follow-up Phase (ITT Population)	127
Table 54 Number (%) of Subjects with the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Related or Possibly Related Adverse Events Occurring During the Follow-up Phase (ITT Population)	128

Table 55 Listing of Subjects with Non-fatal Serious Adverse Events	129
Table 56 Summary of the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Adverse Events by Subjects Who Withdrew from the Study Due to an Adverse Event. Number (%) of Subjects (ITT Population)	130
Table 57 Summary Statistics for Baseline and Change from Baseline for Vital Signs by Visit (ITT Population)	132
Table 58 Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in the Either Paroxetine CR Group) by Whether they were Receiving/Not Receiving Commonly Administered Concomitant Medications (ITT Population)	134
Table 59 Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in Either Paroxetine Group) by Selected Active Medical History Conditions (ITT Population)	137
Table 60 Comparative Summary of Treatment Emergent AEs for Paroxetine CR Intermittent and Continuous Dosing in PMDD. Number (%) of Subjects with Frequently Occurring AEs ($\geq 5\%$ in Either Paroxetine CR Group) (ITT Population)	140
Table 61 Comparative Summary of Follow-up Phase Emergent AEs for Paroxetine CR Intermittent and Continuous Dosing in PMDD. Number (%) of Subjects with Frequently Occurring AEs ($\geq 1\%$ in Either Paroxetine CR Group) (ITT Population)	141

List of Figures

	Page
Figure 1 Flow Chart of Study Design.	26
Figure 2 Adjusted Change from Baseline (+/- 2 s.e.) in Mean Luteal Phase VAS—Mood Scores by Treatment Group (ITT Population)	85
Figure 3 Adjusted Change from Baseline (+/- 2 s.e.) in Mean Luteal Phase VAS Physical Symptoms Scores by Treatment Group (ITT Population) .	90
Figure 4 Adjusted Change from Baseline (+/- 2 s.e.) in PMTS-O Total Score by Treatment Group (ITT Population)	103

List of Modular Appendices

	Page
Protocol and Protocol Amendments	888
Sample Case Report Form	990
Investigators' Curriculum Vitae	1178
Certificates of Analysis	1305

Synopsis

Document Number: HM2002/00207/00 **Study Number:** 029060/717

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder	
Investigator/Study Centers: This was a multicenter study carried out in 53 centers distributed as follows: 10 centers in Canada, 5 centers in Finland, 5 centers in Germany, 7 centers in the Netherlands, 6 centers in Norway, 11 centers in Sweden and 9 centers in the US.	
Publications: None at the time of this report.	
Study period: 25 June 2001 – 9 October 2002	Phase of Development: III
Objectives: The primary objective of this study was to compare the efficacy of intermittent dosing with controlled release (CR) paroxetine (12.5mg and 25mg) with that of placebo for the treatment of Premenstrual Dysphoric Disorder (PMDD). The hypothesis to be tested was that paroxetine treatment results in a greater improvement in symptoms of PMDD compared with placebo treatment. The secondary objective of this study was to evaluate the safety and tolerability of intermittent dosing with paroxetine CR (12.5mg and 25mg) for the treatment of PMDD.	
Methodology: This was a multicenter, randomized, double-blind, placebo-controlled, fixed dose, three-arm parallel group study to compare the efficacy and safety of intermittent treatment with paroxetine CR 12.5mg and paroxetine CR 25mg with placebo in subjects with a diagnosis of PMDD according to DSM-IV criteria A to D. After initial selection of subjects by a telephone interview in reply to advertisements, eligible subjects attended a screening visit (visit 1). Female subjects fulfilling DSM-IV criteria A to C for PMDD completed daily symptom visual analogue scales (VAS) for up to three menstrual cycles (reference cycles) to establish a diagnosis of PMDD. Subjects were required to meet the protocol defined VAS entry criteria for two consecutive menstrual cycles. Subjects who failed to meet the VAS entry criteria during reference cycle 1 were, at the investigator's discretion, entered into an additional reference cycle 1(a) rather than being excluded from the study at this point. Subjects received no medication during reference cycle 1 or 1(a). Following reference cycle 1 or 1(a), eligible subjects entered reference cycle 2 where they received single-blind placebo medication. At the end of the reference phase, eligible subjects diagnosed as having PMDD according to DSM-IV criteria A to D (based on their daily VAS ratings) were randomized to receive one of three possible treatments (paroxetine CR 12.5mg, paroxetine CR 25mg or placebo) in a 1:1:1 ratio for up to three double-blind treatment cycles (TCs).	

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder
Following completion of the three double-blind TCs in this study, subjects returned for a safety follow-up evaluation 14 days after the last dose of study medication. Subjects with ongoing adverse events (AEs) or unresolved laboratory values at the follow-up visit returned for a further safety follow-up evaluation 28 days after the last dose of study medication. Subjects who had withdrawn from the study early, were also required to attend these safety follow-up visits. Efficacy and safety assessments were carried out at scheduled visits at the end of each TC.
Number of subjects: A target total of 324 subjects (108/treatment group) were required for this study.
Diagnosis and main criteria for inclusion: Subjects had to be female outpatients between 18 and 45 years of age (inclusive) with regular menstrual cycles of between 22 and 35 days, and had to meet DSM-IV criteria for PMDD (criteria A-C to be fulfilled at visit 1 screening interview and criterion D in the two to three reference cycles). The condition should have been present for at least the past year during which symptoms were present in at least 9 out of 12 menstrual cycles. In addition the subject had to have a baseline (Visit 3) Clinical Global Impression (CGI) severity of illness score of ≥ 3.
Treatment administration: Paroxetine CR 12.5mg (batch numbers U00150 and U00175) and 25mg (batch numbers U00151 and U00176) was supplied as enteric-coated controlled release tablets for oral administration once daily (morning) during the luteal phase of the subject's menstrual cycle. Subjects were instructed to start taking study medication at an estimated 14 days prior to the start of their next menstrual cycle, and to stop taking study medication on the first day of menses. Matched placebo (batch number N00349) was identical in appearance.
Criteria for evaluation: Efficacy evaluations in this study included PMDD VAS items, Sheehan Disability Scale (SDS) items, Premenstrual Tension Scale (PMTS), CGI severity of illness, CGI global improvement, Patient Global Evaluation (PGE) and Patient Evaluation of Study Medication (PESM) questionnaire. Other evaluations included the EuroQol VAS and EQ-5D questionnaire, the Work Productivity and Activity Impairment (WPAI) questionnaire and the International Classification of Standard Occupations (ICSO-88). Safety evaluations included a full physical examination plus medical and surgical history, prior and concomitant medications, AEs, serious AEs (SAEs), vital signs and laboratory evaluations (clinical chemistry, hematology, thyroid function), and pregnancy test.
Statistical methods: Statistical inferences concerning the efficacy of paroxetine CR were made from the intention-to-treat (ITT) population and per protocol (PP) population (for the primary variable only), using the last observation carried forward (LOCF) dataset at TC 3. The robustness of these results was investigated by the analyses of observed cases (OC) at TC 3. The 70% LOCF dataset was not analyzed, since more than 70% of the subjects from each treatment group were present in the study at the TC 3 endpoint.

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

The primary variable, change from baseline in the mean luteal phase VAS-Mood score at TC 3 LOCF, was analyzed using parametric analysis of covariance. The model on which inference was based included terms for treatment group, center group, baseline score, and age. In addition, the interaction of treatment with each of the other main effects included in the model from the principal analysis was assessed.

All hypothesis tests were two sided. For the primary efficacy variable, hypothesis tests used a nominal 5% level of statistical significance and nominal 95% confidence intervals (CIs) were presented for the TC 3 LOCF endpoint. CIs and significance tests were adjusted for two treatment comparisons using Hochberg's modification to the Bonferroni inequality.

Secondary efficacy variables were analyzed using a model including terms for treatment group, center group, baseline score, and age. Only the ITT population was analyzed for the secondary efficacy variables. No adjustments were made for multiple treatment comparisons; hypothesis tests used a 5% level of significance and 95% CIs were presented. The interaction of treatment with the other main effects was not assessed for any of the secondary efficacy variables.

Continuous efficacy variables were analyzed using analysis of covariance techniques, with results presented as point estimates, 95% CIs (nominal 95% CIs for the primary efficacy variable) and associated p-values for the adjusted mean differences between each dose level of paroxetine CR and placebo.

Categorical efficacy variables were analyzed using logistic regression techniques with results presented as adjusted odds ratios, 95% CIs around the estimated odds ratios and associated p-values.

Summary: Three hundred and sixty-six subjects comprised the ITT population (paroxetine CR 25mg: 116 subjects; paroxetine CR 12.5mg 130 subjects; placebo: 120 subjects). The baseline demographic characteristics of the three treatment groups were similar, with respect to age, height, weight, BMI and race. The mean age of subjects ranged from 35.9 to 37.2 years, and the majority of subjects ($\geq 96.2\%$) were white. The treatment groups were also similar with respect to their baseline scores for all efficacy rating scales. A higher proportion of paroxetine CR treated subjects were withdrawn from the study compared with the placebo group [paroxetine CR 25mg: 29/116 (25.0%); paroxetine CR 12.5mg: 26/130 (20.0%); placebo: 19/120 (15.8%)]. The primary reason for early withdrawal in both of the paroxetine CR groups was "Adverse Event", paroxetine CR 25mg: 16/116 (13.8%); paroxetine CR 12.5mg: 13/130 (10.0%). The primary reason for early withdrawal in the placebo group was "Lack of Efficacy" 6/120 (5.0%).

For the primary efficacy variable, change from baseline in mean luteal phase VAS-Mood score at the TC 3 LOCF endpoint, a statistically significant difference was demonstrated in favor of paroxetine CR 25mg and 12.5mg versus placebo [paroxetine CR 25mg: adjusted mean difference = -10.79mm, 95% CI (-16.46, -5.12), $p < 0.001$; paroxetine CR 12.5mg: adjusted mean difference = -7.66mm, 95% CI (-13.25, -2.08), $p = 0.007$]. The results were supported by the TC 3 OC analysis which also showed statistically significant differences in favor of the two paroxetine CR treatment groups over placebo.

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder			
Summary of Results for the Primary Efficacy Variable, Change from Baseline in Mean Luteal Phase VAS-Mood Score (ITT Population)			
Change from Baseline to:	Treatment Comparisons	Treatment Difference¹	95% CI (p-value) for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	-13.02	-18.98, -7.06 (<0.001)
	Parox CR 12.5mg vs placebo	-7.78	-13.56, -2.01 (0.008)
TC 3 LOCF Endpoint	Parox CR 25mg vs placebo	-10.79	-16.46, -5.12 (<0.001)
	Parox CR 12.5mg vs placebo	-7.66	-13.25, -2.08 (0.007)
CI = Confidence interval; TC = Treatment Cycle; OC = Observed cases; LOCF = Last observation carried forward. 1. Difference in adjusted least square means are shown, adjusted for center group, baseline score and age.			
All of the secondary efficacy variables, including the Regulatory requested variable (VAS total score), showed differences in favor of both paroxetine treatments versus placebo at the TC 3 LOCF endpoint. For both paroxetine CR treatment groups, these differences were statistically significant for the majority of secondary efficacy variables, including the VAS total score.			
Whilst there was evidence that both paroxetine CR treatments were superior to placebo for the majority of the efficacy variables, the magnitude of the response was greater in the paroxetine CR 25mg group than in the paroxetine CR 12.5mg group.			
Summary of Results for Secondary Efficacy Variables (ITT Population)			
Change from Baseline Efficacy Variable	Treatment Comparisons	Treatment Difference¹	95% CI (p-value) for Treatment Difference
VAS Physical Symptoms	Parox CR 25mg vs placebo	-5.28	-12.26, 1.69 (0.137)
	Parox CR 12.5mg vs placebo	-6.57	-13.42, 0.29 (0.060)
VAS Total Score	Parox CR 25mg vs placebo	-77.82	-133.47, -22.16 (0.006)
	Parox CR 12.5mg vs placebo	-73.13	-127.91, -18.36 (0.009)
AUC in VAS-Mood Score	Parox CR 25mg vs placebo	-8.13	-12.26, -3.99 (<0.001)
	Parox CR 12.5mg vs placebo	-6.81	-10.88, -2.73 (<0.001)
SDS Social/Leisure	Parox CR 25mg vs placebo	-0.63	-1.45, 0.18 (0.129)
	Parox CR 12.5mg vs placebo	-0.72	-1.49, 0.04 (0.063)
SDS Work	Parox CR 25mg vs placebo	-0.86	-1.59, -0.13 (0.021)
	Parox CR 12.5mg vs placebo	-0.69	-1.36, -0.01 (0.047)
SDS Family/Home	Parox CR 25mg vs placebo	-0.91	-1.73, -0.09 (0.029)
	Parox CR 12.5mg vs placebo	-0.70	-1.47, 0.07 (0.073)
SDS Total	Parox CR 25mg vs placebo	-2.74	-4.97, -0.51 (0.016)
	Parox CR 12.5mg vs placebo	-2.33	-4.40, -0.26 (0.028)
PMTS-O	Parox CR 25mg vs placebo	-3.21	-5.42, -0.99 (0.005)
	Parox CR 12.5mg vs placebo	-1.78	-3.86, 0.30 (0.093)
CGI Severity of Illness	Parox CR 25mg vs placebo	-0.61	-1.03, -0.20 (0.004)
	Parox CR 12.5mg vs placebo	-0.27	-0.67, 0.12 (0.177)

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

Summary of Results for Secondary Efficacy Variables (ITT Population) (Continued)

Responder Efficacy Variable	Treatment Comparisons	% Responders	Odds Ratio ²	95% CI for Odds Ratio	(p-value)
Responders ³	Parox CR 25mg vs placebo	72.3 vs 49.6	3.03	1.66, 5.53	(<0.001)
	Parox CR 12.5mg vs placebo	66.4 vs 49.6	2.49	1.40, 4.45	(0.002)
Responders ⁴	Parox CR 25mg vs placebo	31.3 vs 6.7	7.08	3.03, 16.55	(<0.001)
	Parox CR 12.5mg vs placebo	17.2 vs 6.7	2.91	1.21, 7.01	(0.017)
CGI Global Improvement ⁵	Parox CR 25mg vs placebo	67.6 vs 43.1	3.47	1.87, 6.43	(<0.001)
	Parox CR 12.5mg vs placebo	56.9 vs 43.1	1.97	1.11, 3.50	(0.021)
PGE ⁵	Parox CR 25mg vs placebo	48.0 vs 28.7	2.67	1.44, 4.94	(0.002)
	Parox CR 12.5mg vs placebo	51.8 vs 28.7	3.07	1.69, 5.58	(<0.001)

AUC = Area under the curve.

Note: Results are for the TC 3 LOCF analysis, except for AUC in VAS-Mood which was calculated for the whole treatment phase. All are adjusted for center group, baseline score and age, except for CGI global improvement and PGE which were adjusted for center group and age.

1. Difference in adjusted least square means are shown.
2. The odds ratio represents the odds of improving with paroxetine relative to placebo.
3. Defined by a $\geq 50\%$ reduction from baseline in VAS-Mood scores.
4. Defined as a mean luteal phase VAS-Mood score $\leq$ baseline mean follicular phase VAS-Mood score.
5. A responder was defined as having a score of 1 or 2 at endpoint.

Subjects in all treatment groups showed improvements during the study as measured by a number of Quality of Life assessments, EuroQol VAS, EQ-5D health profile and utility score, and WPAI. There was a statistically significant difference in favor of paroxetine CR 25mg versus placebo, but not for the paroxetine CR 12.5mg comparison for the change from baseline in EuroQol VAS at the TC 3 LOCF endpoint.

The range of exposure to study medication was from 1 to 88 days with over 81% of subjects in each treatment group being exposed to at least 29 days of study medication. The mean number of days exposure to study medication was slightly lower in the paroxetine CR 25mg treatment group compared to the paroxetine CR 12.5mg and placebo groups, paroxetine CR 25mg group: 36.5; paroxetine CR 12.5mg: 38.6; placebo: 40.8.

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

In this study, 89/116 (76.7%) subjects in the paroxetine CR 25mg group, 88/130 (67.7%) subjects in the paroxetine CR 12.5mg group, and 68/120 (56.7%) in the placebo group reported treatment emergent AEs. Commonly reported treatment emergent AEs ($\geq 5\%$ in either paroxetine CR group), which occurred at an incidence at least twice that of placebo were nausea, asthenia, libido decreased, sweating, diarrhea, dizziness, tremor, insomnia and sinusitis. The majority of treatment emergent AEs in the paroxetine CR groups were rated by investigators as mild or moderate in severity, related or possibly related to study medication, and were consistent with the nature of the AEs observed in other psychiatric disorders for which paroxetine CR is approved (depression and panic). For the most frequently reported AEs in the paroxetine treatment groups ($\geq 12\%$ incidence for both paroxetine CR treatment groups), nausea, asthenia and headache, the time to first occurrence was generally during Days 1 to 7, although this was less marked for headache.

The overall incidence of AEs occurring during the "on study medication" time windows for both of the paroxetine CR treatment groups was highest in the first treatment cycle (paroxetine CR 25mg: 61.2%; paroxetine CR 12.5mg: 43.8%), reducing to a range of 29 to 36% during the "on study medication" time windows associated with treatment cycles 2 and 3. After the first treatment cycle, the incidences of AEs for both paroxetine CR treatment groups during each half of the cycle were similar to those for placebo-treated subjects.

Follow-up phase AEs were less frequent overall, than those reported during the treatment phase, but were more prevalent in the paroxetine CR groups than the placebo group, paroxetine CR 25mg: 19/116 (16.4%) subjects; paroxetine CR 12.5mg: 29/129 (22.5%) subjects; placebo: 15/120 (12.5%) subjects. The majority of follow-up emergent AEs in the paroxetine CR groups were rated by investigators as mild or moderate in intensity and unrelated or probably unrelated to study medication.

The number of subjects withdrawn because of an AE was higher in the paroxetine CR 25mg [16/116 (13.8%) subjects] and 12.5mg groups [13/130 (10.0%) subjects] compared to the placebo group [5/120 (4.2%) subjects].

There were no treatment phase or follow-up phase deaths. Seven subjects reported non-fatal SAEs during the treatment or follow-up phases, 2 subjects in the paroxetine CR 25mg treatment group (anaphylactoid reaction and abortion), 3 subjects in the paroxetine CR 12.5mg treatment group (depression with emotional lability, pulmonary embolus, and emotional lability) and 2 subjects in the placebo treatment group (both trauma). One subject reported a non-fatal serious AE five days prior to receiving paroxetine CR 12.5mg (unintended pregnancy). All but one of the SAEs (related anaphylactoid reaction for a subject receiving paroxetine CR 25mg) were considered to be probably unrelated or unrelated to study medication, but the SAEs for two of the subjects were considered to be possibly or probably associated with protocol design or procedures.

Subject vital sign and laboratory data showed no clinically meaningful changes associated with the use of paroxetine CR in subjects with PMDD. The number of subjects with laboratory and vital sign values of potential clinical concern was low.

Title: A double-blind, placebo controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

Conclusions:

- The results of this study have demonstrated that intermittent paroxetine CR provides effective benefit in the treatment of females with PMDD. Paroxetine CR 25mg and 12.5mg were statistically superior to placebo for the primary efficacy variable, change from baseline in mean luteal phase VAS-Mood score at the TC 3 LOCF endpoint, and the majority of the secondary efficacy parameters.
- While paroxetine CR 12.5mg was shown to be statistically superior to placebo for the primary and the majority of the secondary efficacy variables at the TC 3 LOCF endpoint, the estimated differences for paroxetine CR 12.5mg were usually smaller than for paroxetine CR 25mg.
- Intermittent paroxetine CR was generally well tolerated, and the nature of the AEs observed in subjects with PMDD taking paroxetine CR (25mg and 12.5mg) was, in general, comparable to those reported in other psychiatric disorders for which paroxetine CR is approved. The paroxetine CR 12.5mg treatment group experienced slightly fewer AEs than the paroxetine CR 25mg group.

Date of Report: 20 February 2003

Abbreviations

ADECS	Adverse Drug Experience Coding System
AE	Adverse event
ALAT	Alanine aminotransferase
ASAT	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
AUC	Area under the curve
BMI	Body mass index
BUN	Blood urea nitrogen
CGI	Clinical Global Impression
CI	Confidence interval
CR	Controlled release
CRF	Case report form
CRO	Contract research organisation
D & C	Dilatation and curettage
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
ECDEU	Early Clinical Drug Evaluation Unit
eCRF	Electronic case report form
EuroQol	European Quality of Life Questionnaire
FDA	Food and Drug Administration
FT3	Free triiodothyronine
FT4	Free thyroxine
GCP	Good Clinical Practice
GSK	GlaxoSmithKline
HDPE	High-density polyethylene
IEC	Independent Ethics Committee
IUD	Intra uterine device
IR	Immediate release
IRB	Independent Review Board
ISCO 88	International Standard Classification of Occupations
ITT	Intention-to-treat
IU/L	International units per litre
LOCF	Last observation carried forward
MADRS	Montgomery Asberg Depression Rating Scale
MedDRA	Medical Dictionary for Regulatory Activities
MINI	Mini International Neuropsychiatric Interview
NSAIDs	Non-steroidal anti-inflammatory drugs
OC	Observed cases
o.d.	Once daily
OR	Odds ratio
PCV	Packed cell volume
PESM	Patient's Evaluation of Study Medication
PGE	Patient Global Evaluation
PMDD	Premenstrual Dysphoric Disorder
PMS	Premenstrual Syndrome
PMTS-O	Premenstrual Tension Scale (observer rated)

PP	Per protocol
RAMOS	Randomization and Medication Ordering System
RBC	Red blood cells
RC	Reference cycle
RDM	Remote Data Management
SAE	Serious adverse event
SB	SmithKline Beecham
SC	Study cycle
s.d.	Standard deviation
SDS	Sheehan Disability Scale
s.e.	Standard error of the mean
SOP	Standard Operating Procedure
SSRI	Selective serotonin reuptake inhibitor
TC	Treatment cycle
TSH	Thyroid stimulating hormone
VAS	Visual analogue scale
WBC	White blood cells
WHO	World Health Organization
WPAI	Work Productivity and Activity Impairment
WRC-GCP	Worldwide Regulatory Compliance-GCP

1. ETHICS

1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational center ethics committee or institutional review board.

1.2. Ethical Conduct of the Study

This study was conducted in accordance with "good clinical practice" (GCP) and all applicable regulatory requirements, including, where applicable, the 1996 version of the Declaration of Helsinki.

1.3. Subject Information and Consent

Written informed consent was obtained from each subject prior to the performance of any study-specific procedures. Electronic case report forms (eCRFs) and paper diaries were provided for each subject's data to be recorded.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

This was a multicenter study carried out in 53 centers in Canada, Finland, Germany, the Netherlands, Norway, Sweden and the US distributed as follows: 10 centers in Canada, 5 centers in Finland, 5 centers in Germany, 7 centers in the Netherlands, 6 centers in Norway, 11 centers in Sweden and 9 centers in the US (Section 12, [Table 12.2](#). Note, in this data source table Canadian centers have been combined with the US centers and presented as "Country=USA", in error).

The sponsor, GSK, was responsible for administration of this study. Central laboratory facilities were provided by Quest Diagnostics Clinical Trials, Unit B1, Parkway West, Cranford Lane, Heston, Middlesex, UK, TW5 9QA and Quest Diagnostics Clinical Trials, 7600 Tyrone Avenue, Van Nuys, CA 91405, USA.

The authors of this clinical study report were [REDACTED] PhD (Clinical Development and Medical Affairs), [REDACTED] MSc (Biomedical Data Sciences) and [REDACTED] PhD [REDACTED] (Scientific Writing)].

3. INTRODUCTION

Premenstrual Dysphoric Disorder (PMDD) is characterised by cyclically recurring premenstrual (luteal) phase mood, behavioural and somatic symptoms. These symptoms are not limited to the relatively mild and primarily physical symptoms such as bloating, breast tenderness, headache as well as minor mood changes seen in Premenstrual

Syndrome (PMS), but include symptoms such as irritability, tension, dysphoria and affective lability which seriously interfere with the sufferer's social and occupational functioning. It has been noted that, in order to meet the DSM-IV definition of PMDD, the symptoms must be primarily psychological, cognitive or affective in nature (thus the predominant symptoms are depression, anxiety or irritability as opposed to breast swelling or tenderness, abnormal bloating, weight gain etc.) [Steiner, 1996].

These symptoms typically occur during the last week of the luteal phase and begin to remit within a few days of the onset of menses. However, in severe cases, symptoms may begin around ovulation and continue for 2 weeks through the first few days of menses. It has been noted that, symptoms are typically of comparable severity (though not duration) to those of a major depressive episode [American Psychiatric Association, 1994]. In order to meet the DSM-IV diagnosis the symptoms must cause an obvious and marked impairment in the ability to function socially or occupationally in the week prior to menses [American Psychiatric Association, 1994].

It is estimated that at least 75% of women report minor or isolated premenstrual changes [American Psychiatric Association, 1994]. While limited studies suggest an occurrence of "premenstrual syndrome" (variably defined) of 20-50% [American Psychiatric Association, 1994], only some 3-8% of women experience symptoms which may meet the criteria for PMDD [Steiner, 1996].

Paroxetine immediate release (IR) is a potent selective serotonin reuptake inhibitor (SSRI) that is currently registered worldwide for the treatment of depression, panic disorder, obsessive compulsive disorder, post-traumatic stress disorder, generalized anxiety disorder and social anxiety disorder. A controlled release (CR) formulation of paroxetine (paroxetine CR), a Geomatrix^{*} bi-layered capsule which delays the start, and reduces the rate of absorption of paroxetine, was developed to reduce the frequency of adverse events (AEs) associated with paroxetine. This formulation has been approved in the United States for the treatment of major depressive disorder and panic disorder, and studies investigating the effect of continuous dosing with paroxetine CR in the treatment of PMDD have been completed and were submitted in a supplemental new drug application on June 26, 2002 (S-011).

The paroxetine CR doses chosen for this study were based on a number of considerations. Previous studies with the SSRIs indicated that the effective dose for the treatment of PMDD appeared to be at the lower end of the effective dose range for depression. This finding was noted for paroxetine IR [Sundblad, 1997], fluoxetine [Steiner, 1995] and clomipramine [Sundblad, 1992]. In addition, there appeared to be little rationale to study higher doses. Steiner 1995 found that a study of fluoxetine 20mg, 60mg and placebo failed to demonstrate significant superiority for the 60mg dose over the 20mg dose. The higher dosage was however associated with a significantly higher incidence of side-effects (withdrawals due to side-effects were 8/105, 11/102 and 35/106 for placebo, 20mg and 60mg respectively). Finally, the results of three paroxetine IR flexible dose studies have been published to date. While all allowed a flexible dose regimen (10-30mg/day)

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with continuous treatment, in all cases the results indicated that a relatively low dose was effective. The results from two of the studies showed that the mean paroxetine IR dose at study endpoint was 22mg/day [Yonkers, 1996] and 17.3mg/day [Sundblad, 1997], while the results from the third study showed that the majority of subjects titrated to a 20mg/day dose [Eriksson, 1995].

In most trials investigating the effect of serotonin reuptake inhibition in PMDD, the SSRI has been administered continuously throughout the menstrual cycle. However several recent trials suggest that PMDD may be effectively treated by administration of an SSRI intermittently, during luteal phases only [Wikander, 1998; Sundblad, 1993; Steiner, 1997; Young, 1998; Halbreich, 1997; Halbreich, 2000; Jermain, 1999; Freeman, 1999; (GlaxoSmithKline Document Number [BRL-029060/RSD-101J61/1])]. Thus, the onset of action of SSRIs appears to be much shorter when used for PMDD than when used for depression, panic disorder or obsessive compulsive disorder [PPD Development, 2000; Eriksson, 1999].

As described above, PMDD symptoms typically occur during the last week of the luteal phase and begin to remit within a few days of the onset of menses [American Psychiatric Association, 1994]. In some cases, symptoms may begin around ovulation and continue for 2 weeks through the first few days of menses. The intermittent dosing regime needs to take into account the relatively rapid onset of efficacy seen in PMDD [American Psychiatric Association, 1994; Eriksson, 1999] and the duration over which PMDD symptoms may be experienced. Therefore subjects were instructed to start study medication when they estimate themselves to be 14 days prior to the onset of their next menstrual cycle (following discussion with the investigator) and they were instructed to stop study medication on the first day of menses. This methodology for intermittent dosing during the luteal phase only is consistent with other studies in this disease area [Wikander, 1998; Sundblad, 1993; Steiner, 1997; Young, 1998; Halbreich, 1997; Halbreich, 2000; (GlaxoSmithKline Document Number [BRL-029060/RSD-101J61/1])].

Subjects receiving intermittent treatment with sertraline did not report a high frequency of initial side effects each time they started medication; nor did they experience any marked discontinuation symptoms when stopping medication after the onset of menses [Jermain, 1999; Freeman, 1999]. A similar pattern was also seen in a recent study of intermittent dosing with paroxetine IR in subjects with PMDD (GlaxoSmithKline Document Number [BRL-029060/RSD-101J61/1]).

The objectives of the present trial were to evaluate the efficacy and safety of intermittent treatment with paroxetine CR (12.5mg and 25mg) compared with that of placebo for the treatment of PMDD.

4. STUDY OBJECTIVES

The primary objective of this study was to compare the efficacy of intermittent dosing with paroxetine CR (12.5mg and 25mg) with that of placebo for the treatment of PMDD. The hypothesis to be tested was that paroxetine treatment results in a greater improvement in symptoms of PMDD compared with placebo treatment.

The secondary objective of this study was to evaluate the safety and tolerability of intermittent dosing with paroxetine CR (12.5mg and 25mg) for the treatment of PMDD.

5. INVESTIGATIONAL PLAN

5.1. Study Design

5.1.1. Overall Study Design – Description

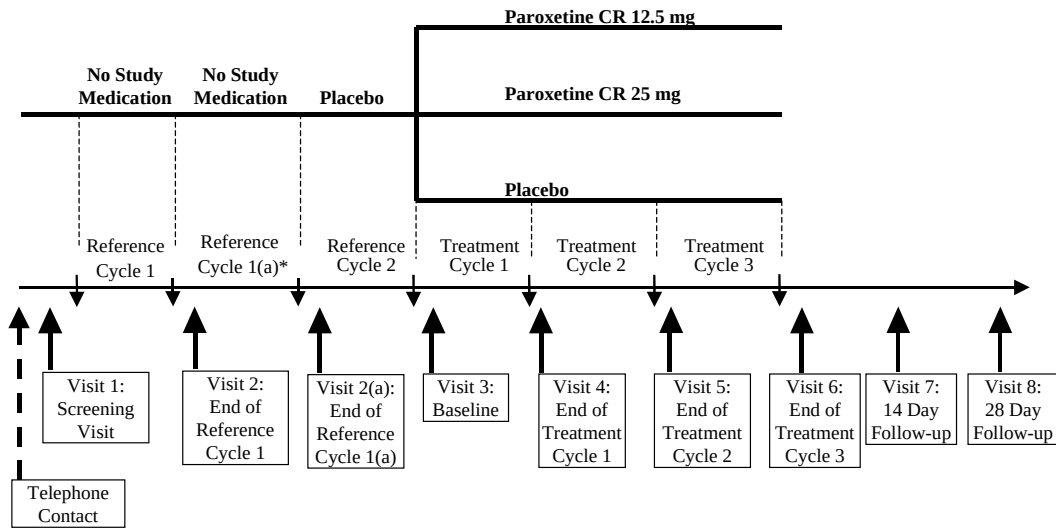
This was a multicenter, randomized, double-blind, placebo-controlled, fixed dose, three-arm parallel group study to compare the efficacy and safety of intermittent treatment with paroxetine CR 12.5mg and paroxetine CR 25mg with placebo in subjects with a diagnosis of PMDD according to DSM-IV criteria A to D.

After initial selection of subjects by a telephone interview in reply to advertisements, eligible subjects attended a screening visit (visit 1). Female subjects fulfilling DSM-IV criteria A to C for PMDD completed daily symptom visual analogue scales (VAS) for up to three menstrual cycles (reference cycles) to establish a diagnosis of PMDD. Subjects were required to meet the protocol defined VAS entry criteria for two consecutive menstrual cycles. Subjects who failed to meet the VAS entry criteria during reference cycle 1 were, at the investigator's discretion, entered into an additional reference cycle 1(a) rather than being excluded from the study at this point. Subjects received no medication during reference cycle 1 or 1(a). Following reference cycle 1 or 1(a), eligible subjects entered reference cycle 2 where they received single-blind placebo medication.

At the end of the reference phase, eligible subjects diagnosed as having PMDD according to DSM-IV criteria A to D (based on their daily VAS ratings) were randomized to receive one of three possible treatments (paroxetine CR 12.5mg, paroxetine CR 25mg or placebo) in a 1:1:1 ratio for up to three double-blind treatment cycles.

Following completion of the three double-blind treatment cycles in this study, subjects returned for a safety follow-up evaluation 14 days after the last dose of study medication. Subjects with ongoing AEs or unresolved laboratory values at the follow-up visit returned for a further safety follow-up evaluation 28 days after the last dose of study medication. Subjects who had withdrawn from the study early, were also required to attend these follow-up visits.

An overview of the study design is given in [Figure 1](#) and an overview of the schedule of assessments and study procedures is presented in [Table 1](#).

Figure 1 Flow Chart of Study Design

* = Patients who did not qualify for inclusion in the study on the basis of their reference cycle 1 diary scores may, at the discretion of the investigator, enter an optional reference cycle 1(a) rather than being withdrawn from the study.

Table 1 Outline of Study Procedures and Assessments

	Screen Visit 1	End of RC 1 ¹ Visit 2	End of RC 1(a) Visit 2(a)	Baseline Visit 3	End of TC 1 Visit 4	End of TC 2 Visit 5	End of TC 3 Visit 6	14 Day FU ² Visit 7	28 Day FU ² Visit 8	EWD Visit ²
Informed Consent	X									
Demography/Medical, Surgical History/MADRS	X									
Vital Signs	X	X	X	X	X	X	X	X	X	X
Prior and Concomitant Medication	X	X	X	X						
Physical Examination	X						X			X
DSM-IV Criteria	X ³	X ³	X ³	X ³						
Inclusion/Exclusion Criteria	X			X						
Dispense Diaries	X	X ⁴	X	X	X					
Collect Diaries		X	X	X	X	X	X			X
Adverse Events		X	X	X	X	X	X	X	X	X
Obstetric/Gynecological/PMDD History			X							
PMDD Treatment History/Psychiatric History			X							
Pregnancy Test/Laboratory Evaluation			X				X	X ⁵		X
Dispense Medication			X	X						
ISCO 88				X						
SDS (Prompt)/PMTS-O/WPAI (Prompt)				X	X	X	X			
EuroQol (Prompt)/Collect Medication/CGI/PGE (Prompt)				X ⁶	X	X	X			X
Concomitant Medication					X	X	X	X	X	X
PESM							X			X
Study Conclusion								X ⁷	X ⁷	

RC=Reference Cycle; TC=Treatment Cycle; FU=Follow-up; EWD=Early Withdrawal; MADRS Montgomery Asberg Depression Rating Scale; ISCO=International Standard Classification of Occupation; SDS=Sheehan Disability Scale; PMTS-O=Premenstrual Tension Scale-Observer Rated; WPAI=Work Productivity and Activities Impairment; EuroQol=European Quality of Life Scale; CGI=Clinical Global Impression; PGE=Patient Global Evaluation; PESM=Patient evaluation of study medicine.

- Subjects who were eligible on the basis of their reference cycle 1 VAS scores did not need to complete reference cycle 1(a). Thus they omitted Visit 2 assessments, and completed Visit 2(a) assessments instead.
- For randomized subjects only.
- Provisional diagnosis of PMDD (On Criteria A-C) was checked at screening (Visit 1). Confirmation of "on-offness" according to the VAS scores was checked during the reference cycles and confirmation of the diagnosis was made at Baseline.
- Only if additional reference cycle required.
- Only repeat labs if required.
- CGI global improvement not assessed at this visit.
- Study conclusion was to be completed at the 14 day FU, except for subjects who required repeat labs or had ongoing AEs for whom it should be completed at 28 Day FU.

5.1.2. Discussion of Study Design, Including the Choice of Control Groups

The study design was based on that used successfully for a number of PMDD studies using continuous and intermittent treatment with paroxetine IR ([GlaxoSmithKline Document Number \[BRL-029060/RSD-101J61/1 \]](#)), and continuous treatment with paroxetine CR ([GlaxoSmithKline Document Number \[BRL-029060/RSD-10127G/1 ; BRL-029060/RSD-10127J/1 ; BRL-029060/RSD-10127L/1 \]](#)). In common with these studies, the study design employed two or three reference cycles to collect data on the subject's symptoms, with a requirement that these symptoms had to meet certain criteria during two consecutive cycles. In this way the diagnosis of PMDD according to DSM-IV criteria was assured.

5.2. Protocol Amendments

The original protocol was approved on March 5, 2001. The protocol was then amended on two occasions as detailed below. Both amendments were approved by the IECs.

5.2.1. Protocol Amendment 1

An amendment to the protocol was approved on July 13, 2001, and was applicable to all centers.

The exclusion criterion relating to gynaecological disease was clarified, stressing that the exclusion was of subjects with diagnosed and clinically significant gynaecological disease (e.g. clinically significant uterine fibroids, ovarian/uterine/cervical carcinoma, or endometriosis).

5.2.2. Protocol Amendment 2

An amendment to the protocol was approved on September 11, 2002, and was applicable to all centers.

This amendment made a number of changes to the statistical section of the protocol to bring it in line with the statistical analysis performed in three recently completed studies which examined continuous paroxetine CR treatment in subjects with PMDD ([GlaxoSmithKline Document Number \[BRL-029060/RSD-10127G/1 ; BRL-029060/RSD-10127J/1 ; BRL-029060/RSD-10127L/1 \]](#)).

5.3. Selection of Study Population

The DSM-IV diagnosis of PMDD required that prospective daily rating of the subject's symptoms had to be carried out over at least two consecutive symptomatic cycles in order to confirm the diagnosis. The need for these "reference cycles" in order to confirm the diagnosis meant that the subject was not randomized into the "treatment cycles" of the study until daily symptom ratings had been carried out for two (or, optionally a third reference cycle could be allowed, see details below) complete menstrual cycles.

The VAS entry criteria stipulated that during two consecutive reference cycles the subject had to rate at least 200% higher (i.e. worse) on one, or at least 100% higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ([\text{mean luteal score} - \text{mean follicular score}] / \text{mean follicular score})$). For these items the mean follicular phase score had to be $\leq 20\text{mm}$ and the mean luteal phase score had to be $\geq 40\text{mm}$. Subjects did not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores were to be $\leq 25\text{mm}$.

To assist with the assessment of the VAS entry criteria for the study, subject eligibility calculation worksheets were provided. These provided detailed information and advice, together with a tabulated guide to help the investigator assess the subject's eligibility regarding VAS scores for the four core symptoms.

In this study, subjects who failed to meet the VAS entry criteria during the first reference cycle (reference cycle 1) could, at the investigator's discretion, enter an additional reference cycle 1(a) rather than be excluded from the study at this point. This applied where the investigator felt that the subject should probably qualify on the VAS scores although they failed to do so in the first reference cycle (e.g. scores just outside the entry criteria or unusual circumstances which caused an elevated follicular phase score). The DSM-IV criteria for PMDD stipulate that subjects must qualify on two consecutive symptomatic cycles. Various scenarios to clarify when a subject would be eligible for the study or excluded are provided in Table 2.

Table 2 Subject Eligibility for Inclusion in the Study Based on Reference Cycle VAS Scores

Reference Cycle 1	Reference Cycle 1(a)	Reference Cycle 2	Decision
Eligible	-	Eligible	Randomise
Eligible	-	Not Eligible	Exclude
Not Eligible	Eligible	Eligible	Randomise
Not Eligible	Eligible	Not Eligible	Exclude
Not Eligible	Not Eligible	-	Exclude

5.3.1. Inclusion Criteria

Subjects were eligible for inclusion in the study if they met the following criteria:

- Female outpatients between 18–45 years of age.
- Subjects had to have regular menstrual cycles (duration between 22-35 days).
- Subjects had to meet DSM-IV criteria for PMDD (criteria A-C to be fulfilled at visit 1 screening interview and criterion D in the two reference cycles).

- The condition should have been present for at least the past year during which symptoms were present in at least 9 out of 12 menstrual cycles (checked at visit 1).
- During two consecutive reference cycles the subject had to rate at least 200% higher (i.e. worse) on one, or at least 100% higher on two or more, of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ([\text{mean luteal score} - \text{mean follicular score}] / \text{mean follicular score})$). For these items the mean follicular phase score had to be ≤ 20 mm and the mean luteal phase score had to be ≥ 40 mm. Subjects did not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores were also to be low and GSK was to be consulted prior to inclusion of a subject if these scores were not ≤ 25 mm.
- The subject had to have a baseline (Visit 3) Clinical Global Impression (CGI) severity of illness score of ≥ 3 .
- The subject had, in the investigator's opinion, to be using an adequate non-hormonal form of contraception. Thus, methods such as intra uterine device (IUD), tubal ligation and double-barrier contraception (any two of diaphragm/spermicidal foam/condom) are acceptable while the use of oral contraceptives or systemic contraception are not.
- The subject had to have given written informed consent to participate in the study.

5.3.2. Exclusion Criteria

The following subjects were not eligible for inclusion in the study:

- Subjects who fulfilled DSM-IV criteria for any Axis 1 disorder (other than PMDD or specific phobias) in the 6 months prior to screening.
- Subjects with severe, clinically significant, co-existing conditions which, in the investigator's opinion, would render the subject unsuitable for the study.
- Subjects with diagnosed and clinically significant gynecological disease (e.g. clinically significant uterine fibroids, ovarian/uterine/cervical carcinoma, or endometriosis).
- Subjects with a screening MADRS score of ≥ 10 during the follicular phase of the menstrual cycle at Visit 1.
- Subjects for whom there was a significant risk of suicide.
- Subjects with any ongoing medication (including herbal medication and any use of sedatives/hypnotics) which in the opinion of the investigator could affect the subject's PMDD symptomatology (within one month prior to the screening visit and for the duration of the study period) except the following permitted treatments: the occasional use of fibrinolysis inhibitors for abundant menstrual bleeding; the occasional use of paracetamol (acetaminophen), acetylsalicylic acid or other non-

steroidal anti-inflammatory drugs (NSAIDs) to treat menstrual cramps or headaches (their use had to be documented in the concomitant medication section of the eCRF).

- Subjects with any previous adequate treatment with an SSRI for premenstrual symptoms (defined as continuous or intermittent treatment for at least 3 consecutive menstrual cycles on an adequate dose equivalent to Prozac 20mg).
- Subjects with a history of hypersensitivity or adverse reaction to paroxetine or other SSRIs.
- Subjects with any previous participation in a psychiatric drug trial (including PMDD trials) in the past 6 months.
- Subjects who were breast-feeding, pregnant or planning to become pregnant during the study period.
- Subjects with any clinically significant abnormality in screening laboratory tests.
- Subjects who had used an investigational drug within 30 days or 5 half-lives (whichever was longer) prior to the screening visit (visit 1).
- Subject characteristics which, in the opinion of the investigator, were likely to reduce compliance with the protocol (e.g. poor medication compliance, poor diary card compliance).

5.3.3. Predetermined Criteria for Subject Withdrawal

Subjects were considered to have completed the study if the investigator tick box indicated that they had completed all visits up to and including the end of menstrual cycle 3 visit and the treatment data indicated that they had actually completed treatment cycle 3 on study medication.

5.3.3.1. Withdrawal prior to randomization

During the reference cycle phase of the study, subjects who were withdrawn were categorized into the following reasons for withdrawal:

- Baseline AE
- Did not meet inclusion/exclusion criteria
- Protocol deviation (including non compliance)
- Lost to follow-up
- Other

5.3.3.2. Withdrawal after randomization

During the double-blind treatment phase of the study, subjects who were withdrawn were categorized into the following reasons for withdrawal:

- AE

- Lack of efficacy
- Protocol deviation (including non compliance)
- Lost to follow-up
- Other

5.4. Investigational Products

5.4.1. Description of Investigational Products

Paroxetine CR 12.5mg and 25mg was supplied as enteric-coated controlled release tablets encapsulated in Supro B capsules comprising an opaque Swedish orange body and cap. Matched placebo was identical in appearance. All study medication was manufactured by GSK. The formulations used in this study are identified in Table 3.

Table 3 Appearance, Formulation, Dosage Strength and Batch Numbers of Drugs Used in Study 29060/717

Study Drugs	Appearance	Formulation	Dose Units	Batch Numbers
Paroxetine CR	Swedish Orange	Supro B	25mg	U00151, U00176
Paroxetine CR	Swedish Orange	Supro B	12.5mg	U00150, U00175
Placebo	Swedish Orange	Supro B	---	N00349

All study medication was provided in 60cc white opaque high density polyethylene (HDPE) bottles with 33mm white, opaque, plastic, child-resistant caps with coated polyester film bonded aluminium foil inner seal.

The single-blind medication for the final reference cycle (reference cycle 2) was supplied as one bottle containing 24 days medication. This bottle was packed separately from the double-blind treatment.

The double-blind medication for each of the three treatment cycles (treatment cycles 1, 2 and 3) was supplied in bottles each containing 24 days medication.

Each randomized subject received three bottles contained in a carton which comprised the double-blind subject pack.

Subjects were instructed to return the carton containing all three bottles at each visit.

For supplies to North American sites, the individual bottle which comprised the single-blind treatment (reference cycle 2) was labelled with a two panel tear-off label. Each of the three individual bottles which comprised double-blind treatment (treatment cycle 1, 2, 3) was labelled with a three panel tear-off label. The left panel was permanently affixed to each bottle and contained the following information:

- Protocol Number
- Job Number (only the single-blind medication)

- Container Number (except for the single-blind placebo medication)
- Contents: i.e. quantity and description of dose form
- Treatment period (i.e. Study Cycle:.....)
- Dosage Directions
- Storage instructions
- "Keep out of reach of children"
- Investigational drug statement
- Sponsor address
- Any other information required by the regulatory authorities in the participating countries

The second and third panels made up the tear-off portion of the label. The second panel contained the blinded disclosure and the third panel contained the container number, protocol number, and fill count along with instructions for the investigator to remove and keep this portion of the label. The tear-off portion was to be affixed to the workbook at the time the medication was dispensed.

The three bottles were presented in a carton which was labelled with a single-panel label. The label text contained the following information:

- Protocol Number
- Container Number
- Contents, i.e. number of bottles and fill count
- Storage instructions
- "Keep out of reach of children"
- Investigational drug statement
- Sponsor address
- Any other information required by the regulatory authorities in the participating countries

For supplies to non-North American Sites, the individual bottle which comprised the single-blind treatment for the final reference cycle (reference cycle 2) was labelled with two labels i.e. a tear-off label and a multi-language re-closable booklet label which was affixed to the opposite face of the bottle.

Each of the three individual bottles which comprised the double-blind treatment (treatment cycles 1, 2, 3) was labelled with two labels i.e. a with a plain white label and a multi-language re-closable booklet label which was affixed to the opposite face of each bottle.

The three bottles were presented in a carton which was also labelled with two labels i.e. a tear-off label and a multi-language re-closable booklet label which was affixed to the opposite face of each carton.

The label text contained the following information:

- Protocol Number
- Job Number
- Container Number (except for single-blind placebo medication)
- Contents i.e.: i.e. quantity and description of dose form
- Treatment period (i.e. Study Cycle:.....)
- Dosage Directions
- Storage instructions
- "Keep out of reach of children"
- "FOR CLINICAL TRIAL USE ONLY"
- Sponsor address
- Any other information required by the regulatory authorities in the participating countries

NB (For all sites): The investigator was required to write the study cycle (SC) number (i.e. 3, 4, and 5) in the space provided on the main label applied to each of the three bottles of study medication (i.e. SC: 3, SC: 4, SC: 5) prior to dispensing the carton containing the three bottles to the subject.

The study medication was to be stored at room temperature (between 20° to 25°C) under secure conditions.

5.4.2. Dosages and Administration

During the final reference cycle (reference cycle 2) subjects received single blind placebo medication (one capsule each morning) during the luteal phase (i.e. last 14 days) of their menstrual cycle.

During the three treatment cycles, subjects were instructed to take one capsule each morning during the luteal phase (i.e. last 14 days) of their menstrual cycle. Thus, study medication started approximately 14 days prior to the expected time of next menses and continued until the first day of menses. During the rest of the menstrual cycle the subjects did not take study medication.

Investigators were responsible for reviewing the details of each of their subjects reference cycles and from this review they were to provide their subjects with clear instructions describing when they should start and stop taking their study medication. For example, a subject with an average cycle length of 30 days was to be instructed to start their study medication on day 17 of their cycle and to stop taking study medication on the first day

of menses. In addition, subjects received written instructions on how and when to take the study medication.

The medication during the three treatment cycles (treatment cycles 1, 2 and 3) was double-blind. Each subject was randomized to receive either paroxetine CR 12.5mg or paroxetine CR 25mg or placebo throughout the three treatment cycles.

5.4.3. Dose Rationale

The doses of paroxetine CR (12.5mg and 25mg) chosen for this study were based on a number of considerations. Previous studies with the SSRIs indicated that the effective dose for the treatment of PMDD appeared to be at the lower end of the effective dose range for depression. This finding was noted for paroxetine IR [Sundblad, 1997], fluoxetine [Steiner, 1995] and clomipramine [Sundblad, 1992]. In addition, there appeared to be little rationale to study higher doses. Steiner, 1995 found that a study of fluoxetine 20mg, 60mg and placebo failed to demonstrate significant superiority for the 60mg dose over the 20mg dose. The higher dosage was however associated with a significantly higher incidence of side-effects (withdrawals due to side-effects were 8/105, 11/102 and 35/106 for placebo, 20mg and 60mg respectively). Finally, the results of three paroxetine IR flexible dose studies have been published to date. While all allowed a flexible dose regimen (10-30mg/day) with continuous treatment, in all cases the results indicated that a relatively low dose was effective. The results from two of the studies showed that the mean paroxetine IR dose at study endpoint was 22mg/day [Yonkers, 1996] and 17.3mg/day [Sundblad, 1997], while the results from the third study showed that the majority of subjects titrated to a 20mg/day dose [Eriksson, 1995].

5.4.4. Blinding

Active paroxetine CR and placebo capsules were identical in appearance and all packaging maintained the double-blind nature of the study for the treatment cycles.

All centers were supplied with an initial supply of the single-blind medication for reference cycle 2.

Each subject was randomized to one of the three treatment arms by the GSK Randomization and Medication Ordering System (RAMOS). The investigator phoned into this system to register the subject at the start of single-blind medication. A randomization number and a container number was issued when the subject was randomized at the start of the double-blind phase of the study, which determined which subject pack was dispensed. The blinded status of the GSK monitors, investigators, and subject was maintained at all times. Complete instructions were supplied at the time of study initiation.

For supplies to North American sites, each of the three individual bottles for the double-blind supply had a three panel label attached to the outside of the bottle, of which one contained the code for the blinded medication. In order to unblind a subject treatment, an alcohol wipe was needed to remove the black protective ink. GSK had to be notified of any case of code-breaking.

For supplies to non-North American sites, individual subject code breaks were provided to the investigator and the study monitor. These contained the container number and the treatment allocation. In order to unblind a subject treatment the disclosure panel had to be scratched with a coin. GSK Clinical Research and Product Development held a copy of the master randomization code. These were provided for use in emergency situations only. All opened and unopened envelopes had to be returned to GSK at the end of the study. GSK had to be notified of any case of code-breaking.

5.4.5. Treatment Assignment

Subjects were randomized to one of three treatment arms (paroxetine CR 12.5mg, paroxetine CR 25mg or placebo) in a 1:1:1 ratio using a computer generated randomization code which was generated by the GSK Coding Memo System.

From an operational point of view, in order to assign medication to a subject the investigator phoned the GSK RAMOS virtual randomization system to register a subject. A separate call to the GSK RAMOS system was made to randomize the subject. At this call the randomization number and container number were issued; these determined the medication that the subject was dispensed.

5.4.6. Assessment of Compliance

Every effort was to be made to encourage subject compliance with the dosage regimen as per protocol. All subjects were to be instructed to return their medication pack, with any unused drug to the investigator at each scheduled visit and at the end of the study. A record of the supplies dispensed, taken and returned was made in the eCRF at the appropriate visits.

If there were any significant irregularities in compliance, in the opinion of the investigator, the subject was to be withdrawn from the study. This included subjects who did not take the study medication during the correct stage of their menstrual cycles (i.e. during the last 14 days). If a subject missed more than three consecutive days medication, GSK were to be contacted to confirm whether the subject was to be withdrawn from the study.

5.4.7. Treatment of Investigational Product Overdose

GSK was to be informed of any incidence of overdose (suspected or confirmed and irrespective of whether it involved study medication) within 24 hours, and the event documented as a serious AE (SAE). Details of any signs or symptoms and their management, including details of any antidote(s) administered, were to be recorded in the subject's eCRF.

The symptoms of overdose with paroxetine include nausea, vomiting, tremor, dilated pupils, dry mouth and irritability. There is no specific antidote. Treatment should consist of those general measures employed in the management of overdose with an antidepressant. The stomach was to be emptied either by the induction of emesis, lavage, or both. Following evacuation, 20 to 30g of activated charcoal was to be administered

every 4 to 6 hours during the first 24 hours after ingestion. Supportive care with frequent monitoring of vital signs and observation was indicated.

5.5. Prior and Concomitant Medications and Non-Drug Therapies

All prior medications taken within one month of the screening visit and all concomitant medications taken during the study, whether a prescribed medication, non-prescribed medication or herbal medication, were to be recorded in the subject's eCRF with the total daily dose, route of administration, indication, start date and end date or notation that medication was continuing beyond study end.

5.5.1. Permitted Medications

The occasional use of fibrinolysis inhibitors for abundant menstrual bleeding and the occasional use of paracetamol (acetaminophen), acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs) to treat menstrual cramps or headaches was allowed during the study.

5.5.2. Prohibited Medications

Any ongoing medication (including herbal medication and any use of sedatives/hypnotics) which in the opinion of the investigator could affect the subject's PMDD symptomatology (within one month prior to the screening visit and for the duration of the study period) was prohibited. Subjects were also excluded from the study if they had participated in a psychiatric drug trial (including PMDD trials) in the 6 months prior to the present study, and were also excluded from the study if they had used an investigational drug within 30 days or 5 half-lives (whichever was longer) prior to the screening visit (visit 1).

5.6. Study Assessments and Procedures

5.6.1. Rating Scales

This section describes the rating scales used in this study.

5.6.1.1. Daily PMDD VAS Symptom Scores

Subjects were provided with diaries and instructed to complete VAS ratings for the 11 individual PMDD symptoms described in the DSM-IV: irritability, tension, depressed mood, affective lability, decreased interest, difficulty concentrating, lack of energy, change in appetite, change in sleep pattern, feeling out of control and physical symptoms. The subject indicated the severity of the symptom by marking a position between two extremes (0mm, no symptoms and 100mm, the worst severity of that symptom which the subject had experienced) on a 100mm long horizontal line for each item. Subjects were instructed to complete VAS ratings on a daily basis throughout the study each evening before going to bed. Completed diaries containing the VAS ratings were collected and reviewed with the investigator at the next scheduled clinic visit.

The VAS-Mood score (the mean of the VAS scores for the 4 core PMDD symptoms: irritability, tension, depressed mood and affective lability) has been shown to be sensitive to change in drug treatment studies for PMDD, and its reliability and validity have also been demonstrated [Steiner, 1999].

5.6.1.2. Premenstrual Tension Scale Observer Rated (PMTS-O)

The Premenstrual Tension Scale (PMTS-O) was completed at baseline (visit 3), the end of treatment cycle 1 (visit 4), the end of treatment cycle 2 (visit 5) and the end of treatment cycle 3 (visit 6) for the luteal phase that had just ended (see Table 1). The questionnaire was included in the subject's eCRF and was completed by the investigator.

The PMTS-O has been used in subjects with PMDD to assess the severity of premenstrual symptoms [Steiner, 1999]. The PMTS-O assesses symptoms in ten different domains: irritability and hostility, tension, efficiency, dysphoria, motor co-ordination, mental-cognitive functioning, eating habits, sexual drive and activity, physical symptoms and social impairment. The 10 domains are scored with severity criteria ranging from 0 to 4 in eight domains and 0 to 2 in two domains, to give a maximum score of 36. A score of zero demonstrates no symptoms and a score of 36 indicates the most severe symptoms.

5.6.1.3. Clinical Global Impression (CGI) Scale

Both the Clinical Global Impression (CGI) -global improvement and the CGI severity of illness items were measured in this study. The CGI global improvement and CGI severity of illness were completed at baseline (visit 3) (CGI severity of illness only), the end of treatment cycle 1 (visit 4), the end of treatment cycle 2 (visit 5), the end of treatment cycle 3 (visit 6) and early withdrawal if applicable (see Table 1). The CGI global improvement and CGI severity of illness were included in the subject's eCRF and were completed by the clinician for the premenstrual phase which had just ended.

The CGI is a widely accepted measure of clinical improvement in a variety of psychiatric disorders. These items have been extensively used in psychopharmacologic trials since their introduction into the Early Clinical Drug Evaluation Unit (ECDEU) Assessment Manual for Psychopharmacologic Trials published by the US National Institute of Mental Health [Guy, 1976]. The CGI is rated by the clinician based on all information available at the time of rating.

Both the CGI global improvement and CGI severity of illness items are rated on a 1-7 scale. For the CGI global improvement item, the clinician indicates his/her assessment of the subject's total improvement or worsening compared with that individual's condition at the start of the study (whether or not the change is judged to be due to drug treatment). Typically, a score of 1 "very much improved" or 2 "much improved" is considered a responder. For the CGI severity of illness item, the clinician indicates his/her assessment of the subject's severity of illness considering their total clinical experience with the particular population being studied.

5.6.1.4. Montgomery and Asberg Depression Rating Scale (MADRS)

Subjects completed the MADRS at screening (visit 1) which was scheduled to take place in the follicular phase of the cycle. The MADRS was used to assess depressive symptoms; the timing of the assessment was such that the results of the MADRS would be unaffected by underlying PMDD symptomatology. The MADRS was included in the subject's eCRF and was completed by the investigator.

The MADRS is an internationally recognized and validated measurement for the assessment of depressive symptoms [Montgomery, 1979]. The MADRS is a clinician rated scale and consists of 10 individual questions, each rated on a seven point scale ranging from 0 (not present) to 6 (very severe).

5.6.1.5. Sheehan Disability Scale (SDS)

Subjects completed the Sheehan Disability Scale (SDS) at baseline (visit 3), the end of treatment cycle 1 (visit 4), the end of treatment cycle 2 (visit 5) and the end of treatment cycle 3 (visit 6) for the luteal phase that had just ended (see Table 1). The questionnaire was included in the subject's diary.

The SDS is an internationally recognized measure of disability (impairment) [Sheehan, 1983]. It is widely used, not only in psychiatry but also in many other chronic mental illnesses because of its generic design. It is a patient-rated scale which consists of three items; work, social life/leisure activities and family life/home responsibilities. Each item consists of a scale on which the subject circles a number from 0 ("not at all") to 10 ("very severely") in response to questions on how much these aspects of their lives are impaired.

The SDS has been shown to be very sensitive to change in drug treatment studies in psychiatry [Sheehan, 1996] and its reliability and validity have also been demonstrated in subjects with panic disorder [Leon, 1992]. The original publication of the scale does not endorse a minimum improvement on the SDS which would be considered clinically meaningful. However, the anchoring of descriptive terms "mildly" (1-3), "moderately" (4-6) and "markedly" (7-9) mean that changes within a subject are readily interpretable.

5.6.1.6. Patient Global Evaluation (PGE)

Subjects completed the PGE questionnaire at baseline (visit 3), the end of treatment cycle 1 (visit 4), the end of treatment cycle 2 (visit 5), the end of treatment cycle 3 (visit 6) and early withdrawal if applicable for the premenstrual phase that had just ended (see Table 1). The questionnaire was included in the subject's diary.

The PGE is a patient-rated scale which is similar in design to the clinician-rated CGI global improvement item. Subjects were asked to indicate their assessment of any improvement or worsening of symptoms compared with the start of the study. The PGE is rated on a scale of 1 ("very much improved") to 7 ("very much worse").

5.6.1.7. Patient Evaluation of Study Medication (PESM) Observer Rated

The PESM questionnaire was completed by the investigator at the end of treatment cycle 3 (visit 6) or early withdrawal if applicable (see [Table 1](#)). The investigator asked the subject "Did you find the medication sufficiently beneficial to ask for it again ?", if the subject replied "no" or "not sure", she was asked to specify the reason (i.e. lack of efficacy, side effects, anti-medication, other), and the response was recorded in the subject's eCRF by the investigator.

5.6.1.8. EuroQol

Subjects completed the EuroQol questionnaire at baseline (visit 3), the end of treatment cycle 1 (visit 4), the end of treatment cycle 2 (visit 5), the end of treatment cycle 3 (visit 6) and early withdrawal if applicable (see [Table 1](#)). The questionnaire was included in the subject's diary.

The EuroQol is a simple but effective standardized instrument designed for use as a measure of health outcome [[Health Policy, 1990](#)]. Applicable to a wide range of health conditions and treatments, it provides both a compact descriptive profile and a single index value that can be used as part of a pharmaco-economic evaluation. The EuroQol enables an accurate self-description of current health-related quality of life to be easily recorded.

The EuroQol has two components: the health state classification (EQ-5D) and the VAS. The EQ-5D comprises five questions corresponding to five different dimensions of health (mobility, self-care, usual activity, pain/discomfort, anxiety/depression). Subjects respond by indicating 1 (no problem), 2 (some or moderate problem(s)), 3 (unable or extreme problem(s)). The numerical combination of responses across the five questions categorizes subjects into one of 243 standard health states. The subject's health state is converted into a utility score using a predefined population-based table of coefficients (the EuroQol tariff). The VAS provides an overall summary rating of the subject's current health-related quality of life. The VAS has end points of 100 (best imaginable health state) at the top, and 0 (worst imaginable health state) at the bottom. The subject rates her current health state by drawing a line to the point on the scale that best corresponds with her own health state that day.

5.6.1.9. Work Productivity and Activity Impairment (WPAI)

Subjects completed the WPAI questionnaire at baseline (visit 3), the end of treatment cycle 1 (visit 4), the end of treatment cycle 2 (visit 5) and the end of treatment cycle 3 (visit 6) based on the luteal phase that had just ended (see [Table 1](#)). The questionnaire was included in the subject's diary.

The WPAI questionnaire is a valid and reliable measure of the benefit and costs of pharmaceutical interventions [[Reilly, 1993](#)]. The scale consists of 6 items which capture information on the effect of health problems on both the subject's work and regular daily activities. It may be either observer-rated or self-rated by the subject. The WPAI was self-rated in this study.

5.6.1.10. International Standard Classification of Occupations (ISCO-88)

Subjects completed the International Standard Classification of Occupations (ISCO-88) questionnaire at baseline. The ISCO-88 captures 10 employment classifications (e.g. professional, technician, military) [[International Labour Office](#)].

5.6.2. Demographic and Baseline Assessments

Demographic data (date of birth, race, height, weight), vital signs, and medical and surgical history were collected at the screening visit.

Baseline characteristics including psychiatric history, obstetrics/gynecological history, PMDD history and previous treatment for PMDD were assessed at the end of reference cycle 1 (visit 2) or end of reference cycle 1(a) [visit 2(a)].

Baseline efficacy and quality of life data were collected at the end of reference cycle 2 (visit 3).

5.6.3. Efficacy Assessment

5.6.3.1. Primary efficacy endpoint

The primary measure of efficacy was the change from baseline in the mean luteal phase VAS-Mood score at the treatment cycle 3 last observation carried forward (LOCF) endpoint. The mean luteal phase VAS score for each symptom was the mean of the last five days of the menstrual cycle, calculated for each subject. The VAS-Mood score was defined as the mean of luteal phase VAS scores for the four core PMDD symptoms: irritability, tension, depressed mood and affective lability. Further information on the handling and analysis of the primary efficacy endpoint data can be found in the Statistical Appendix ([Attachment 1](#)).

5.6.3.2. Secondary efficacy endpoints

- Change from baseline in the mean luteal phase VAS Physical Symptoms score at the treatment cycle 3 endpoint. Mean luteal phase score is the mean of the last 5 days of the menstrual cycle, calculated for each subject.
- Change from baseline in the mean luteal phase VAS total score at the treatment cycle 3 endpoint (Regulatory requested variable).
- Change from baseline in area under the curve (AUC) for treatment cycles 1-3 in daily luteal phase VAS-Mood scores, adjusting for the total number of luteal days.
- Change from baseline in the individual items of the Sheehan Disability Scale (SDS) (work, social life and family life) at the treatment cycle 3 endpoint.
- Change from baseline in the SDS total score at the treatment cycle 3 endpoint.
- Change from baseline in the observer rated Premenstrual Tension Scale (PMTS-O) total score at the treatment cycle 3 endpoint.

- Change from baseline in the CGI - severity of illness score at the treatment cycle 3 endpoint.
- Proportion of responders defined by a 50% reduction from their baseline luteal phase VAS-Mood score at the treatment cycle 3 endpoint.

Percentage change is defined as:

$$\% \text{ Change} = \frac{(VAS - Mood_{\text{endpoint}} - VAS - Mood_{\text{baseline}})}{VAS - Mood_{\text{baseline}}} \times 100$$

- The proportion of responders defined by a mean luteal phase VAS-Mood score at the treatment cycle 3 endpoint of less than or equal to their baseline mean follicular phase VAS-Mood score.
- The proportion of subjects who scored 1 or 2 (very much improved or much improved) on the CGI – global improvement item at the treatment cycle 3 endpoint.
- The proportion of subjects who scored a 1 or 2 (very much improved or much improved, respectively) on the PGE (subject-rated) at the treatment cycle 3 endpoint.

5.6.3.3. Other efficacy endpoints

The following have been summarized by descriptive statistics with no formal statistical analysis performed:

- Change from baseline in each individual VAS item score at the treatment cycle 3 endpoint.
- PESH (observer-rated) at treatment cycle 3 endpoint, or early withdrawal.

5.6.4. Quality of Life and Employment Status

The main quality of life and employment status endpoint was:

- Change from baseline in the EuroQol VAS score at the treatment cycle 3 endpoint.

The following variables were summarized only, no formal statistical analyses were performed:

- Change from baseline in the weighted EQ-5D health profile score based on the EuroQol tariff (EQ-5D utility).
- EQ-5D health profiles at baseline and treatment cycle 3.
- Overall work productivity score from the WPAI
- ISCO-88 (visit 3).

5.6.5. Safety Assessments

5.6.5.1. Adverse events

An AE was any noxious, pathological or unintended change in anatomical, physiological or metabolic functions as indicated by physical signs, symptoms and/or laboratory changes occurring in any phase of the clinical study whether associated with the study medication or placebo and whether or not considered to be drug related. This included exacerbation of a pre-existing condition or event, intercurrent illness, drug interaction or the significant worsening of the disease under investigation that was not recorded elsewhere in the eCRF under specific efficacy assessments. Anticipated day-to-day fluctuations of pre-existing conditions, including the disease under study, that did not represent a clinically significant exacerbation or worsening were not considered AEs. Discrete episodes of chronic conditions occurring during the study were reported as AEs in order to assess changes in frequency or severity.

Any pre-existing conditions or signs and/or symptoms present in a subject prior to the start of the study were recorded on the medical history and physical examination form within the subject's eCRF. AEs (serious and non-serious) which occurred after informed consent was obtained, but prior to administration of single-blind placebo medication in reference cycle 2 were documented on the significant medical history and physical examination form within the subject's eCRF. AEs (serious and non-serious), which occurred during the administration of single-blind placebo medication in reference cycle 2, and AEs occurring after administration of single-blind placebo medication in reference cycle 2 but prior to administration of the first dose of randomized study medication, were documented on the baseline AEs report form within the subject's eCRF. AEs occurring on or after administration of the first dose of randomized double-blind study medication were reported on the AE form within the subject's eCRF. All AEs were documented, whether or not they were considered drug related.

AEs were evaluated by the investigator at each visit. AEs not previously documented were recorded in the AEs record form within the subject's eCRF. The nature of the event, date and time of onset, outcome, course (intermittent or constant), maximum intensity, any change in study drug administration and investigator assessment of relationship to study drug were to be recorded. Details of changes to the dosage schedule or any corrective therapy were documented on the appropriate pages of the subject's eCRF.

AEs that were already documented within the subject's eCRF and designated as ongoing were reviewed at subsequent visits as necessary. If these events resolved, the appropriate pages in the eCRF were completed. If an AE increased in frequency or severity during the study a new record of the event was started.

The maximum intensity of an AE was assigned to one of the following categories:

Mild:	an AE which was easily tolerated, caused minimal discomfort and did not interfere with everyday activities.
Moderate:	an AE which was sufficiently discomforting to interfere with normal daily activities.
Severe:	an AE which prevented normal everyday activities.

Every effort was made to explain each AE and assess its relationship, if any, to study medication. Causality was assessed using the following categories:

Unrelated:	the AE was definitely not related to the test drug.
Probably unrelated:	cause and effect relationship between the drug and the AE was not demonstrated, was improbable but not impossible.
Possibly related:	a direct cause and effect relationship between the drug and the AE was not demonstrated but was possible or likely.
Related:	there was a direct cause and effect relationship between the AE and the study drug.

All AEs were coded from the verbatim term using the World Health Organization (WHO) adverse event codelist, and then mapped by the Adverse Drug Experience Coding System (ADECS) to give a body system and preferred term.

5.6.5.2. Serious adverse events

A SAE was any event which was fatal, life threatening, disabling/incapacitating or resulted in hospitalization, prolonged a hospital stay or was associated with congenital abnormality, cancer or overdose (either accidental or intentional)¹. In addition, any event which the investigator regarded as serious or which suggested any significant hazard, contraindication, side effect or precaution that was associated with the use of the drug was documented as a SAE.

Any SAE which occurred at any time after randomization or within 30 days of receiving the last dose of study medication, whether or not related to study medication, was to be reported to the sponsor within 24 hours. In addition, any SAE occurring after informed consent was obtained, but prior to randomization, which the investigator assessed as related to study procedures/design (including single-blind placebo medication) was also to be reported to the sponsor within 24 hours. Instances of death, cancer or congenital

¹ Elective surgery or routine clinical procedures which required hospitalization but were not the result of an adverse event, were not to be considered as serious adverse events.

abnormality if brought to the attention of the investigator at any time after cessation of study medication and considered by the investigator to be possibly related to study medication, were to be reported to the sponsor.

SAEs were documented on a SAE form, and the event captured on the AEs page of the subject's eCRF.

5.6.5.3. Pregnancies

Subjects who became pregnant during the study were to be withdrawn from the study immediately. Subjects were instructed to notify the investigator if it was determined after completion of the study that they became pregnant either during the treatment phase of the study or within 30 days. Whenever possible, a pregnancy was to be followed to term, any premature terminations reported, and the status of the mother and child was to be reported to the sponsor after delivery.

5.6.5.4. Clinical laboratory evaluations

All laboratory assessments were carried out centrally by Quest Diagnostics Ltd. The following haematological and clinical chemistry parameters were assessed at the end of reference cycle 1(a) [visit 2(a)], at the at Visit 6 (end of treatment cycle 3) and/or at the early withdrawal visit if a subject was withdrawn early from the study. Serum pregnancy tests were also conducted at these timepoints.

- Haematology - haemoglobin, hematocrit (PCV), red blood cells (RBCs), total and differential white blood cell counts, platelets.
- Clinical Chemistry – blood urea nitrogen (BUN), creatinine, total bilirubin, alkaline phosphatase, alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT).
- Serum Pregnancy Test

In addition, thyroid function tests [thyroid stimulating hormone (TSH), FT3 and FT4] were carried out at visit 2(a).

Laboratory assessments were to be repeated if clinically significant abnormalities were detected, and followed up until resolved or stabilised. Clinically significant abnormalities in laboratory parameters or positive pregnancy tests were to be recorded as AEs. The criteria for defining abnormalities of potential clinical concern for laboratory parameters are presented in Section 5.8.6.5.

5.6.5.5. Vital signs

Sitting blood pressure (systolic and diastolic) and pulse rate were measured at each clinic visit. If clinically significant abnormalities were detected they were to be followed up until the abnormality had resolved or stabilized. Vital sign values of potential clinical concern were identified and tabulated. The criteria for defining vital sign changes of potential clinical concern are provided in Section 5.8.6.5.

5.7. Data Quality Assurance

To ensure that the protocol-stipulated study procedures were well understood and performed as consistently as possible across all investigator sites, a sponsor representative reviewed the protocol, eCRF and safety reporting procedures with the investigator and his/her staff responsible for the conduct of the study at the investigative site prior to the enrolment of any subjects at the site. Multi-investigator meetings were held on 14 June 2001 in Oslo, Norway, and 21 June 2001 in Toronto, Canada.

This study employed a remote data entry (RDM) system with a laptop computer to collect all of the information which the investigator would otherwise have captured in a paper CRF. Each site received a laptop computer and all site staff participated in specialized training on the use of the RDM system. Each investigator and authorized staff member received unique passwords used to log on to the system. As with traditional paper CRFs, sites were required to retain source documentation to support all RDM entries. The subject diary data was collected using paper diaries.

Adherence to the protocol requirements and verification of data generation accuracy was achieved through monitoring visits to each investigator site. Subsequent data handling and reporting processes were subject to in-process quality control. All the above procedures were performed according to methodologies detailed in SmithKline Beecham and GSK Standard Operating Procedures (SOPs).

This study was subject to audit by GSK's department of Worldwide Regulatory Compliance-GCP (WRC-GCP). The following center was audited:

- [REDACTED] Sweden (center [REDACTED])

In addition, at the time of writing this report a site audit was planned for the following center:

- [REDACTED] the Netherlands (center [REDACTED])

5.8. Data Analysis Methods

5.8.1. Timings of Planned Analyses

At database freeze, once all protocol violations and deviations had been identified and once the intention-to-treat (ITT) and per protocol (PP) populations had been established, the blinding of the treatment randomization was broken and the final data analyses performed.

5.8.1.1. Interim analyses and data monitoring

No interim analyses of efficacy or safety were performed on unblinded data.

5.8.1.2. Changes in the conduct of the study or planned analyses

Following a regulatory review of study 717 by the Food and Drug Administration (FDA), an additional analysis of the sum of the individual VAS items (VAS Total) was requested by the regulators. Since the request was made after study closure the Statistical Analysis plan, and not the protocol, was amended to incorporate this extra analysis.

There were no other changes in the conduct of the study or in the planned analysis.

5.8.2. Sample Size Considerations

This study was powered to demonstrate a difference of 16.3mm between paroxetine CR (12.5mg and 25mg) and placebo, in mean change from baseline to treatment cycle 3 in VAS-MOOD score. The mean difference of 16.3mm was recommended to GSK as a target difference by an opinion leader in the PMDD research area based on the results of a single previous study [Brown, 1999]. Based on data presented from an earlier study of fluoxetine continuous dosing [Steiner, 1995; Brown, 1999] and from a paroxetine study [PPD Development, 2000] a common standard deviation of 30mm was assumed for the change in VAS-MOOD score at the treatment cycle 3 LOCF endpoint. A total of 86 evaluable subjects in each of the three study arms would provide 90% power to detect a difference of 16.3mm. To adjust for the two treatment comparisons a two-sided alpha level of 0.025 has been used. Assuming a 20% attrition rate, the target number of subjects randomized to each treatment group was increased to 108, a total of 324 subjects overall.

The robustness and sensitivity of the sample size calculation was considered in order to assess the impact on the power of the study should the observed standard deviation be higher or lower than expected.

Given a fixed sample size and a difference of 16.3mm the size of the standard deviation affected the power of the study to detect this difference between the treatment groups, as shown below:

Standard Deviation		Power (%) with 86 evaluable subjects per group	Evaluable subjects required per group for 90% Power
SD maximum	40	65	151
	35	78	116
SD best	30	90	86
	25	97	60
SD minimum	20	>99	39

The minimum standard deviation value of 20 was chosen based on data from the placebo and intermittent paroxetine dosing arms from a recent study [PPD Development, 2000] and the maximum value was chosen in order to be symmetric about the assumed value.

5.8.3. Analysis Populations

Two subject populations were analyzed: ITT and PP. Primary inferences have been based on the ITT population.

5.8.3.1. ITT population

The modified ITT population, referred to as the ITT population, consisted of all randomized subjects who received at least one dose of study medication and had at least one post-baseline assessment.

5.8.3.2. PP population

The PP population comprised the subset of the ITT population who met all the following criteria:

- Had no major protocol violation with regard to inclusion or exclusion criteria.
- Had no major protocol violation between randomization and completion of the active treatment phase of the study (treatment cycles 1-3).
- Had no break in study medication for more than 3 consecutive days or compliance outside 80-120% during the active treatment phase of the study (treatment cycles 1-3).
- Had been exposed to randomized study medication for at least one luteal phase (i.e. last 14 days) of a menstrual cycle.

Only the primary efficacy variable was analyzed using the PP population. The PP population was not to be analyzed if it comprised more than 95%, or less than 50%, of the subjects in the ITT population. Subjects to be excluded from the PP efficacy analysis were identified prior to unblinding of the study.

5.8.4. Treatment Comparisons

The paroxetine arms versus placebo comparisons of change from baseline in the mean luteal phase VAS-Mood score at the treatment cycle 3 LOCF endpoint in the ITT population were the primary comparisons of interest in this study.

For this study to be considered a success, a clinically and statistically significant difference had to be observed (after adjustment for multiple comparisons) between the placebo arm and either of the paroxetine arms.

Other comparisons of interest included a LOCF analysis of the secondary endpoints at the treatment cycle 3 visit. In addition, an analysis of the primary and secondary efficacy variables based on the 70% LOCF dataset and the observed cases (OC) dataset at the

treatment cycle 3 visit was also to be performed. A PP analysis of the primary endpoint only will be performed if the PP population comprises between 50% and 95% (inclusive) of the subjects in the ITT population.

Differences among the treatment groups were estimated as paroxetine CR minus placebo, and 95% confidence intervals (CIs) (nominal for the primary endpoint only) were constructed around the estimated differences.

The difference between the two paroxetine arms was not of central scientific interest and was presented for the primary variable alone for information only.

5.8.5. General Considerations for Data Analyses

5.8.5.1. Multicenter studies

In multicenter studies low recruiting centers may cause problems when trying to model the center effect. Therefore, prior to database freeze a review of the blinded data was undertaken to determine the size of each center and small centers were combined. The process for combining centers was first performed on the ITT population and then repeated on the PP population.

Each center was assigned a category type according to the speciality of the primary investigator as follows:

- Obstetrics/gynaecological specialist
- Psychiatric specialist
- GP or primary health care

Any center which contributed less than 12 subjects to the ITT population was combined with other low recruiting centers based on their speciality type as described below. These categories were chosen in an attempt to achieve reasonable homogeneity in factors which could affect the primary response.

First, the total number of subjects within each speciality type was determined separately by region (North America vs Europe). If within the region this total was less than 12 for a speciality type, and there were two or more centers, then these were to be combined together before aggregating with a center of the same type in the other region. Otherwise the algorithm was to be performed for each region as follows.

Within each investigator type, the low recruiting centers were combined with each other to obtain an aggregated center type. This was achieved by ranking each of these centers on the basis of the number of subjects in the ITT population, the center with the smallest number of subjects being ranked one. Centers with equal numbers of subjects were ranked depending on center number, the lowest center number being allocated the lowest rank. The center with the lowest rank was then combined with the center with the highest rank. The center with the second lowest rank was combined with the center with the second largest rank and so on. This procedure was repeated until there were no aggregated centers with less than 12 subjects.

For those centers with at least 12 subjects, the individual centers, along with any pooled centers, were used as the adjustment factor in all statistical analyses.

5.8.5.2. Other strata and covariates

The model on which inference was based included terms for treatment group, center group, baseline score of efficacy measures and age (in years) at start of study. These terms are believed to be predictors of response.

As a supportive analysis of the primary endpoint, interactions with treatment were investigated as described in Section 5.8.8.1. In addition, any significant treatment interactions observed were to be tabulated and presented graphically. For those interactions with a continuous covariate the treatment effect was also to be plotted against the following pre-defined categories:

- VAS-Mood score at baseline: quartiles of the observed values;
- age (years): 18-25, 26-35, ≥ 36 .

5.8.5.3. Multiple comparison/multiplicity

Since each active dose group was compared against placebo, an adjustment was made for the primary analysis alone to reduce the incidence of spurious results and thereby protect the validity of the inferences between each dose of paroxetine and placebo. For the primary endpoint, nominal 95% CIs are presented and hypothesis tests (two sided) used a nominal 5% level of statistical significance. CIs and significance tests were adjusted for two treatment comparisons using Hochberg's modification to the Bonferroni inequality [Hochberg, 1988]. For the purpose of applying Hochberg's method to the calculation of adjusted CIs, comparisons were ordered on the basis of the corresponding p-value.

As the analysis of the secondary variables was to provide supportive evidence only, no adjustment was made to the significance level for these variables. Hypothesis tests used a 5% level of significance and 95% CIs were presented.

5.8.6. Data Handling Conventions

Further information relating to this section can be found in the Statistical Appendix ([Attachment 1](#)).

5.8.6.1. Treatment of missing data

For each subject, missing data for a rating scale at a particular visit was handled as follows:

The efficacy variables based on composite scores are listed below. Rather than discard a value if component items were missing at a given timepoint the methods described next were used to derive a score, provided that the criteria for the number of allowable missing items is satisfied.

1. Visual Analogue Scale (VAS) individual symptom items: For each of the eleven VAS items a mean score for the luteal or follicular phase was only to be calculated if scores were available for at least four of the five designated days.
2. VAS–Mood score: If mean symptom scores were available for at least three of the four core symptoms then a composite VAS-Mood score was to be derived as the average of the mean item scores; otherwise the VAS-Mood score was assigned as missing at this timepoint. In addition, to calculate a VAS-Mood score for a single day (used for the subject profile plots and area under the curve), data had to be available for at least three of the four core symptoms otherwise the value was set to missing.
3. VAS total score: Provided that at least 10 of the 11 items were available the total score was calculated as:

$$\frac{\text{No. items in the scale} * \text{Total score for answered items}}{\text{No. items answered}}$$

i.e., the mean of the observed data multiplied by the total number of items in the scale.

4. Area Under the Curve (AUC) for VAS–Mood: For a given baseline or treatment cycle the VAS–Mood AUC was to be calculated only if data were available for at least four of the five designated luteal days. AUC was calculated as specified in Section 5.8.6.3. If there was one missing score, and this occurred on the first or the last day, then the AUC calculation was to be based on the available data from the other four days with i running from 0 to 3. Otherwise, if the missing score occurs on the second, third or fourth day then this value will be imputed as the average of the observed values from the day before and the one after this missed data point. In this instance it will be assumed that there are 5 days-worth of data (i.e., i runs from 0 to 4).
5. MADRS: This scale, collected only at screening (i.e., visit 1), comprised 10 individual questions each rated on a 7 point scale from 0 (mild or not present) to 6 (severe). Provided that at least 9 of the 10 questions were answered the total score will be calculated as:

$$\frac{\text{No. items in the scale} * \text{Total score for answered items}}{\text{No. items answered}}$$

i.e., the mean of the observed data multiplied by the total number of items in the scale.

6. PMTS-O: The PMTS-O consisted of 10 questions from which the total score was calculated. Items 1-6, 9 and 10 consisted of 5 response categories: 0 = No symptoms to 4 = Severe symptoms; Items 7 and 8, 'Eating Habits' and 'Sexual Drive and Activity' consisted of only 3 response categories: 0 = No symptoms to 2 = Severe symptoms.

If a single item was missing the total was to be calculated using the following formula:

$$\text{Total Score} = \frac{\text{Observed Total Score} \times (1 + \text{Denominator of the missing value})}{\text{Sum of denominators of the non-missing values}}$$

Here the total score was adjusted for the missing value by assuming that this value was a weighted average of the answered questions. Since this total was only to be imputed when there was one missing value, the formula can be simplified to:

3 item missing question: i.e., Observed total score $\times (1 + 2/34)$

5 item missing question: i.e., Observed total score $\times (1 + 4/32)$

Note, the 2/34 and 4/32 can be considered as correction factors which allow for the scale on which the missing question was rated.

If more than 1 response was missing then the subject's PMTS-O data was to be excluded at that particular timepoint.

7. EQ-5D health profiles: If at a given timepoint one or more of the five dimensions was missing then the digit summary and weighted tariff were not to be derived for that timepoint.

Missing data for the remaining variables was handled as follows:

1. CGI global improvement and severity of illness and PGE: For these variables, data on subjects who had a score of 0 (i.e., not assessed) or missing data were not to be included for that particular timepoint. For LOCF analyses, the last non-zero post-baseline score was carried forward.
2. SDS: If an individual item (i.e., work, social life or family life) was missing or unassessed at a visit, then that subject's data was to be excluded from the analysis of that particular SDS item score at that timepoint.

If a subject had any one of the three SDS items (work, social life, family life) missing or unassessed at a visit, the total score was not to be calculated for that visit (i.e. no adjustment were made for missing values).
3. WPAI: For each question, subjects with no data were excluded from the denominator in the summary tables.
4. ISCO-88: Subjects with no data for this question were excluded from the denominator in the summary tables.
5. EuroQol VAS: Subjects with missing data were excluded from summary tables and analyses at that timepoint.

Having applied these rules, a subject was considered evaluable for a given change from baseline efficacy analysis if they had a baseline and a post-baseline non-missing value (at least one for the LOCF analysis or at a specific timepoint for the OC analysis) i.e., baseline values were not carried forward.

5.8.6.2. Luteal phase evaluability

Post-screening visits associated with a given menstrual cycle were scheduled to occur between days 1-3 of the next menstrual cycle. In this study, visit-related efficacy and

health economic data (i.e., PMTS-0, CGI, SDS, PGE, EuroQol and WPAI) refer to the symptomatic luteal phase of the given cycle.

Assuming that a subject could accurately recall their luteal phase symptoms for up to a week after the end of a cycle, the relevant visit associated data (i.e., PMTS-0, CGI, SDS, PGE, EuroQol and WPAI) was considered evaluable for a given cycle if the assessment was completed during the interval from the stop date of this menstrual cycle and up to and including day 7 of the next menstrual cycle.

Note: Luteal phase evaluability was only to be determined for the baseline and treatment cycle data. Only one evaluable measure per cycle (collected at a scheduled or withdrawal visit) has been included in the summary tables. However, all values are presented in the data listings sorted in chronological order.

5.8.6.3. Derived and transformed data

For both the ITT and PP populations the primary inferences were based on the LOCF dataset at the protocol defined treatment cycle 3 endpoint. The LOCF dataset contained all evaluable data for the treatment cycle 3 assessment, plus the last evaluable on-treatment assessment for subjects who had a missing assessment at this timepoint or had withdrawn early from the study. For subjects with insufficient data from treatment cycle 3, data from the last treatment cycle visit with sufficient data were carried forward.

Two additional datasets were to be analyzed to assess the robustness of the results. These were the LOCF dataset at the latest time point where at least 70% of the subjects in each treatment group remain in the study (70% LOCF) and an OC dataset at the treatment cycle 3 endpoint.

In the LOCF dataset, the last available on-therapy observation for a subject was used to estimate subsequent missing data points. In the OC dataset, efficacy data were evaluated only at the time-point when they were collected; no data were carried forward to estimate missing data points. In both datasets, efficacy and quality of life visit-associated data were excluded from the analysis if the subject had discontinued study medication seven or more days prior to the visit. These data were listed, but not summarized.

Derived variables were calculated as follows:

VAS–Mood: For each subject, the VAS–Mood score was the mean of VAS symptom scores for the four core PMDD symptoms. Each symptom score was the mean of the scores for the designated days of the follicular or luteal phase (i.e., days 6-10 or the last five days) of the cycle.

VAS total: For each subject, the VAS total score was the sum of the eleven individual VAS items. Each symptom score was the mean of the scores for the designated days of the follicular or luteal phase (i.e., days 6-10 or the last five days) of the cycle.

Body Mass Index: This was defined as weight/height^2 (kg/m^2).

Area Under the Curve: Each subject's VAS–Mood profile was summarised by calculating the AUC at baseline and the treatment cycles during the last five days of the luteal phase based on available data using the trapezoidal rule [Altman, 1999]:

$$\frac{1}{2} \sum_{i=0}^{n-1} (t_{i+1} - t_i)(y_i + y_{i+1})$$

for $n+1$ measurements of y_i VAS–Mood scores at day t_i (i runs from 0 to n).

For each subject the AUCs derived from the separate post-baseline visits were added together. This total was then standardized by dividing by the total number of luteal phase days used in the calculation to obtain an average level over the 1-3 luteal phases considered. The subject's AUC at baseline was similarly standardized. Note, these weighted mean scores are on the same scale as the VAS–Mood.

5.8.6.4. Assessment windows

Visit Assignments

For the visit-associated data, all visits up to and including the baseline assessment were assigned based on the visit specified by the investigator on the eCRF page. This approach was also used to assign visits for the laboratory and vital signs data prior to the start of randomized medication and to assign the active medication dosing and compliance data to a treatment cycle.

Because of the long intervals between visits, and use of placebo run-in study drug during reference cycle 2, efficacy or pharmacoeconomic data relating to earlier menstrual cycles was not carried forward if the baseline data was missing. In addition, any data of this type assigned to baseline with a corresponding visit date on or after the first dose of active medication was considered non-evaluable and not included in the tables or analyses.

For each subject a baseline measure was assigned for each laboratory and vital signs parameter by taking the last non-missing value prior to the start of randomized active medication.

All efficacy and pharmacoeconomic visit data collected after the baseline visit date and up to and including the last day of follow-up (see Post-treatment section below) was assigned to a treatment cycle by comparing the visit date for the scale against the subject's menstrual cycle dates as recorded on the patient diary card as follows:

- Assessments performed up to and including the day prior to the menstrual cycle stop date of treatment cycle 2 were assigned to the end of treatment cycle 1 visit. Those occurring in the interval from the treatment cycle 2 stop date up to and including the day prior to the menstrual cycle stop date of treatment cycle 3 were assigned to the end of treatment cycle 2 visit, and measures taken on the menstrual cycle stop date of treatment cycle 3 up to the last day of follow-up were assigned to the end of treatment cycle 3 visit.

Efficacy and pharmacoeconomic data collected at the early withdrawal visit were slotted to a treatment cycle using these rules. Although the intervals for each treatment cycle varied, each cycle had the same luteal phase evaluable window (see Section 5.8.6.2) used for tabulations and analyses.

Vital sign and laboratory data collected after the baseline visit up to the last dose of active medication date were assigned to a treatment cycle using the same approach. Note, this baseline visit could be a reference, treatment cycle or early withdrawal visit provided the visit date was prior to the start of active medication.

Pre-treatment

Pre-treatment was split into two periods: i) prior to placebo run-in and ii) from the start date of taking placebo run-in study medication to the day before the first dose of randomized study drug medication was taken.

On-treatment

This period ran from the day that the first dose of randomized study medication was taken up to the day that the study drug was permanently discontinued. Note, within this session the active treatment phase (i.e., when randomized study drug was taken) occurred only during the luteal phase of each menstrual cycle.

An assessment was considered to be on-treatment if the assessment date (or the start date for AE data) overlapped with the on-treatment interval.

Post-treatment

For efficacy, pharmacoeconomic and safety data, the post-treatment period was divided into follow-up and post follow-up as follows:

- Follow-up: Efficacy and pharmacoeconomic data were considered to be in the follow-up period if the assessment was ≤ 7 days after the last day of randomized treatment. For safety data this window was extended to ≤ 14 days (≤ 30 days for SAEs).
- Post follow-up: Any efficacy, pharmacoeconomic or safety assessment or event which took place after the follow-up period was considered to be post-follow-up. This data was not tabulated but is presented in data listings.

These windows were used for reporting all the safety data. For efficacy and pharmacoeconomic data the period following the day after baseline up to and including the last day that the study drug was permanently discontinued was denoted as the "efficacy treatment" phase and was combined with the "follow-up" phase in tabulations and listings and presented as "treatment cycle 1, 2 or 3".

For the assessment of AEs and medications during the follow-up phase the follow-up denominator comprised the subset of the ITT population who met at least one of the following criteria:

- Had at least one assessment from the following after the last dose of study medication: laboratory values, vital signs, CGI, MADRS, PESM, PGE, PMTS-O, SDS, EuroQol or WPAI.
- Experienced an AE with a start date or an end date after the last dose of study medication.
- Had a prior or concomitant medication categorised as post-treatment (see Section 5.8.7.5).

5.8.6.5. Values of clinical concern

Laboratory values outside the normal range and of potential clinical concern were flagged. The criteria for defining laboratory values of potential clinical concern are detailed in Section 15, [Table 15.29](#) and presented in [Table 4](#). Before laboratory values were flagged as above or below the ranges of clinical concern, they were converted to SmithKline Beecham (SB) preferred units. The normal ranges were also converted to SB preferred units before any multiplier was applied to obtain the clinical concern range. For reporting purposes data is presented in SB preferred units.

The normal range and clinical concern flags for differential laboratory parameters (basophils, eosinophils, lymphocytes, monocytes and neutrophils) were assigned based on percentage units. The value as a percentage (e.g. lymphocytes = 30%) was then converted to the SB preferred unit by taking the percentage of the white blood cell count (e.g. if WBC = $9.3 \times 10^9/\text{L}$, then the absolute lymphocyte count = 30% of $9.3 = 2.79 \times 10^9/\text{L}$).

Table 4 Normal Range and Criteria of Potential Clinical Concern for Laboratory Parameters

Laboratory Tests Groupings	Age (Years)	Normal Range	Units	Potential Clinical Concern Criteria
Hematology				
Hemoglobin	18-46	120.04 – 156.30	g/L	≤ 95
Hematocrit	18-46	35 – 46	%	≤ 32
RBC	18-46	3.9 – 5.2	x10 ¹² /L	≥ 10
WBC	18-46	3.8 – 10.8	x10 ⁹ /L	≤ 2.8 or ≥ 16
Neutrophil Bands	18-46	-	%	≥ 10
Neutrophils Segmented	18-46	40 – 75	%	≤ 15
Lymphocytes	18-46	16 – 46	%	≥ 75
Monocytes	18-46	0 – 12	%	≥ 15
Eosinophils	18-46	0 – 7	%	≥ 10
Basophils	18-46	0 – 2	%	≥ 10
Platelet Count	18-46	130 – 400	x10 ⁹ /L	≤75 or ≥700
Clinical Chemistry				
Total Bilirubin	18-46	0 – 22	micromol/L	≥ 34.2
ASAT	18-46	0 – 42	IU/L	≥ 150
ALAT	18-46	0 – 48	IU/L	≥ 165
Alkaline Phosphatase	18-19	30 – 165	IU/L	≥ 390
Alkaline Phosphatase	20-46	20 – 125	IU/L	≥ 390
Creatinine	18-46	44 – 124	micromol/L	≥ 176.8
BUN	18-46	2.5 – 9	mmol/L	≥ 10.71
Thyroid Hormones				
TSH	18-46	0.4 – 5.5	MU/L	≥ 10
FT3	18-46	3.5 – 6.5	pmol/L	≤ 1.75 or ≥ 13.0
FT4	18-46	10.3 – 23.2	pmol/L	≤ 5.15 or ≥ 46.4

The criteria for defining changes in vital signs of potential clinical significance are presented in [Table 5](#). Blood pressure and heart rate were evaluated by tabulating the number of subjects in each treatment group with values outside clinically important ranges of potential clinical significance or with changes from baseline of clinical importance. In addition for blood pressure and heart rate, summary statistics for absolute values and changes from baseline were presented by treatment group. Vital signs of potential clinical concern were flagged.

Table 5 Criteria for Assessment of Vital Signs Changes of Potential Clinical Concern

Parameter	Normal Range	Change from Baseline of Potential Clinical Concern	
		Decrease	Increase
Systolic BP (mmHg)	90 – 180	≥ 30	≥ 40
Diastolic BP (mmHg)	50 – 105	≥ 20	≥ 30
Pulse Rate (bpm)	50 – 120	≥ 30	≥ 30
Weight	-	≥ 7%	≥ 7%

5.8.7. Study Population

5.8.7.1. Disposition of subjects

Two subject populations were defined: ITT population and PP population ([Section 5.8.3](#)). Subjects in each population were listed by treatment group. The number of subjects by study status (screened, randomized, completed, early withdrawal) and population (ITT and PP) was summarized by treatment group, and also by treatment group and country, for all subjects.

Subject conclusion data was listed for the ITT population. The number and percentage of subjects either completing the study or withdrawing early (by reason for withdrawal) was tabulated by treatment group for the ITT population and the PP population. The reasons for early withdrawal were categorized as recorded in the eCRF.

In addition, the number and percentage of subjects in the ITT population withdrawing or still in the study was summarized by visit. The cumulative percentage of subjects in the ITT population who withdrew from the study was summarized by reason for withdrawal and treatment group.

5.8.7.2. Protocol violations

Among the ITT population, subjects violating any of the following inclusion/exclusion criteria during the study were considered as having a protocol violation and were not included in the PP population:

- no primary diagnosis of PMDD according to DSM-IV criteria;
- PMDD symptoms were not present in the majority of menstrual cycles in the 12 months prior to screening;
- insufficient “on-offness” of premenstrual symptoms;
- insufficient score on the CGI severity of illness at baseline (i.e. score of < 3);
- hormonal contraception use;

- history of Axis I disorder (other than specific phobias) within 6 months prior to screening;
- subjects with diagnosed and clinically significant gynecological disease(s);
- out of range score on MADRS at screening (i.e. score of ≥ 10);
- ongoing medication which may have affected PMDD symptomatology;
- pregnant or lactating women;
- study medication non-compliance (see Section 5.8.7.6)

Protocol violations were identified programmatically where possible, and by clinical review of blinded listings (e.g. listings of AEs, medical history, psychiatric history and concomitant medications). The protocol violations were identified on the database before the study was unblinded. All protocol violations were listed by treatment group for the ITT population. The number of subjects in each treatment group with protocol violations, and the reasons for exclusion from the PP population were summarized for the ITT population.

5.8.7.3. Protocol deviations

The following criteria were considered as protocol deviations. Subjects in the ITT population without a protocol violation, but with any of these deviations from the protocol inclusion/exclusion criteria were included in the PP population:

- age outside permitted range;
- irregular or out of range menstrual cycles;
- inadequate or non-use of contraception for women of childbearing age. Subjects were classified as having a protocol deviation if they met this criterion provided that they were not identified as a protocol violator for hormonal contraception usage.
- severe, clinically significant, concurrent disease;
- at risk of committing suicide;
- previous adequate treatment with SSRIs for premenstrual syndrome;
- intolerance to paroxetine or other SSRIs;
- participation in psychiatric drug trial in the 6 months prior to screening;
- clinically significant abnormality in screening laboratory tests;
- use of investigational drug within 30 days or 5 half-lives prior to screening;
- unable to comply with the study procedure and assessments.

Protocol deviations were identified before the study was unblinded. Protocol deviations were listed by treatment group for the ITT population. The number of subjects in each treatment group with protocol deviations were summarized for the ITT population.

5.8.7.4. Demographic and baseline characteristics

The number and percentage of subjects by age group, race and by treatment group were tabulated for the ITT and PP populations. Summary statistics (n, mean, standard deviation, median, minimum and maximum) for age, height, weight, BMI and by treatment group were tabulated for the ITT and PP populations.

Baseline characteristics were summarized by treatment group for the ITT population. Summary statistics (n, mean, standard deviation, median, minimum and maximum) for the efficacy rating scales at baseline were presented by treatment group for the ITT population.

5.8.7.5. Prior and concomitant medications

At the screening visit investigators were requested to record medications taken within the last month. Prior and concomitant medication and usage during the post-treatment period was defined using the start and stop dates, and ongoing fields recorded in the eCRFs relative to the first and last dose dates of randomized study medication.

Prior and concomitant medications were coded using the Anatomical Therapeutic Chemical (ATC) classification of WHO. Medication was considered as prior, concomitant or post-treatment as shown schematically below:

Start and stop dates (?=missing date)			Prior	Concomitant	Post-treatment
Pre-treatment	On-treatment	Post-treatment			
X—————X			Y	N	N
X—————	—————X		Y	Y	N
—					
X—————	—————	—————X	Y	Y	Y
—					
	X———X		N	Y	N
	X—————	—————X	N	Y	Y
		X—————X	N	N	Y
?—————X			Y	N	N
	?—————X		Y*	Y	N
		?—————X	Y*	Y*	Y
X—————?			Y	Y*	Y*
	X—————?		N	Y	Y*
		X—————?	N	N	Y

Where medication was stopped on-treatment or post-treatment and no start date was recorded it was assumed that the medication was ongoing from the pre-treatment phase. If a medication was started pre-treatment or on-treatment and no stop date was recorded

then usage was assumed to be ongoing provided that the investigator had indicated that the medication was continuing into the relevant phase (see "*" in the above diagram).

If a medication was started or stopped on the same day of taking the first or last dose of randomized study drug then this was considered as a concomitant medication. Note, a medication could be counted in more than one phase.

5.8.7.6. Treatment compliance

Study medication compliance and dosing were listed by treatment group. The number and percentage of subjects who were compliant and non-compliant was tabulated by visit and treatment group. The compliance of subjects with respect to their assigned treatment regimen was assessed in three ways:

- Capsule compliance: This was assessed at each visit during the study where capsules were returned using the following algorithm:
$$\% \text{ compliance} = [(\text{capsules dispensed} - \text{capsules returned}) \times 100] / \text{days}$$
where days was the interval from the first to last dose of study medication during the cycle i.e., stop date – start date +1. This calculation was based only on data recorded in the study medication panel of the eCRF. For a given cycle, subjects were considered to be compliant if this calculation was within 80-120%.
 - Interruption in study drug: To be compliant subjects must not have had a break in study medication for more than 3 consecutive days between the medication start and stop dates in a given dosing period. This was based on the investigator question in the study medication panel of the eCRF.
 - Adherence with regard to taking medication during the luteal phase: A subject was considered compliant for a given cycle if they started taking study drug at least 7 days prior to Day 1 of the next cycle, had discontinued on Day 1 or Day 2 of the next cycle, and for all cycles (apart from the placebo run-in reference cycle), had a break of at least 7 days between discontinuation of medication on the previous cycle and the start of medication in this cycle. Here the medication start and stop dates were based on data in the study medication panel of the eCRF, and the dates for menstrual cycle days were taken from the subject diary.

For each subject, each component of compliance was calculated for each menstrual cycle in which they took study medication. For each of these criteria a subject was assigned as compliant, non-compliant or as "unknown" in the situation where a required component data item such as the study drug start or stop date for a cycle was missing.

An individual was considered to be overall compliant for a given cycle if they satisfied all three compliance definitions. Otherwise, if a subject was confirmed as non-compliant for at least one of the definitions they were assigned as overall non-compliant and the remaining subjects with "unknown" status for any one of the three criteria, were assigned as "unknown" for overall compliance for that cycle.

5.8.8. Efficacy Analyses

5.8.8.1. Primary efficacy measure

The primary comparison of interest for all study variables was each dose of paroxetine CR versus placebo in the ITT population at treatment cycle 3 endpoint using the LOCF data. Analysis of the 70% LOCF endpoint and the treatment cycle 3 OC data were used to provide supportive evidence. Analysis of the primary variable was performed on the ITT population and PP population.

The primary variable, change from baseline in the protocol defined mean luteal phase VAS-Mood score at treatment cycle 3 LOCF, was analyzed using parametric analysis of covariance (PROC GLM and PROC MIXED in SAS). The model on which inference was based included terms for treatment group, center group, baseline score, and age.

The assumptions of normality and homogeneity of variance were assessed by inspection of normal probability plots and residual plots. Standardized residuals versus predicted, and standardized residuals versus covariate plots were also produced to aid in the diagnostics. The Shapiro-Wilk test for normality was also applied to the residuals. If the model assumptions were strongly violated, a non-parametric analysis adjusting for the pre-specified covariates was also to be undertaken using the methods developed by Zinc and Koch [Zinc, 2001]. This non-parametric analysis of covariance within the SAS system using the macro NparCov was chosen to provide a more precise estimate of the treatment effect compared to other non-parametric methods without covariate adjustment. If parametric and non-parametric analyses were performed on the primary endpoint then the results from both analyses were to be presented. If the conclusions were quantitatively the same then inference was to be based on the parametric results, otherwise inference would be based on the non-parametric results.

In addition, the interaction of treatment with each of the other main effects included in the model from the principal analysis were assessed. This was achieved by adding separately each interaction to the model and assessing the statistical significance. In the event that more than one interaction was found to be statistically significant ($p < 0.1$), the interactions were to be modelled together to assess their joint significance. For those terms which do interact with treatment, results were presented within each category (see Section 5.8.5.2) of the interacting variable, in addition to the overall presentation from the principal analysis.

The results of the primary analysis are presented as point estimates, nominal 95% confidence intervals and associated p-values for the adjusted mean differences between treatments. Hypothesis tests used a nominal 5% level of statistical significance. Confidence intervals and significance tests were adjusted for two treatment comparisons using Hochberg's modification to the Bonferroni inequality [Hochberg, 1988]. For the purpose of applying Hochberg's method to the calculation of adjusted confidence intervals, comparisons were ordered on the basis of the corresponding p-values.

A repeated measures model was fitted to the observed VAS-Mood treatment cycle 1 to 3 change from baseline data, correcting for dropout and accounting for the fact that

measurements taken on the same subject over time tend to be correlated. The model for the mean response includes the primary analysis covariates i.e., treatment group, centre grouping, baseline VAS-Mood, and age, along with treatment group by cycle and baseline score by cycle interaction terms. The covariance was modelled using a separate unstructured covariance matrix for the individuals' profiles in each treatment group. The model was fitted using restricted maximum likelihood applying the methods of Kenward and Roger [Kenwood, 1997] to obtain estimates of the treatment differences in mean VAS-Mood scores at treatment cycle 3. Under this likelihood-based approach, dropout is assumed to be random which allows the probability of a subject to drop out to depend on their observed response measurement history.

5.8.8.2. Secondary efficacy measures

Each secondary efficacy variable was analyzed using the model specified for the primary analysis (Section 5.8.8.1), except for CGI global improvement and PGE where a baseline score is not available.

Analyses were performed only on the ITT population. Furthermore, no adjustment was made for multiple comparisons for secondary efficacy measures; 95% confidence intervals are presented. The interaction of treatment with the other main effects was not assessed for any of the secondary variables.

Continuous secondary efficacy variables (change from baseline in: VAS physical symptom and VAS total score, PMTS-O, SDS items and total, AUC in VAS-Mood and CGI severity of illness) were analyzed using analysis of covariance techniques. Results were presented as point estimates, 95% confidence intervals and associated p-values for the adjusted mean differences between each dose level of paroxetine CR and placebo.

As for the primary analysis, the fitted models were to be evaluated by graphical diagnostics (see Section 5.8.8.1). If for a given model the assumptions were strongly violated, then non-parametric methods adjusting for the pre-specified covariates (i.e., treatment, center, age and corresponding baseline score) were also to be performed [Zinc, 2001].

Categorical secondary efficacy variables (the proportion of subjects with 50% reduction in baseline luteal phase VAS-Mood score, the proportion of subjects with a mean luteal phase VAS-Mood score $\leq$ baseline mean follicular phase VAS-Mood score, proportion of responders on the CGI global improvement and the proportion of responders on the PGE) were analyzed using logistic regression techniques. Results were presented as adjusted odds ratios, 95% confidence intervals around the estimated odds ratios and associated p-values.

Continuous data were summarized by means, standard deviations, medians, ranges and number of subjects, and categorical data were summarized by counts and proportions.

5.8.8.3. Other efficacy measures

No formal statistical analysis was performed on the remaining efficacy variables: change from baseline in the individual raw VAS item scores at each treatment cycle and PESM at treatment cycle 3 or early withdrawal. Summary statistics (means, standard deviations, medians, ranges and number of subjects) were provided for the ITT population.

5.8.8.4. Quality of life and employment status

Analyses of the quality of life data were performed on the ITT population as an additional measure of paroxetine CR effect. Results of the EuroQol VAS scores are presented as summary statistics (means, standard deviations, medians, ranges and number of subjects) by treatment group. The number and percentage of subjects in each category of the EuroQol EQ-5D health profile was tabulated by treatment group and visit. Results of the EQ-5D utility score are presented as summary statistics.

An analysis of covariance model was also fitted to the change from baseline in EuroQol VAS endpoint, additionally adjusting for employment status (as captured in question 1 of the WPAI). The results were presented as point estimates, 95% CIs and associated p-values for the adjusted mean differences between paroxetine CR and placebo.

The number and percentage of subjects in each category of occupation per the ISCO-88 were tabulated by treatment group. Impact on work productivity was assessed using the WPAI. In addition to the number and percentage of subjects employed and unemployed at each timepoint, summary statistics were tabulated by visit and treatment group for the number of hours worked, number of hours missed from work because of health problems and number of hours missed from work for other reasons. The number and percentage of subjects with health problems affecting productivity while working and the number and percentage of subjects with health problems affecting regular daily activities (other than work) were recorded and categorized by response at each visit. No hypothesis testing was performed on these data.

5.8.9. Safety Analyses

Safety reporting was performed only on the ITT population.

5.8.9.1. Adverse events

All AEs were coded from the verbatim term using the World Health Organization (WHO) adverse event codelist, and then mapped by ADECS to give a body system and preferred term, however the SAE terms in the SAE subject narratives were coded using the Medical Dictionary for Regulatory Activities (MedDRA).

AEs, SAEs and AEs leading to withdrawal were tabulated and listed by treatment group and subject for body system and preferred term. Individual case narratives for, SAEs and AEs leading to withdrawal are provided in Section 15, [Table 15.36](#) and [Table 15.37](#) respectively (there were no deaths during the study). A table which identifies all subjects with narratives is located in Section 15, [Table 15.35](#).

The number (%) of subjects in each treatment group with AEs was compared both for overall incidence and by body system and preferred term. Counts and percentages were also presented for SAEs, AEs leading to withdrawal, AEs by severity, AEs by relationship to study drug and time to first occurrence.

- Pre-treatment AEs for the ITT population, were defined as any AE or SAE with an onset date on or after the start of placebo run-in medication and prior to the start of randomized study drug medication. In addition, any SAE which was considered by the investigator as related to study design or procedures which occurred after study start (i.e., after informed consent has been obtained) but prior to administration of the first dose of randomized study medication was considered as a pre-treatment SAE.

For screen-only and randomized non-ITT subjects all events recorded on the study eCRF AE panels are presented.

Emergent AEs were defined as any AE which emerged during treatment or follow-up, or which worsened relative to the pre-treatment state. Emergent AEs were summarized as follows:

- Treatment phase AEs were defined as and AE or SAE where the onset date was on or after the start of double-blind medication and before or on the last day of double-blind study medication.
- Follow-up phase AEs were defined as any AE or SAE where the onset date was after the last date of randomized treatment but within 14 days (or 30 days for an SAE) from the last randomized treatment date.

If the AE onset date was missing and the AE was reported in the eCRF Baseline AE panel then this will be assigned as a pre-treatment AE, otherwise if it was recorded in the AE panel then it was assumed that this was incident in the treatment phase only.

In order to take account of the intermittent nature of the treatment in this study, any AE (i.e., not necessarily "emergent") with a start date between the first day of randomized study medication drug and up to 14 days after the last day of randomized treatment (i.e. the follow-up period as described in Section 5.8.6.4) was assigned based on the AE start date to one of the following 6 time windows :

- On study medication during treatment cycle 1
- Off study medication following treatment cycle 1
- On study medication during treatment cycle 2
- Off study medication following treatment cycle 2
- On study medication during treatment cycle 3
- Off study medication following treatment cycle 3

For all three "off treatment" periods the time window extended to a fixed period of 14 days from the last dose of study medication, or alternatively up to the day prior to the start of medication in the next cycle if earlier.

The denominator for each "on study medication" period was based on the number of subjects who progressed to that window, which was determined by data recorded in the study medication panel of the eCRF. For the "off study medication" periods, the denominator was based on the assumption that those subjects who started active medication for a cycle also participated in the subsequent "off study medication" interval.

The number and percentage of AEs in each window is presented by treatment group, by severity. For those AEs with multiple occurrences in a given window only the highest severity report is included in the table. In addition, the AEs are presented by combining severity counts within each time window for each treatment group.

5.8.9.2. Laboratory values

Summary statistics are presented for the laboratory data (hematology and blood chemistry) by visit and for change from baseline. Each subject's baseline measurement for a given parameter was classified into one of 5 categories:

- Lower than a pre-determined clinically important range
- Below the normal range
- Within the normal range
- Above the normal range
- Higher than a pre-determined clinically important range

"Endpoint" values, defined as the last available value on treatment or during follow-up i.e. within 14 days of the last study dose will be classified using the same procedures. The proportion in each category at each timepoint, and transition from baseline was examined by cross-tabulating the assigned post-baseline levels against the baseline categories. Individual case narratives for subjects who had a laboratory value outside the pre-determined clinically important range are provided in Section 15, [Table 15.38](#). A table which identifies all subjects with narratives is located in Section 15, [Table 15.35](#).

5.8.9.3. Vital signs

Summary statistics of the absolute values at entry are presented for blood pressure, heart rate, weight, height and body mass index. In addition, summaries of change are presented for blood pressure and heart rate. Additionally, for blood pressure, heart rate and weight the number of subjects in each treatment group with values outside pre-determined clinically important ranges and/or with changes from baseline of clinical importance has been tabulated.

6. STUDY POPULATION RESULTS

This section presents study population data including the number and distribution of subjects, the number of subjects withdrawn from the study and reason for withdrawal, the number of subjects in each of the populations analyzed, and the number of protocol violators and deviators. Also described here are demographic characteristics for each population and baseline characteristics for the ITT population. Baseline characteristics presented include baseline scores in efficacy rating scales (VAS-Mood, VAS total score, individual VAS items, SDS items, CGI severity of illness, PMTS-O), PMDD history, obstetrics and gynecological history, psychiatric co-morbidity, and current medical conditions. Prior and concomitant medications and subject compliance data are also presented.

6.1. Populations Analyzed

Two subject populations were defined: ITT population and PP population.

The ITT population consisted of all subjects who had been randomized, had received at least one dose of double-blind study medication and for whom at least one post-baseline assessment was available. Primary inference for efficacy and safety was based on this population. The ITT population consisted of a total of 366 subjects. Of these 116 received paroxetine CR 25mg, 130 received paroxetine CR 12.5mg and 120 received placebo.

The PP population was a subset of the ITT population and consisted of subjects who had no protocol violations with regard to inclusion or exclusion criteria; had no protocol violations between randomization and completion of the double-blind treatment phase of the study (treatment cycles 1 to 3); had no break in study medication for more than 3 consecutive days or compliance outside 80-120% during the double-blind treatment phase of the study (treatment cycles 1 to 3); and had taken double-blind study medication for at least one luteal phase of a menstrual cycle. The PP population consisted of a total of 269 subjects. Of these 74 received paroxetine CR 25mg, 99 received paroxetine CR 12.5mg and 96 received placebo. Protocol violations which required the subject to be removed from the PP population are summarized in [Section 6.3](#). Analyses were based on the ITT and PP populations. The number of subjects in the ITT and PP populations are summarized in Section 12, [Table 12.1](#).

6.2. Disposition of Subjects

6.2.1. Number and Distribution of Subjects

A total of 1615 subjects from 53 centers in Europe, Canada and the US were screened, of whom 373 were randomized to receive double-blind treatment. Details of reasons for withdrawal prior to randomization, are given in Section 12, [Table 12.5](#). Seven subjects were randomized but did not fulfil the criteria for inclusion into the ITT population. Six of these subjects did not receive any double-blind study medication, and the remaining subject lacked a post-baseline assessment. The ITT population consisted of 366 subjects. A summary of the numbers of subjects in each treatment group by study status and

population is presented in Table 6. The numbers of subjects in each treatment group by study status and population is presented by country in Section 12, [Table 12.2](#). (Note, in Section 12, [Table 12.2](#) Canadian centers have been combined with the US centers and presented as "Country=USA", in error.)

Table 6 The number of Subjects by Study Status and Population (All Subjects)

Study Stage	Treatment Groups			Total
	Parox CR 25mg	Parox CR 12.5mg	Placebo	
Screened	-	-	-	1615
Screening Failures	-	-	-	797
Run-in Failures	-	-	-	445
Randomized	119	131	123	373
Completed ¹	87	104	101	292
Early Withdrawal ²	32	27	22	81
ITT Population	116	130	120	366
PP Population	74	99	96	269

Data Source: Section 12, [Table 12.1](#).

1. Subjects were considered to have completed the study if the investigator tick box indicated that they had completed all visits up to and including the end of menstrual cycle 3 visit and the treatment data indicated that they had actually completed treatment cycle 3 on study medication.
2. For randomized subjects, the investigator tick box states that the subject did not complete the study, or, the investigator tick box states that the subject did complete the study but the treatment data indicates that they did not complete treatment cycle 3 on study medication.

6.2.2. Number of Subjects Present at Each Visit

Table 7 shows the number and percentage of subjects remaining in the study at each visit for the ITT population. The percentage of subjects still in the study at the end of treatment cycle 3 was higher in the placebo group [101/120 (84.2%) subjects], compared to the paroxetine CR 25mg and 12.5mg groups [87/116 (75.0%) subjects and 104/130 (80.0%) subjects, respectively].

Table 7 Summary of Number (%) of Subjects Remaining in the Study at Each Visit (ITT Population)

Visit	Treatment Group					
	Parox CR 25mg N =116		Parox CR 12.5mg N =130		Placebo N =120	
Baseline	116	(100.0)	130	(100.0)	120	(100.0)
End of Treatment Cycle 1	101	(87.1)	120	(92.3)	117	(97.5)
End of Treatment Cycle 2	96	(82.8)	110	(84.6)	108	(90.0)
End of Treatment Cycle 3	87	(75.0)	104	(80.0)	101	(84.2)

Data Source: Section 12, [Table 12.8](#).

Remaining in the Study = subjects completing the cycle on treatment.

The number of randomized ITT subjects who completed the study is presented by country and center in Section 12, [Table 12.10](#). (Note, in Section 12, [Table 12.10](#) Canadian centers have been combined with the US centers and presented as "Country=USA", in error.)

6.2.3. Number of Subjects Withdrawn from the Study

Table 8 shows the number and percentage of subjects withdrawn pre-randomization and the reason for withdrawal. The primary reason for withdrawal pre-randomization was "Did not meet inclusion/exclusion criteria", 754/1242 (60.7%) subjects, followed by "Other Reason" which included the subject withdrawing consent, 218/1242 (17.6%) subjects.

Table 8 Number (%) of Subjects Who were Withdrawn Pre-Randomization by Reason for Withdrawal (Screening Only Population)

Reason for Pre-Randomization Withdrawal	Treatment Group	
	No Therapy Dispensed N = 1242	
Baseline Adverse Event	3	(0.2)
Did Not Meet Inclusion/Exclusion Criteria	754	(60.7)
Protocol Deviation (Including Non-Compliance)	133	(10.7)
Lost to Follow-Up	134	(10.8)
Other Reason	218	(17.6)
Total Withdrawn	1242	(100.0)

Data Source: Section 12, [Table 12.5](#).

[Table 9](#) shows the number and percentage of subjects withdrawn from the treatment phase of the study and by reason for withdrawal for the ITT population. The proportion of subjects who withdrew prematurely was lower in the placebo treatment group [19/120 (15.8%) subjects], compared with the paroxetine CR 25mg and 12.5mg groups, [29/116 (25.0%) subjects and 26/130 (20.0%) subjects respectively].

The primary reason for early withdrawal in both of the paroxetine CR groups was "Adverse Event", paroxetine CR 25mg: 16/116 (13.8%); paroxetine CR 12.5mg: 13/130 (10.0%). The primary reason for early withdrawal in the placebo group was "Lack of Efficacy" 6/120 (5.0%).

The proportion of subjects withdrawing due to an AE was higher in the paroxetine CR 25mg and 12.5mg groups [16/116 (13.8%) and 13/130 (10.0%) respectively] compared to the placebo group [5/120 (4.2%)], but the proportions withdrawing due to lack of efficacy were lower for the paroxetine CR 25mg and 12.5mg groups [2/116 (1.7%) and 2/130 (1.5%), respectively] compared to the placebo group [6/120 (5.0%)].

Table 9 Number (%) of Randomized Subjects Who Completed the Study or were Withdrawn by Reason for Withdrawal (ITT Population)

Reason for Study Conclusion	Treatment Groups					
	Parox CR 25mg N = 116		Parox CR 12.5mg N =130		Placebo N =120	
Completed Study ¹	87	(75.0)	104	(80.0)	101	(84.2)
Total Withdrawn ²	29	(25.0)	26	(20.0)	19	(15.8)
Adverse Event	16	(13.8)	13	(10.0)	5	(4.2)
Lack of Efficacy	2	(1.7)	2	(1.5)	6	(5.0)
Protocol Deviation (Including Non-Compliance)	2	(1.7)	4	(3.1)	2	(1.7)
Lost to follow-up	3	(2.6)	1	(0.8)	0	
Other Reason	2	(1.7)	3	(2.3)	2	(1.7)
Programmatically Assigned ³	4	(3.4)	3	(2.3)	4	(3.3)

Data Source: Section 12, [Table 12.6](#).

1. Subjects were considered to have completed the study if the investigator tick box indicated that they had completed all visits up to and including the end of menstrual cycle 3 visit and the treatment data indicated that they had actually completed treatment cycle 3 on study medication.
2. Investigator tick box states that the subject did not complete the study, or, the investigator tick box states that the subject did complete the study but the treatment data indicates that they did not complete treatment cycle 3 on study medication.
3. Investigator tick box states that the subject completed the study, but the treatment data indicated that the subject did not complete treatment cycle 3 on study medication.

The cumulative percentage of subjects withdrawing from the study by visit and reason for withdrawal is given for the ITT population in [Table 10](#).

For both paroxetine CR treatment groups, the majority of withdrawals due to an AE had occurred by treatment cycle 1, whereas withdrawals due to an AE in the placebo group occurred later in the study. Withdrawals due to lack of efficacy occurred throughout the study for all 3 treatment groups, although the proportions were higher for the placebo treatment group.

Table 10 Cumulative Percentage of Subjects Withdrawn Over Time by Reason for Withdrawal (ITT Population)

TC	Parox CR 25mg N=116				Cumulative Withdrawn (%) Parox CR 12.5mg N=130				Placebo N=120			
	AE	LOE	Oth	Tot	AE	LOE	Oth	Tot	AE	LOE	Oth	Tot
1	9.5	0.9	2.6	12.9	5.4	0.8	1.5	7.7	0.8	1.7	0	2.5
2	12.1	0.9	4.3	17.2	9.2	0.8	5.4	15.4	3.3	3.3	3.3	10.0
3	13.8	1.7	9.5	25.0	10.0	1.5	8.5	20.0	4.2	5.0	6.7	15.8

Data Source: Section 12, [Table 12.9](#).

TC=Treatment cycle; AE=adverse event; LOE=lack of efficacy; Oth=Other and includes protocol deviation, lost to follow-up, other reason based on the eCRF and those assigned programatically as withdrawals; Tot=Total.

The number and percentage of subjects withdrawing from the study and the reason for withdrawal for the PP population is provided in Section 12, [Table 12.7](#). The primary reason for early withdrawal from the PP population in both of the paroxetine CR groups was “Adverse Event”, and in the placebo group was “Lack of efficacy”.

6.3. Protocol Violations and Deviations

Protocol violations and deviations are described in Section 5.8.7.2 and Section 5.8.7.3 respectively.

Protocol violations required the subject to be removed from the PP population because the violation may have had a bearing on the effectiveness of the treatment. The protocol violations were identified and flagged on the database before the study was unblinded. The number of subjects in each treatment group, and the protocol violations are summarized in Table 11. A higher proportion of subjects in the paroxetine CR 25mg treatment group violated the protocol sufficiently to be excluded from the PP population compared with the paroxetine CR 12.5mg and placebo groups [paroxetine CR 25mg: 42/116 (36.2%); paroxetine CR 12.5mg 31/130 (23.8%); placebo: 24/120 (20.0%)]. The most common protocol violation for all three treatment groups was “Study Medication Non-Compliance”, however it should be noted that the criteria applied for this study (see Section 5.8.7.6) were very stringent compared with those used in previous paroxetine CR PMDD studies.

A higher proportion of subjects in the paroxetine CR 25mg treatment group violated the protocol with “Insufficient on-offness of premenstrual symptoms” compared with the other treatment groups, and higher proportions of subjects in both paroxetine CR treatment groups violated the protocol with “Study Medication Non-Compliance” compared to the placebo group.

Table 11 Number (%) of Subjects Excluded from the Per Protocol Analyses by Protocol Violation (ITT Population)

	Treatment Groups		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Total number of subjects with at least one protocol violation¹	42 (36.2)	31 (23.8)	24 (20.0)
History of Axis I disorder (other than specific phobias)	0	0	1 (0.8)
Ongoing medication which could affect PMDD symptomatology	6 (5.2)	1 (0.8)	5 (4.2)
Pregnant or lactating women	1 (0.9)	1 (0.8)	0
Study medication non-compliance ²	29 (25.0)	26 (20.0)	17 (14.2)
Insufficient “on-offness” of premenstrual symptoms	11 (9.5)	5 (3.8)	4 (3.3)
Hormonal contraception use	0	2 (1.5)	1 (0.8)

Data Source: Section 12, [Table 12.3](#).

1. A subject may have more than one protocol violation leading to exclusion.
2. Based on percentage and luteal phase compliance and interruption in study drug criteria.

Protocol deviations were considered to have little effect on treatment and did not warrant subject withdrawal from the PP population. The number of subjects in each treatment group with protocol deviations are provided in Section 12, [Table 12.4](#). Overall, 4 subjects in the ITT population with protocol deviations were included in the PP population, zero from the paroxetine CR 25mg group, 2 from the paroxetine CR 12.5mg group (one “severe, clinically significant disease”, and one “outside permitted age range”) and 2 from the placebo group (both “outside permitted age range”).

6.4. Demographics and Other Baseline Characteristics

6.4.1. Demographic Characteristics

Table 12 summarizes demographic characteristics by treatment group for the ITT population. The demographic characteristics of the three treatment groups were generally similar, with respect to age, height, weight, BMI and race. The mean age of subjects ranged from 35.9 to 37.2 years, and the majority of subjects ($\geq 96.2\%$) were white.

The demographics of the PP population were similar to the ITT population (Section 12, [Table 12.13](#) and [Table 12.17](#)).

Table 12 Demographic Characteristics (ITT Population)

	Treatment Groups		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Age: Years			
Mean (s.d.)	37.2 (5.39)	35.9 (6.01)	36.9 (5.51)
Median	38.0	36.0	37.5
Range	19.0-46.0	20.0-46.0	22.0-46.0
18 – 25: n (%)	5 (4.3)	10 (7.7)	2 (1.7)
26 – 35: n (%)	31 (26.7)	45 (34.6)	44 (36.7)
≥ 36 : n (%)	80 (69.0)	75 (57.7)	74 (61.7)
Height: cm			
Mean (s.d.)	165.4 (6.71)	166.0 (6.13)	166.8 (6.62)
Median	165.0	166.0	167.3
Range	147.3-186.0	149.9-183.0	152.4-181.0
Weight: kg			
Mean (s.d.)	66.0 (11.19) ¹	68.7 (13.88)	68.7 (13.01)
Median	65.0	66.0	65.8
Range	45.0-99.5	47.5-132.9	50.0-114.0
BMI: kg/m²			
Mean (s.d.)	24.1 (3.44) ¹	24.9 (4.49)	24.7 (4.75)
Median	23.9	23.9	23.4
Range	17.1-34.4	18.0-44.7	17.9-44.7
Race: No. (%)			
White	116 (100.0)	125 (96.2)	118 (98.3)
Black	0	3 (2.3)	1 (0.8)
Oriental	0	1 (0.8)	1 (0.8)
Other	0	1 (0.8)	0

Data Source: Section 12, [Table 12.12](#) and [Table 12.16](#).

1. For weight and BMI N=115 for paroxetine CR 25mg treatment group.

Demographic details of the screening only subjects are presented in Section 12, [Table 12.11](#) (race and age group) and Section 12, [Table 12.14](#) (age). Demographic details of the randomized non-ITT subjects are presented in Section 12, [Table 12.15](#).

6.4.2. Baseline Characteristics

Table 13 summarizes the mean baseline score by treatment group in the following efficacy rating scales: VAS-Mood (depressed mood, tension, affective lability, and irritability); VAS total score; individual item VAS scores; SDS total, work, social life and family life scores; PMTS-O total score; and CGI severity of illness. The treatment groups were similar with respect to their baseline scores for all these efficacy rating scales.

Table 13 Baseline Scores in Efficacy Rating Scales by Treatment Group (ITT Population)

Instrument	Treatment Groups								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	Mean	s.d.	n	Mean	s.d.	n	Mean	s.d.
VAS-Mood Score	116	54.4	24.46	130	52.2	21.35	119	55.7	21.52
VAS Total Score	116	545.2	252.77	130	522.0	232.29	119	539.3	220.67
Individual VAS Item Score									
Irritability	115	62.6	23.12	130	58.3	22.22	119	63.8	21.06
Tension	116	53.7	27.59	130	50.7	25.28	118	52.0	26.58
Depressed Mood	116	49.0	29.11	130	47.9	24.86	119	52.1	24.27
Affective Lability	116	52.7	27.98	130	51.9	22.92	119	55.1	26.10
Decreased Interest	116	44.2	31.00	130	39.9	26.73	119	43.6	26.84
Difficult Concentrating	116	40.5	30.94	130	38.0	27.19	119	38.0	26.23
Lack of Energy	116	50.8	29.59	130	45.9	28.50	119	47.5	28.10
Change in Appetite	116	46.8	29.97	130	47.2	29.44	119	44.5	29.55
Change in Sleep Pattern	116	46.7	31.41	130	43.9	31.04	119	46.6	29.99
Feeling out of Control	116	43.8	31.07	130	40.8	28.57	119	40.8	30.56
Physical Symptoms	116	54.6	28.05	130	57.5	29.13	119	55.4	29.02
SDS									
Total Score	82	17.6	6.38	108	16.8	7.46	104	17.2	6.88
Social/Leisure Item	85	5.9	2.67	110	5.7	2.69	104	6.0	2.79
Work Item	82	5.0	2.60	108	4.8	2.74	104	4.8	2.41
Family/Home Item	85	7.0	2.34	110	6.1	2.87	104	6.4	2.80
PMTS-O Total Score	93	21.9	6.39	116	21.9	6.38	107	21.3	5.55
CGI Severity of Illness	93	4.7	0.98	116	4.7	0.95	107	4.6	0.84

Data Source: Section 13, [Table 13.5](#), [Table 13.15.3](#), [Table 13.16](#), [Table 13.17](#), [Table 13.18](#), [Table 13.19](#), [Table 13.20](#), [Table 13.21](#), [Table 13.22](#), [Table 13.23](#), [Table 13.24](#), [Table 13.25](#), [Table 13.26](#), [Table 13.29](#), [Table 13.32](#) and [Table 13.33](#).

6.4.3. History of PMDD

Summary statistics relating to the history of PMDD are shown in [Table 14](#). The age of onset of PMDD and duration if symptoms persisted were similar across the treatment groups. In the majority of subjects, PMDD had persisted since initial onset, ranging from 92.5 to 96.2% in the three treatment groups. The age of onset of PMDD ranged from 11 to 42 years, with a mean age of approximately 26 years. The mean duration of PMDD

symptoms, where they persisted, was approximately 10 years. The duration of the longest episode if symptoms did not persist, and duration of the current episode if symptoms did not persist, were both noticeably longer for subjects in both paroxetine CR treatment groups compared to placebo-treated subjects (duration of longest episode - paroxetine CR 25mg: 11.0 years; paroxetine CR 12.5mg: 10.1 years; placebo: 6.5 years, duration of the current episode – paroxetine CR 25mg: 8.2 years; paroxetine CR 12.5mg: 7.0 years; placebo: 3.9 years). However, it should be noted that the numbers of subjects that these latter two parameters were based on were small.

Table 14 Summary Statistics for Persistency of PMDD, Age at Onset of PMDD Symptoms and Duration of PMDD Symptoms (ITT Population)

Baseline Parameter	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Persisted since initial onset?			
No: n (%)	7 (6.0)	5 (3.8)	9 (7.5)
Yes n (%)	108 (93.1)	125 (96.2)	111 (92.5)
Age (years) at onset of PMDD			
N =	115	130	120
Mean (s.d.)	26.5 (7.56)	25.7 (7.41)	26.8 (7.57)
Median	28.0	27.0	27.0
Range	11.0-42.0	11.0-39.0	12.0-42.0
Duration (years) if persisted			
N =	108	125	111
Mean (s.d.)	10.5 (7.02)	10.5 (7.41)	10.4 (7.35)
Median	9.3	9.0	8.5
Range	1.0-34.0	0.9-33.0	1.0-33.0
Duration (years) of longest episode¹			
N =	7	5	9
Mean (s.d.)	11.0 (4.58)	10.1 (7.35)	6.5 (3.79)
Median	10.0	11.0	7.2
Range	5.0-19.0	0.5-18.0	1.0-12.0
Duration (years) of current episode¹			
N =	7	5	9
Mean (s.d.)	8.2 (4.40)	7.0 (6.69)	3.9 (3.69)
Median	9.0	5.0	3.0
Range	1.5-15.0	0.5-18.0	0.3-12.0

Data Source: Section 12, [Table 12.26](#).

1. Recorded only if PMDD symptoms had not persisted from initial onset.

[Table 15](#) shows the relationship of the onset of PMDD symptoms by category (childbirth, menarche, sterilization, oral contraception, other, nothing specified). Apart from “nothing specified”, childbirth most commonly coincided with the onset of PMDD symptoms for all three treatment groups, ranging from 29.2 to 35.4% of subjects.

Table 15 Relationship to Onset of PMDD Symptoms by Category. Number (%) of Subjects (ITT Population)

Onset of PMDD Coincided with:	Treatment Group					
	Parox CR 25mg N = 116		Parox CR 12.5mg N = 130		Placebo N = 120	
Total	115	(99.1)	130	(100.0)	120	(100.0)
Childbirth	40	(34.5)	46	(35.4)	35	(29.2)
Menarche	14	(12.1)	19	(14.6)	12	(10.0)
Sterilization	4	(3.4)	1	(0.8)	2	(1.7)
Stopping Oral Contraception	5	(4.3)	9	(6.9)	9	(7.5)
Starting Oral Contraception	1	(0.9)	1	(0.8)	5	(4.2)
Other	8	(6.9)	11	(8.5)	13	(10.8)
Nothing Specified	47	(40.5)	50	(38.5)	46	(38.3)

Data Source: Section 12, [Table 12.25](#).

Note: A subject could be in more than one category.

The number of subjects who had received treatment for PMDD prior to inclusion in this study is summarized in Table 16. The proportions of subjects who had received previous treatment for PMDD were similar for the three treatment groups, paroxetine CR 25mg: 62/116 (53.4%) subjects; paroxetine CR 12.5mg: 61/130 (46.9%) subjects; placebo: 58/120 (48.3%) subjects. The most common previous treatments (>13%) for PMDD were oral contraception or hormone preparations, pyridoxine (vitamin B6), gamma-linolenic acid (evening primrose oil) and other treatments.

Table 16 Number (%) of Subjects by Previous Treatment for PMDD (ITT Population)

Treatment	Treatment Group					
	Parox CR 25mg N = 116		Parox CR 12.5mg N = 130		Placebo N = 120	
Total	62	(53.4)	61	(46.9)	58	(48.3)
Antidepressants, Anxiolytics, Lithium or other Psychotropic Drugs	3	(2.6)	5	(3.8)	3	(2.5)
Oral Contraception or Hormone Preparation	16	(13.8)	18	(13.8)	19	(15.8)
Pyridoxine (Vitamin B6)	25	(21.6)	20	(15.4)	21	(17.5)
Gamma-Linolenic Acid (Evening Primrose Oil)	21	(18.1)	19	(14.6)	18	(15.0)
NSAIDs	11	(9.5)	14	(10.8)	9	(7.5)
Tryptophan	1	(0.9)	0		0	
Mefenamic Acid	1	(0.9)	1	(0.8)	0	
Diuretics	6	(5.2)	6	(4.6)	8	(6.7)
Clonidine	0		1	(0.8)	0	
Calcium	2	(1.7)	0		2	(1.7)
Other Treatments	16	(13.8)	22	(16.9)	16	(13.3)

Data Source: Section 12, [Table 12.28](#).

Subjects can have more than one treatment in the "other treatments" category.

6.4.4. Obstetrics and Gynecological History

The obstetrics and gynecological history of subjects is summarized by treatment group in [Table 17](#). There were no major differences between treatment groups in any of the

parameters. The majority of subjects had experienced 1 or more pregnancies (range 80.8 to 85.3%), and had 1 or more children (range 76.7 to 78.4%). Approximately 20 to 28% of subjects had experienced 1 or more miscarriages, had 1 or more terminations or had undergone 1 or more dilatation and curettage (D & C) procedures. Heavy periods were experienced by between 37 and 52% of subjects and painful periods were experienced by between 50 and 60% of subjects.

Table 17 Obstetrics and Gynecological History by Treatment Group. Number (%) of Subjects (ITT Population)

Obstetrics and Gynecological History	Treatment Group					
	Parox CR 25mg N = 116		Parox CR 12.5mg N = 130		Placebo N = 120	
Number of Pregnancies						
None	17	(14.7)	25	(19.2)	21	(17.5)
1	16	(13.8)	18	(13.8)	19	(15.8)
2	37	(31.9)	34	(26.2)	34	(28.3)
3	21	(18.1)	30	(23.1)	25	(20.8)
4	12	(10.3)	12	(9.2)	10	(8.3)
>4	13	(11.2)	11	(8.5)	11	(9.2)
Number of Children						
None	25	(21.6)	30	(23.1)	28	(23.3)
1	22	(19.0)	23	(17.7)	25	(20.8)
2	43	(37.1)	49	(37.7)	44	(36.7)
3	18	(15.5)	22	(16.9)	11	(9.2)
4	6	(5.2)	5	(3.8)	10	(8.3)
>4	2	(1.7)	1	(0.8)	2	(1.7)
Number of Spontaneous Miscarriages						
None	84	(72.4)	104	(80.0)	95	(79.2)
1	26	(22.4)	20	(15.4)	18	(15.0)
2	4	(3.4)	3	(2.3)	3	(2.5)
3	1	(0.9)	1	(0.8)	2	(1.7)
4	1	(0.9)	1	(0.8)	2	(1.7)
>4	0		1	(0.8)	0	
Number of Terminations						
None	90	(77.6)	95	(73.1)	95	(79.2)
1	18	(15.5)	30	(23.1)	19	(15.8)
2	5	(4.3)	3	(2.3)	2	(1.7)
3	3	(2.6)	1	(0.8)	3	(2.5)
4	0		1	(0.8)	1	(0.8)
Number of D & Cs						
None	89	(76.7)	95	(73.1)	91	(75.8)
1	16	(13.8)	30	(23.1)	19	(15.8)
2	8	(6.9)	3	(2.3)	7	(5.8)
3	2	(1.7)	0		2	(1.7)
4	1	(0.9)	1	(0.8)	1	(0.8)
>4	0		1	(0.8)	0	
Heavy Periods ?						
No	72	(62.1)	64	(49.2)	58	(48.3)
Yes	44	(37.9)	66	(50.8)	62	(51.7)
Painful Periods ?						
No	53	(45.7)	52	(40.0)	59	(49.2)
Yes	63	(54.3)	78	(60.0)	61	(50.8)

Data Source: Section 12, [Table 12.27](#).

6.4.5. Psychiatric Co-morbidity

Subjects who fulfilled DSM-IV criteria for Axis 1 disorders (other than PMDD or specific phobias) in the 6 months prior to the start of the study, and subjects with a MADRS score of ≥ 10 during the follicular phase of their menstrual cycle (screening visit) were excluded from this study ([Section 5.3.2](#)). Summary statistics for MADRS total score at the screening visit are presented for the ITT population in Section 12, [Table 12.29](#). The mean MADRS scores at screening were low indicating that no clinically relevant depressive symptomatology existed; the MADRS total score ranged from 0 to 9 with a mean score of 1.2 (s.d. 1.79).

Psychiatric co-morbidity was assessed with a standard psychiatric interview including the MINI performed at the end of reference cycle 1 or 1(a) [Visit 2 or 2(a)]. The number of subjects with a prior or concomitant co-morbid psychiatric illness was 7/116 (6.0%) and 9/130 (6.9%) in the 25mg and 12.5mg paroxetine CR groups, respectively, and 5/120 (4.2%) in the placebo group ([Table 18](#)). The most frequently occurring co-morbidity in all treatment groups was a major depressive episode.

Of the 21 subjects with a prior or concomitant psychiatric illness only 3 had a co-morbid psychiatric illness that was ongoing during the treatment phase of the study (paroxetine CR 25mg group: 2 subjects; placebo: 1 subject), although for one subject in the paroxetine CR 12.5mg treatment group it was not known if the illness was in the past or present.

Table 18 **Number (%) of Subjects with Other Psychiatric Disorders from Full Psychiatric History and MINI Interview (ITT Population)**

Psychiatric Disorder Decoded		Treatment Group					
		Parox CR 25mg N = 116		Parox CR 12.5mg N = 130		Placebo N = 120	
Total		7	(6.0)	9	(6.9)	5	(4.2)
(Hypo) Manic Episode	Total	1	(0.9)	1	(0.8)	1	(0.8)
	Past	1	(0.9)	1	(0.8)	1	(0.8)
Agoraphobia	Total	0		1	(0.8)	0	
	Past	0		1	(0.8)	0	
Bulimia Nervosa	Total	0		1	(0.8)	0	
	Past	0		1	(0.8)	0	
Major Depressive Episode	Total	4	(3.4)	5	(3.8)	3	(2.5)
	Past	3	(2.6)	5	(3.8)	3	(2.5)
	Present	1	(0.9)	0		0	
Other (DSM-IV Code – 300.29)	Total	1	(0.9)	1	(0.8)	1	(0.8)
	Present	1	(0.9)	0		1	(0.8)
	Unknown	0		1	(0.8)	0	
Panic Disorder	Total	1	(0.9)	1	(0.8)	0	
	Past	1	(0.9)	1	(0.8)	0	
Suicidality	Total	0		2	(1.5)	0	
	Past	0		2	(1.5)	0	

Data Source: Section 12, [Table 12.24](#).

A subject may have more than one psychiatric disorder.

6.4.6. Other Current Medical Conditions

Section 12, [Table 12.18](#) and [Table 12.19](#) summarize prior and current significant medical or surgical conditions for the screening-only population and randomized non-ITT population, respectively.

Summaries of prior and current significant medical or surgical conditions are presented for the ITT population in Section 12, [Table 12.20](#) and [Table 12.21](#) (prior conditions), and Section 12, [Table 12.22](#) and [Table 12.23](#) (current conditions). No major differences were observed in the treatment groups with respect to the nature of the prior or current medical conditions reported, and there were no differences in the proportions of subjects in each treatment group with current medical conditions. Among the prior conditions there were only two notable differences between the treatment groups. These were for influenza, where there were more subjects in the paroxetine CR 25mg treatment group compared with the paroxetine CR 12.5mg and placebo groups [paroxetine CR 25mg: 13/116 (11.2%) subjects; paroxetine CR 12.5mg: 5/130 (3.8%) subjects; placebo: 4/120 (3.3%) subjects] and contraceptive management, where there were fewer subjects in the paroxetine CR 25mg treatment group compared with the paroxetine CR 12.5mg and

placebo groups [paroxetine CR 25mg: 1/116 (0.9%) subjects; paroxetine CR 12.5mg: 5/130 (3.8%) subjects; placebo: 8/120 (6.7%) subjects]

The number of subjects in the ITT population reporting prior medical conditions was 93/116 (80.2%) subjects in the paroxetine CR 25mg group, 103/130 (79.2%) subjects in the paroxetine CR 12.5mg group and 103/120 (85.8%) subjects in the placebo group. The most common prior medical conditions ($\geq 15\%$ in any treatment group) were headache, female genital disorders other, female genital operations and nose/mouth operations.

The number of subjects in the ITT population reporting current medical conditions was 83/116 (71.6%) subjects in the paroxetine CR 25mg group, 87/130 (66.9%) subjects in the paroxetine CR 12.5mg group and 77/120 (64.2%) subjects in the placebo group. The most common current medical conditions ($\geq 15\%$ in any treatment group) were headache and female genital disorders other.

6.5. Previous and Concomitant Medications

The criteria for determining whether a medication was prior, concomitant, follow-up or prior and concomitant are described in Section 5.8.7.5.

Prior medications are summarized in Section 12, [Table 12.30](#) and [Table 12.31](#) for the screening only and randomized non-ITT population respectively.

Prior and/or concomitant medications are summarized for the ITT population in Section 12, [Table 12.32](#) and [Table 12.33](#) (prior), Section 12, [Table 12.34](#) and [Table 12.35](#) (treatment phase concomitant) and Section 12, [Table 12.36](#) and [Table 12.37](#) (follow-up phase). For Section 12, [Table 12.30](#), [Table 12.31](#), [Table 12.32](#), [Table 12.34](#) and [Table 12.36](#) the medications are summarized using the WHO ATC generic terms and the Level 1 drug classification system. In the ATC Level 1 classification system, medications that are part of combination products may be counted in more than one ATC level. For Section 12, [Table 12.33](#), [Table 12.35](#) and [Table 12.37](#), the medications are summarized using only the generic term and are displayed by decreasing frequency. In these tabulations the generic components of each medication are counted only once.

A summary of the most commonly used ($\geq 5\%$) prior medications is provided in [Table 19](#) for the ITT population. The use of prior medications was reported for 82/116 (70.7%) and 89/130 (68.5%) subjects in the paroxetine CR 25mg and 12.5mg groups, respectively, and 83/120 (69.2%) subjects in the placebo group. The most commonly reported prior medications were paracetamol and ibuprofen.

Table 19 Summary of Most Frequently Administered ($\geq 5\%$ in Any Treatment Group) Prior Medications by Generic Term and Treatment Group. Number (%) of Subjects (ITT Population)

Medications	Treatment Group					
	Parox CR 25mg N = 116		Parox CR 12.5mg N = 130		Placebo N = 120	
Total	82	(70.7)	89	(68.5)	83	(69.2)
Paracetamol	36	(31.0)	47	(36.2)	41	(34.2)
Ibuprofen	35	(30.2)	39	(30.0)	27	(22.5)
Acetylsalicylic Acid	7	(6.0)	7	(5.4)	11	(9.2)
Codeine Phosphate	7	(6.0)	4	(3.1)	4	(3.3)
Vitamins NOS	7	(6.0)	7	(5.4)	9	(7.5)
Caffeine	6	(5.2)	6	(4.6)	4	(3.3)
Naproxen	6	(5.2)	4	(3.1)	5	(4.2)
Ascorbic Acid	3	(2.6)	3	(2.3)	7	(5.8)
Calcium	2	(1.7)	1	(0.8)	7	(5.8)
Diclofenac	0		2	(1.5)	6	(5.0)
Pseudoephedrine Hydrochloride	1	(0.9)	3	(2.3)	6	(5.0)

Data Source: Section 12, [Table 12.33](#).

Prior medications includes medication that were 'prior' or 'prior and go on to be concomitant'.

A summary of the most commonly used ($\geq 5\%$) concomitant, and follow-up study medications is provided in [Table 20](#) for the ITT population. During the treatment phase, concomitant medication use was reported for 78/116 (67.2%) and 75/130 (57.7%) subjects in the paroxetine CR 25mg and 12.5mg groups, respectively, and 81/120 (67.5%) subjects in the placebo group. The most commonly observed concomitant medications were analgesics.

During the follow-up phase, concomitant medication use was reported for 63/116 (54.3%) and 61/129 (47.3%) subjects in the paroxetine CR 25mg and 12.5mg groups, respectively, and 52/120 (43.3%) subjects in the placebo group. Similar to those medications used during the treatment phase, the most commonly observed follow-up concomitant medications were analgesics.

Table 20 Summary of Most Frequently Administered ($\geq 5\%$ in Any Treatment Group) Concomitant Medications During the Treatment Phase and Follow-up Phase by Generic Term and Treatment Group. Number (%) of Subjects (ITT Population)

Medications	Treatment Group					
	Parox CR 25mg		Parox CR 12.5mg		Placebo	
Treatment Phase Medications: N=	116		130		120	
Total	78	(67.2)	75	(57.7)	81	(67.5)
Paracetamol	30	(25.9)	26	(20.0)	40	(33.3)
Ibuprofen	26	(22.4)	33	(25.4)	24	(20.0)
Vitamins NOS	7	(6.0)	4	(3.1)	8	(6.7)
Loratadine	6	(5.2)	3	(2.3)	1	(0.8)
Acetylsalicylic acid	3	(2.6)	10	(7.7)	9	(7.5)
Ascorbic Acid	1	(0.9)	3	(2.3)	9	(7.5)
Calcium	2	(1.7)	1	(0.8)	6	(5.0)
Follow-up Phase Medications: N=	116		129		120	
Total	63	(54.3)	61	(47.3)	52	(43.3)
Paracetamol	12	(10.3)	10	(7.8)	15	(12.5)
Ibuprofen	9	(7.8)	17	(13.2)	9	(7.5)
Vitamins NOS	8	(6.9)	3	(2.3)	8	(6.7)
Ascorbic Acid	0		2	(1.6)	6	(5.0)
Calcium	2	(1.7)	2	(1.6)	6	(5.0)

Data Source: Section 12, [Table 12.35](#) and [Table 12.37](#).

Treatment phase medications include medications that were 'concomitant' or 'prior and concomitant'.

Follow-up medications may include medications which were 'concomitant' or 'prior and concomitant' which continued into the follow-up phase in addition to those initiated in the follow-up phase.

6.6. Treatment Compliance

A summary of overall subject compliance with the dosing regimen by treatment group is provided in [Table 21](#). For each treatment group study medication compliance during each treatment cycle was over 75%.

Table 21 **Number (%) of Subjects who were Overall Compliant with Study Medication (ITT Population)**

	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	N	% ¹	n	N	% ¹	n	N	% ¹
Baseline ²	109	116	94.0	110	130	84.6	109	120	90.8
End of TC 1	89	116	76.7	107	130	82.3	107	120	89.2
End of TC 2	87	100	87.0	98	118	83.1	104	115	90.4
End of TC 3	82	94	87.2	96	110	87.3	91	107	85.0

Data Source: Section 12, [Table 12.39](#).

n = the number of subjects who were compliant; N = the total number of subjects for whom compliance data is available; TC = Treatment Cycle.

Note: Overall compliance: $\geq 80\%$ and $\leq 120\%$ capsule compliance, investigator had indicated that subject did not have a break in treatment of > 3 days and adherence to luteal phase dosing. % capsule compliance = $[(\text{capsules dispensed} - \text{capsules returned}) \times 100] / \text{duration of dosing (days)}$. Where duration is stop date – start date + 1.

1. Percentages are based on the total number of subjects for whom data is available.
2. Baseline was the end of reference cycle 2.

The proportions of subjects by study medication capsule compliance by menstrual cycle for the ITT population are shown in Section 12, [Table 12.38](#). Luteal phase compliance is shown by cycle in Section 12, [Table 12.39](#).

7. EFFICACY RESULTS

This section presents the analyses of the efficacy data for the primary, all secondary and all “other” efficacy variables. These analyses were conducted using the ITT population. Also described here is the analysis of efficacy data for the PP population; this analysis is limited to the primary variable only.

Two analysis datasets were used to summarize the results: the LOCF and OC datasets at the end of treatment cycle 3. The end of treatment cycle 3 OC results are presented as supportive evidence for the treatment cycle 3 LOCF results. The 70% LOCF dataset was not analyzed since more than 70% of subjects in each treatment group remained in the study at the treatment cycle 3 endpoint.

Primary inferences were based on the ITT population LOCF dataset at the protocol-defined treatment cycle 3 endpoint. The LOCF dataset contained all evaluable data for the treatment cycle 3, plus the last evaluable on-treatment assessment for subjects who had a missing assessment at this timepoint or had withdrawn early from the study.

[Section 5.8](#) provides a description of analysis methods.

7.1. Primary Efficacy Results

The protocol-defined primary measure of efficacy was the change from baseline in mean luteal phase VAS-Mood score at the treatment cycle 3 LOCF endpoint. Primary inference was based on the treatment difference between the paroxetine CR 25mg and 12.5mg groups versus placebo for the covariate adjusted model (center group, baseline VAS-Mood score and age) at the treatment cycle 3 LOCF endpoint.

A summary of adjusted change from baseline in mean luteal phase VAS-Mood score for the ITT population is presented in [Table 22](#).

A statistically significant difference was demonstrated in favor of paroxetine CR 25mg and 12.5mg versus placebo for the treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: adjusted mean difference = -10.79mm, 95% CI (-16.46, -5.12), $p < 0.001$; paroxetine CR 12.5mg: adjusted mean difference = -7.66mm, 95% CI (-13.25, -2.08), $p = 0.007$]. The results of the treatment cycle 3 OC analysis were similar to the results of the treatment cycle 3 LOCF endpoint analysis. Statistically significant differences were observed in favor of the two paroxetine CR treatment groups over placebo.

Table 22 Summary and Analysis of Adjusted Change from Baseline in Mean Luteal Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	302	-38.06	2.23	-25.04	2.09	-13.02	-18.98, -7.06	<0.001
	Parox CR 12.5mg vs placebo	302	-32.83	2.08	-25.04	2.09	-7.78	-13.56, -2.01	0.008
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	353	-34.73	2.09	-23.94	2.03	-10.79	-16.46, -5.12	<0.001
	Parox CR 12.5mg vs placebo	353	-31.61	2.00	-23.94	2.03	-7.66	-13.25, -2.08	0.007

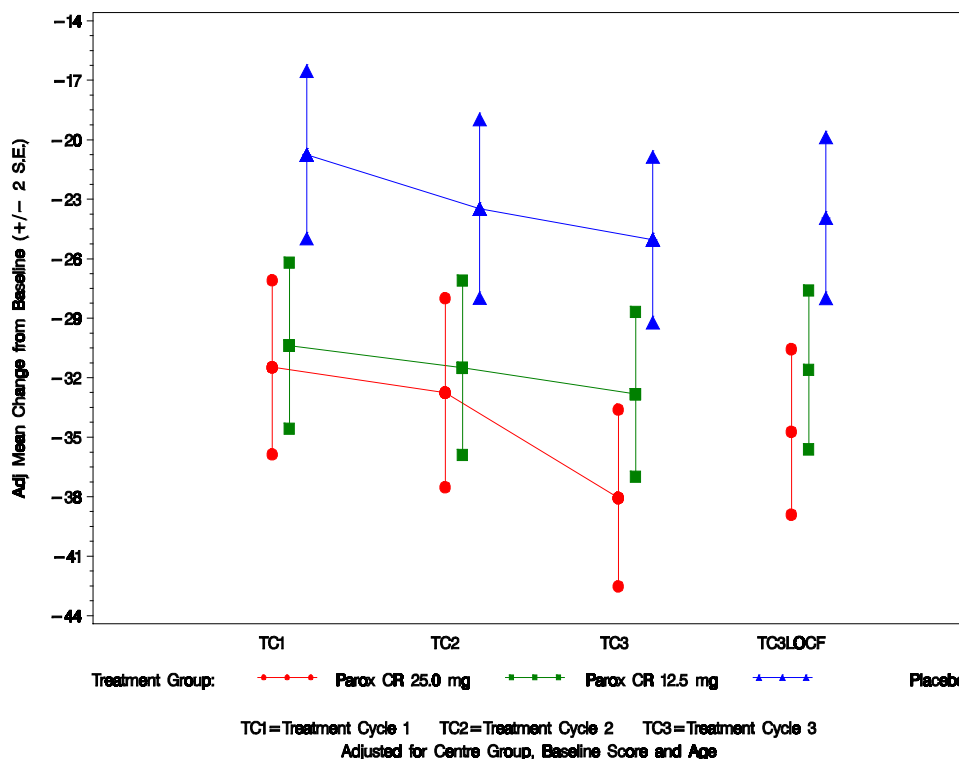
Data Source: Section 13, [Table 13.1](#) and [Table 13.3](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Figure 2 shows the adjusted mean change from baseline (± 2 s.e.) in mean luteal phase VAS-Mood scores for the OC cases at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint for the ITT population. All three treatment groups demonstrated a large average decrease in mean luteal phase VAS-Mood score at the end of treatment cycle 1. The greatest initial decrease was in the paroxetine CR 25mg group, followed closely by the paroxetine CR 12.5mg group and then the placebo group. This order was maintained at treatment cycles 2 and 3 with further decreases in VAS-Mood score for all treatment groups, particularly for the paroxetine CR 25mg group at treatment cycle 3. The treatment cycle 3 OC and LOCF endpoint results show the advantage of the paroxetine CR 25mg and 12.5mg treatments compared to placebo.

Figure 2 Adjusted Change from Baseline (± 2 s.e.) in Mean Luteal Phase VAS-Mood Scores by Treatment Group (ITT Population)



Data Source: Section 16, [Figure 13.1](#).

The treatment difference (95% CI) for the change from baseline in mean luteal phase VAS-Mood score for the ITT population is shown in Section 16, [Figure 13.2](#).

Investigation of the model diagnostics indicated that the data did not satisfy the assumptions of normality. Therefore, a non-parametric analysis adjusting for the pre-specified covariates was performed. This analysis yielded similar results to the parametric analysis.

In further analyses, the homogeneity of the treatment effect was examined by assessing the interaction of treatment with each of the other main effects in the primary model. There were no significant interactions between treatment and any of the covariates.

The results of the analysis of adjusted change from baseline in mean luteal phase VAS-Mood score for the PP population showed differences in favor of paroxetine CR 25mg and 12.5mg versus placebo that were statistically significant for the treatment cycle 3 LOCF [paroxetine CR 25mg: adjusted mean difference = -13.91mm, 95% CI (-20.43, -7.38), $p < 0.001$; paroxetine CR 12.5mg: adjusted mean difference = -9.35mm, 95% CI (-15.42, -3.29), $p = 0.003$] and treatment cycle 3 OC endpoints (Section 13, [Table 13.2](#) and [Table 13.4](#)).

A repeated measures analysis was performed on all the observed VAS-Mood treatment cycle 1 to treatment cycle 3 change from baseline data, correcting for dropout and accounting for the fact that measurements taken on the same subject over time tend to be correlated. Under this likelihood-based approach where dropout was assumed to be random i.e., the probability of a subject dropping out depends on their observed response measurement history, the population average estimate of the treatment difference for change in mean VAS-Mood at treatment cycle 3 for paroxetine CR 25mg versus placebo was -11.49mm, 95% CI (-17.33, -5.65), $p < 0.001$. The estimated treatment difference for change in mean VAS-Mood at treatment cycle 3 for paroxetine CR 12.5mg versus placebo was -6.91mm, 95% CI (-12.79, -1.03), $p = 0.021$. (Statistical Appendix, [Attachment 1](#)).

Summary statistics for mean luteal phase VAS-Mood scores are presented in ([Table 23](#)). Summary statistics for mean luteal phase VAS-Mood scores grouped by center are presented in Section 13, [Table 13.7](#). Individual subject profile plots of the daily VAS-Mood score for the ITT population are shown in Section 16, [Figure 13.3](#).

Table 23 Summary Statistics for Mean Luteal Phase VAS-Mood Scores (ITT Population)

Treatment Cycle Statistics	Parox CR 25mg	Treatment Group Parox CR 12.5mg	Placebo
Baseline			
N	116	130	119
Mean (s.d.)	54.4 (24.46)	52.2 (21.35)	55.7 (21.52)
Median	48.9	47.0	55.4
Range	13.6-99.4	14.7-100.0	13.1-96.3
Treatment Cycle 1			
N	109	120	118
Mean (s.d.)	22.0 (22.91)	23.2 (22.57)	33.6 (27.39)
Median	12.6	15.6	27.5
Range	0.3-93.9	1.0-100.0	1.0-100.0
Treatment Cycle 2			
N	98	113	109
Mean (s.d.)	20.3 (25.50)	21.7 (21.16)	30.8 (25.59)
Median	8.3	15.2	21.7
Range	0.8-95.1	1.0-82.4	0.1-98.9
Treatment Cycle 3			
N	93	105	105
Mean (s.d.)	16.2 (19.72)	21.4 (21.39)	29.6 (24.34)
Median	8.2	11.0	24.7
Range	0.0-90.4	1.0-87.9	0.0-94.5

Data Source: Section 13, [Table 13.5](#)

N is the number of subjects with an assessment.

Summary statistics for the mean luteal phase VAS-Mood score at baseline were similar across the three treatment groups, paroxetine CR 25mg: 54.4mm (s.d. 24.46); paroxetine CR 12.5mg group: 52.2mm (s.d. 21.35); placebo: 55.7mm (s.d. 21.52), ([Table 23](#)).

Summary statistics for mean luteal phase VAS-Mood scores and mean luteal phase VAS-Mood scores grouped by center are presented for the PP population in Section 13, [Table 13.6](#) and [Table 13.8](#), respectively.

Of the 366 subjects in the ITT population, a total of 13 subjects (3.6%) were not included in the treatment cycle 3 LOCF primary analysis of the VAS-Mood endpoint [paroxetine CR 25mg: 4/116, (3.4%); paroxetine CR 12.5mg: 8/130 (6.2%); placebo: 1/120 (0.8%)]. The subject in the placebo group had VAS data for treatment cycles 2 and 3 but lacked a baseline measure. All the subjects in the paroxetine CR groups had baseline VAS data but no post-baseline data. Of the remaining 353 subjects included in the treatment cycle 3 LOCF analysis, 51 subjects did not have an evaluable mean luteal VAS-Mood score at treatment cycle 3 OC [paroxetine CR 25mg: 19/112 (17.0%); paroxetine CR 12.5mg: 17/122 (13.9%); placebo: 15/119 (12.6%)]. For the primary LOCF analysis, a value was carried forward from either treatment cycle 1 or treatment cycle 2 for these 51 subjects (Statistical Appendix, [Attachment 1](#)).

The number of subjects with a missing mean luteal phase VAS-Mood Score by treatment cycle is shown in Section 13, [Table 13.47](#). The number of subjects with a missing mean luteal phase VAS Score for the Core PMDD Symptoms is summarized in Section 13,

[Table 13.48](#). The number of subjects with a missing daily luteal phase VAS Score for the Core PMDD Symptoms is summarized in Section 13, [Table 13.49](#).

7.2. Secondary Efficacy Results

Investigation of the model diagnostics for each of the continuous secondary efficacy variables indicated that the treatment cycle 3 LOCF data did not satisfy the assumptions of normality for the AUC, SDS (total and all individual items), CGI severity of illness and EuroQol VAS endpoints. Therefore, a non-parametric analysis adjusting for covariates was performed on the treatment cycle 3 LOCF and OC datasets for these variables. Each of these analyses yielded similar results to the parametric analyses described in the following sections.

7.2.1. Change from Baseline in VAS Physical Symptoms Score

Summary statistics for the mean luteal phase VAS physical symptoms score for the ITT population are presented in Section 13, [Table 13.11](#).

A summary of the adjusted mean change from baseline in luteal phase VAS physical symptoms score for the ITT population, adjusted for center group, baseline score, and age, is presented in [Table 24](#).

There were no statistically significant differences between the paroxetine CR treatment groups and placebo for the treatment cycle 3 LOCF endpoint, although the results were numerically in favor of the paroxetine CR groups [paroxetine CR 25mg: adjusted mean difference = -5.28mm, 95% CI (-12.26, 1.69), $p=0.137$; paroxetine CR 12.5mg: adjusted mean difference = -6.57mm, 95% CI (-13.42, 0.29), $p=0.060$]. Similar results were observed for the treatment cycle 3 OC analysis for the paroxetine CR 25mg treatment group. However, the treatment cycle 3 OC analysis showed a statistically significant difference in favor of the paroxetine CR 12.5mg treatment group over placebo.

Table 24 Summary and Analysis of Adjusted Change from Baseline in Mean Luteal Phase VAS Physical Symptoms Score Adjusted for Center Group, Baseline Group and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	301	-20.72	2.87	-14.25	2.70	-6.47	-14.18, 1.24	0.100
	Parox CR 12.5mg vs placebo	301	-22.49	2.67	-14.25	2.70	-8.25	-15.69, -0.80	0.030
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	352	-19.17	2.56	-13.89	2.49	-5.28	-12.26, 1.69	0.137
	Parox CR 12.5mg vs placebo	352	-20.46	2.46	-13.89	2.49	-6.57	-13.42, 0.29	0.060

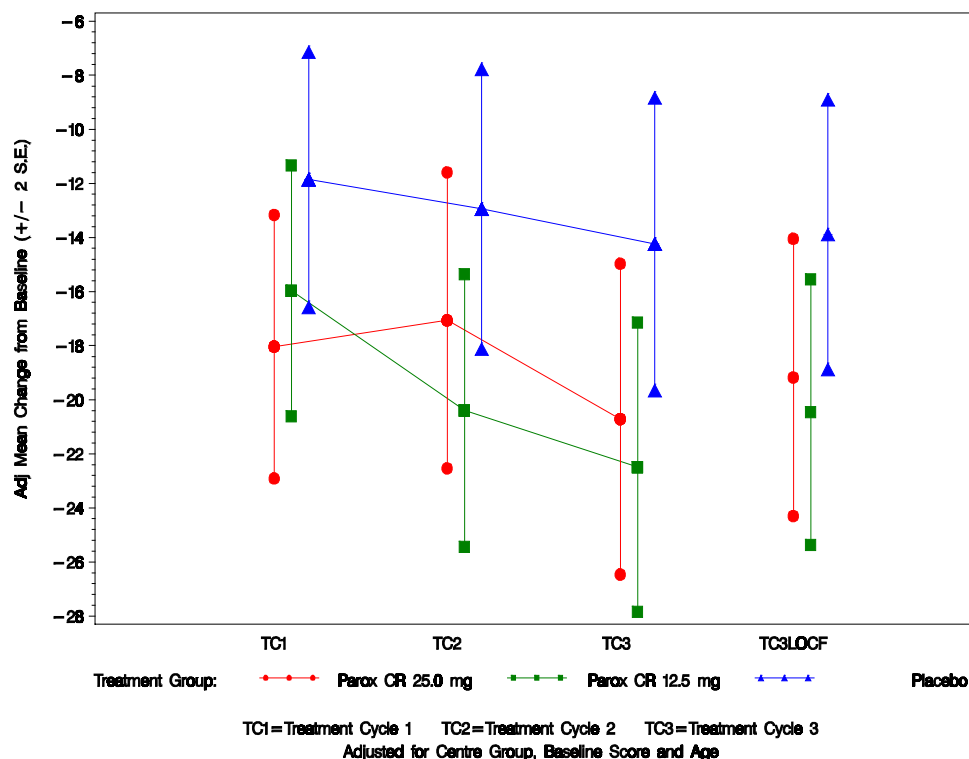
Data Source: Section 13, [Table 13.9](#) and [Table 13.10](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Figure 3 shows the adjusted mean change from baseline (± 2 s.e.) in mean luteal phase VAS physical symptom score for the OC cases at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint for the ITT population. All three treatment groups demonstrated a large decrease in VAS physical symptom score at the end of treatment cycle 1. The greatest initial decrease was in the paroxetine CR 25mg group, followed closely by the paroxetine CR 12.5mg group and then the placebo group. The treatment cycle 3 OC and LOCF endpoint results show the advantage of the paroxetine CR 25mg and 12.5mg treatments compared to placebo.

Figure 3 Adjusted Change from Baseline (± 2 s.e.) in Mean Luteal Phase VAS Physical Symptoms Scores by Treatment Group (ITT Population)



Data Source: Section 16, [Figure 13.4](#).

7.2.2. Change from Baseline in Mean Luteal Phase VAS Total Score (Regulatory Requested Variable)

A summary and analysis of adjusted change from baseline in mean luteal phase VAS total score, adjusted for center group, baseline score, and age, for the ITT population is presented in [Table 25](#).

Statistically significant differences were demonstrated in favor of paroxetine CR 25mg and paroxetine CR 12.5mg versus placebo for the treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: adjusted mean difference = -77.82mm, 95% CI (-133.47, -22.16),

p=0.006; paroxetine CR 12.5mg: adjusted mean difference = -73.13mm, 95% CI (-127.91, -18.36), p=0.009].

The results of the treatment cycle 3 OC analysis were similar to the treatment cycle 3 LOCF endpoint analysis. Statistically significant differences were observed in favor of the two paroxetine CR treatment groups over placebo.

Table 25 Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS Total Score Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	302	-313.32	22.46	-214.23	20.96	-99.09	-159.14, -39.05	0.001
	Parox CR 12.5mg vs placebo	302	-296.52	20.87	-214.23	20.96	-82.29	-140.22, -24.35	0.006
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	353	-283.54	20.51	-205.72	19.88	-77.82	-133.47, -22.16	0.006
	Parox CR 12.5mg vs placebo	353	-278.85	19.64	-205.72	19.88	-73.13	-127.91, -18.36	0.009

Data Source: Section 13, [Table 13.15.1](#) and [Table 13.15.2](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Section 16, [Figure 13.7.1](#) shows the mean change from baseline (± 2 s.e.) in mean luteal phase VAS total score for the OC data at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint.

Summary statistics for mean luteal phase VAS total score and percentage change from baseline in mean luteal phase VAS total score are shown in Section 13, [Table 13.15.3](#) and [Table 13.15.4](#) respectively.

7.2.3. Proportion of Responders Defined by a 50% Reduction from their Baseline Luteal Phase VAS-Mood Score

The proportion of subjects having a 50% reduction from baseline in mean luteal phase VAS-Mood score is presented in Table 26.

At the treatment cycle 3 LOCF endpoint 81/112 (72.3%) subjects in the paroxetine CR 25mg group and 81/122 (66.4%) subjects in the paroxetine CR 12.5mg group were classed as responders compared to 59/119 (49.6%) subjects in the placebo group.

Table 26 Summary of the Percentage of Subjects Responding (50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score) (ITT Population)

	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	N	%	n	N	%	n	N	%
TC 1 OC	75	109	68.8	80	120	66.7	55	118	46.6
TC 2 OC	71	98	72.4	75	113	66.4	60	108	55.6
TC 3 OC	74	93	79.6	74	105	70.5	56	104	53.8
TC 3 LOCF Endpoint	81	112	72.3	81	122	66.4	59	119	49.6

Data Source: Section 13, [Table 13.12](#).

n = the number of subjects who responded; N = the total number of subjects for whom data is available;
TC = Treatment Cycle.

[Table 27](#) shows the odds ratio (95% CI) for responders (50% reduction from baseline in mean luteal phase VAS-Mood score) for the ITT population. The odds of being a responder on paroxetine CR 25mg relative to the odds of being a responder on placebo at the treatment cycle 3 LOCF endpoint was 3.03 (95% CI [1.66, 5.53], $p < 0.001$) indicating a statistically significant benefit for paroxetine CR 25mg over placebo, and this was also the case for paroxetine CR 12.5mg with an odds ratio of 2.49 (95% CI [1.40, 4.45], $p = 0.002$).

The results of the treatment cycle 3 OC analysis were similar to the results of the treatment cycle 3 LOCF endpoint analysis. Statistically significant differences were observed in favor of the two paroxetine CR treatment groups over placebo.

Table 27 Summary of Logistic Regression for Subjects with a 50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons	Odds Ratio ¹	Pairwise Comparisons	
			95% CI for Odds Ratio	p-value
TC 3 OC	Parox CR 25mg vs placebo	3.93	1.97, 7.85	<0.001
	Parox CR 12.5mg vs placebo	2.50	1.33, 4.71	0.005
TC 3 LOCF Endpoint	Parox CR 25mg vs placebo	3.03	1.66, 5.53	<0.001
	Parox CR 12.5mg vs placebo	2.49	1.40, 4.45	0.002

Data Source: Section 13, [Table 13.13.1](#)

TC = Treatment Cycle

1. The odds ratio represents the odds of improving with paroxetine CR relative to placebo.

Section 16, [Figure 13.5](#) shows the odds ratio (95% CI) for responders (50% reduction from baseline in mean luteal phase VAS-Mood score) for the ITT population.

Summary statistics for the percentage change from baseline in mean luteal phase VAS-Mood score for the ITT population are shown in Section 13, [Table 13.13.2](#).

7.2.4. Proportion of Responders Defined by Mean Luteal Phase VAS-Mood Score $\leq$ Baseline Mean Follicular Phase VAS-Mood Score

The proportion of subjects with a mean luteal phase VAS-Mood score $\leq$ baseline mean follicular phase VAS-Mood score is presented in Table 28. This endpoint represents complete alleviation of luteal phase PMDD symptomatology. At the treatment cycle 3 LOCF endpoint 35/112 (31.3%) subjects in the paroxetine CR 25mg group and 21/122 (17.2%) subjects in the paroxetine CR 12.5mg group were responders compared to 8/120 (6.7%) subjects in the placebo group.

Table 28 Summary of the Percentage of Subjects Responding (Mean Luteal Phase VAS-Mood Score $\leq$ Baseline Mean Follicular Phase VAS-Mood Score) (ITT Population)

	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	N	%	n	N	%	n	N	%
TC 1 OC	19	109	17.4	21	120	17.5	4	118	3.4
TC 2 OC	29	98	29.6	19	113	16.8	10	109	9.2
TC 3 OC	33	93	35.5	21	105	20.0	7	105	6.7
TC 3 LOCF Endpoint	35	112	31.3	21	122	17.2	8	120	6.7

Data Source: Section 13, [Table 13.14.1](#).

n = the number of subjects who responded; N = the total number of subjects for whom data is available;

TC = Treatment Cycle.

Table 29 shows the odds ratio (95% CI) for responders (mean luteal phase VAS-Mood score $\leq$ baseline mean follicular phase VAS-Mood score) for the ITT population. The odds of being a responder on paroxetine CR 25mg relative to the odds of being a responder on placebo at the treatment cycle 3 LOCF endpoint was 7.08 (95% CI [3.03 , 16.55], $p < 0.001$) indicating a statistically significant benefit for paroxetine CR 25mg over placebo, and this was also the case for paroxetine CR 12.5mg with an odds ratio of 2.91 (95% CI [1.21 , 7.01], $p = 0.017$).

The results of the treatment cycle 3 OC analysis were similar to the results of the treatment cycle 3 LOCF endpoint analysis. Statistically significant differences were observed in favor of the two paroxetine CR treatment groups over placebo.

Table 29 Summary of Logistic Regression for Subjects with a Mean Luteal Phase VAS-Mood Score $\leq$ Baseline Mean Follicular Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons	Odds Ratio ¹	Pairwise Comparisons	
			95% CI for Odds Ratio	p-value
TC 3 OC	Parox CR 25mg vs placebo	8.31	3.35, 20.63	<0.001
	Parox CR 12.5mg vs placebo	3.62	1.43, 9.16	0.007
TC 3 LOCF Endpoint	Parox CR 25mg vs placebo	7.08	3.03, 16.55	<0.001
	Parox CR 12.5mg vs placebo	2.91	1.21, 7.01	0.017

Data Source: Section 13, [Table 13.14.2](#).

TC = Treatment Cycle

1. The odds ratio represents the odds of improving with paroxetine CR relative to placebo.

Section 16, [Figure 13.6](#) shows the odds ratio (95% CI) for responders (mean luteal phase VAS-Mood score $\leq$ baseline mean follicular phase VAS-Mood score) for the ITT population.

7.2.5. Change from Baseline in AUC for Luteal Phase VAS-Mood Scores

The AUC in the observed case dataset was used to summarize the daily luteal phase VAS-Mood scores across the treatment phase (treatment cycles 1-3).

Summary statistics for luteal phase AUC VAS-Mood scores for the ITT population are presented in Section 13, [Table 13.45](#). A summary and analysis of change from baseline for AUC luteal phase VAS-Mood scores adjusted for center group, baseline score, and age, for the ITT population is presented in [Table 30](#).

Statistically significant differences were demonstrated in favor of paroxetine CR 25mg and 12.5mg versus placebo for change from baseline in AUC daily luteal phase VAS-Mood score, paroxetine CR 25mg: adjusted mean difference = -8.13mm [95% CI (-12.26, -3.99), $p < 0.001$; paroxetine CR 12.5mg: adjusted mean difference = -6.81mm [95% CI (-10.88, -2.73), $p < 0.001$].

Table 30 Summary of the Analysis of Change from Baseline in AUC Luteal Phase VAS-Mood Score Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Phase	Parox CR 25mg vs placebo	353	-26.32	1.52	-18.19	1.48	-8.13	-12.26, -3.99	<0.001
	Parox CR 12.5mg vs placebo	353	-25.00	1.46	-18.19	1.48	-6.81	-10.88, -2.73	<0.001

Data Source: Section 13, [Table 13.43](#) and [Table 13.44](#).

Note: The AUC was calculated for the treatment phase as a whole, based on OC data.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

7.2.6. Change from Baseline in Individual SDS Item Scores

A summary and analysis of adjusted change from baseline in the SDS individual item scores, adjusted for center group, baseline score and age, for the ITT population are presented in [Table 31](#).

Statistically significant differences were demonstrated in favor of paroxetine CR 25mg versus placebo for the SDS work and family/home item scores and for paroxetine CR 12.5mg for the SDS work item score for the treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: work adjusted mean difference -0.86 points, 95% CI (-1.59, -0.13), $p=0.021$; family/home adjusted mean difference -0.91 points, 95% CI (-1.73, -0.09), $p=0.029$; paroxetine CR 12.5mg: work adjusted mean difference -0.69 points, 95% CI (-1.36, -0.01), $p=0.047$]. There were no statistically significant differences between the paroxetine CR treatment groups and placebo for the SDS social/leisure item scores (and for the family/home item for the paroxetine CR 12.5mg group) at the treatment cycle 3 LOCF endpoint, although the differences between paroxetine CR treatment and placebo were always numerically in favor of the paroxetine treatment.

The results of the treatment cycle 3 OC analysis were similar to the results of the treatment cycle 3 LOCF endpoint analysis, with all differences between paroxetine CR treatments and placebo being numerically in favor of the paroxetine treatment, but only the paroxetine CR 25mg SDS work item difference was statistically significant.

Table 31 Summary and Analysis of Adjusted Change from Baseline in SDS Individual Item Scores Adjusted for Center Group, Baseline Score and Age (ITT Population)

		Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)								
Social/Leisure									
	TC 3 OC								
	TC 3 LOCF Endpt								
Work									
	TC 3 OC								
	TC 3 LOCF Endpt								
Family/Home									
	TC 3 OC								
	TC 3 LOCF Endpt								

Data Source: Section 13, [Table 13.27](#) and [Table 13.28](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Section 16, [Figure 13.8.1.1](#), [Figure 13.8.1.2](#) and [Figure 13.8.1.3](#) show the adjusted mean change from baseline (± 2 s.e.) in SDS individual item scores for the OC data at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint for the ITT population.

Summary statistics for the SDS individual item scores (social/leisure, work and family/home) for the ITT population are presented in Section 13, [Table 13.29](#).

7.2.7. Change from Baseline in Total SDS Item Score

A summary and analysis of adjusted change from baseline in the SDS total score, adjusted for center group, baseline score and age, for the ITT population is presented in [Table 32](#).

Statistically significant differences were demonstrated in favor of paroxetine CR 25mg and 12.5mg versus placebo for the SDS total score for the treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: adjusted mean difference -2.74 points, 95% CI $(-4.97, -0.51)$, $p=0.016$; paroxetine CR 12.5mg: adjusted mean difference -2.33 points, 95% CI $(-4.40, -0.26)$, $p=0.028$].

The results of the treatment cycle 3 OC analysis showed a statistically significant benefit in favor of paroxetine CR 25mg versus placebo, but the difference for the paroxetine CR 12.5mg versus placebo comparison, although numerically in favor of paroxetine CR 12.5mg, was not statistically significant.

Table 32 Summary and Analysis of Adjusted Change from Baseline in SDS Total Score Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	186	-10.34	1.08	-7.33	0.92	-3.01	-5.79, -0.23	0.034
	Parox CR 12.5mg vs placebo	186	-9.68	0.94	-7.33	0.92	-2.35	-4.91, 0.20	0.071
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	269	-9.40	0.86	-6.66	0.74	-2.74	-4.97, -0.51	0.016
	Parox CR 12.5mg vs placebo	269	-8.98	0.75	-6.66	0.74	-2.33	-4.40, -0.26	0.028

Data Source: Section 13, [Table 13.27](#) and [Table 13.28](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Section 16, [Figure 13.8.2](#) shows the adjusted mean change from baseline (± 2 s.e.) in SDS total score for the OC cases at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint.

Summary statistics for the SDS total score for the ITT population are presented in Section 13, [Table 13.29](#).

7.2.8. Change from Baseline in the Observer Rated PMTS-O Total Score

A summary and analysis of adjusted change from baseline in PMTS-O total scores, adjusted for center group, baseline score, and age, for the ITT population is presented in [Table 33](#).

A statistically significant difference was demonstrated in favor of paroxetine CR 25mg versus placebo for the treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: adjusted mean difference = -3.21 points, 95% CI (-5.42, -0.99), $p=0.005$]. Although not statistically significant, the paroxetine CR 12.5mg versus placebo comparison was numerically in favor of paroxetine CR 12.5mg.

The results of the treatment cycle 3 OC analysis were similar to the treatment cycle 3 LOCF endpoint analysis. Compared to placebo, both paroxetine CR treatment were superior, but only the paroxetine CR 25mg treatment difference was statistically significant.

Table 33 Summary and Analysis of Adjusted Change from Baseline in PMTS-O Total Scores Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	209	-11.99	1.03	-8.47	0.92	-3.52	-6.24, -0.79	0.012
	Parox CR 12.5mg vs placebo	209	-10.63	0.89	-8.47	0.92	-2.15	-4.66, 0.35	0.091
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	290	-11.42	0.84	-8.22	0.76	-3.21	-5.42, -0.99	0.005
	Parox CR 12.5mg vs placebo	290	-10.00	0.74	-8.22	0.76	-1.78	-3.86, 0.30	0.093

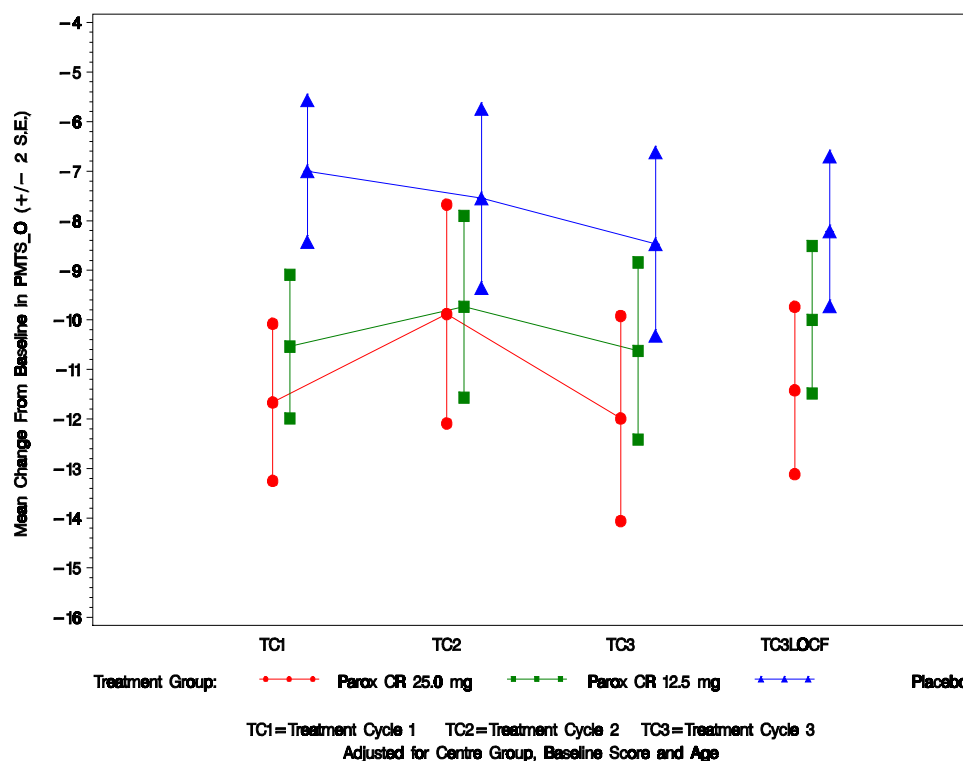
Data Source: Section 13, [Table 13.30](#) and [Table 13.31](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Figure 4 shows the adjusted mean change from baseline (± 2 s.e.) in PMTS-O total score for the OC cases at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint for the ITT population. All three treatment groups demonstrated a large decrease in the PMTS-O total score at the end of treatment cycle 1. The greatest initial decrease was in the paroxetine CR 25mg group, followed by the paroxetine CR 12.5mg group and then the placebo group. The treatment cycle 3 OC and LOCF endpoint results show the advantage of the paroxetine CR 25mg and 12.5mg treatments compared to placebo.

Figure 4 Adjusted Change from Baseline (± 2 s.e.) in PMTS-O Total Score by Treatment Group (ITT Population)



Data Source: Section 16, [Figure 13.9](#).

Summary statistics for the PMTS-O total scores for the ITT population are presented in Section 13, [Table 13.32](#).

7.2.9. Change from Baseline in CGI Severity of Illness Score

A summary of baseline and change from baseline in CGI severity of illness score for the ITT population is given in Section 13, [Table 13.33](#). At baseline the mean CGI severity of illness score was 4.7 for both paroxetine CR treatment groups and 4.6 for the placebo group, indicating that on average subjects were moderately to markedly ill at baseline. At the end of treatment cycle 3, the mean change from baseline CGI severity of illness score

was -2.4 and -2.1 for the paroxetine CR 25mg and 12.5mg treatment groups respectively, compared to -1.9 for the placebo group.

The number (%) of subjects in each category of the CGI severity of illness score is summarized by visit for the ITT population in Section 13, [Table 13.35](#). The number of subjects in each category of the CGI severity of illness item was comparable between treatment groups at baseline. At baseline the proportions of subjects assessed as being moderately, markedly, severely or extremely ill were 85/93 (91.4%) for paroxetine CR 25mg subjects, 105/116 (90.5%) for paroxetine CR 12.5mg subjects, and 100/107 (93.5%) for placebo subjects. At the treatment cycle 3 endpoint, the proportions of such subjects were, 12/75 (16.0%) for paroxetine CR 25mg subjects, 22/81 (27.2%) for paroxetine CR 12.5mg subjects, and 29/82 (35.4%) for placebo subjects, showing the advantage of paroxetine CR treatment. This effect of treatment with paroxetine CR was also demonstrated in the proportion of subjects rated as normal or borderline mentally ill at baseline, zero, compared with the treatment cycle 3 endpoint: 50/75 (66.7%) subjects in the paroxetine CR 25mg group, 43/81 (53.1%) subjects in the paroxetine CR 12.5mg group and 36/82 (43.9%) subjects in the placebo group.

The number (%) of subjects by change from baseline in the CGI severity of illness is presented for the ITT population in Section 13, [Table 13.36](#). A summary and analysis of adjusted change from baseline in CGI severity of illness scores, adjusted for center group, baseline score and age is presented in [Table 34](#).

A statistically significant difference was demonstrated in favor of paroxetine CR 25mg versus placebo for the treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: adjusted mean difference = -0.61 points, 95% CI (-1.03, -0.20), $p=0.004$]. The result for paroxetine CR 12.5mg was numerically in favor of paroxetine CR 12.5mg, but not statistically significant.

The results of the treatment cycle 3 OC analysis showed non-significant numerical benefit for the paroxetine CR treatment groups versus placebo.

Table 34 Summary of Analysis for Change from Baseline in CGI Severity of Illness Scores Adjusted for Center Group, Baseline Score and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	209	-2.36	0.20	-1.92	0.18	-0.44	-0.96, 0.08	0.094
	Parox CR 12.5mg vs placebo	209	-2.09	0.17	-1.92	0.18	-0.17	-0.65, 0.30	0.470
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	294	-2.36	0.16	-1.75	0.14	-0.61	-1.03, -0.20	0.004
	Parox CR 12.5mg vs placebo	294	-2.02	0.14	-1.75	0.14	-0.27	-0.67, 0.12	0.177

Data Source: Section 13, [Table 13.34.1](#) and [Table 13.34.2](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

Section 16, [Figure 13.10](#) shows the adjusted mean change from baseline (± 2 s.e.) in the CGI severity of illness score for the OC cases at treatment cycles 1 to 3 and the treatment cycle 3 LOCF endpoint.

7.2.10. Proportion of Responders on the CGI Global Improvement Item Scale

The number (%) of subjects in each category of the CGI global improvement item at endpoint is summarized for the ITT population in Section 13, [Table 13.39](#).

The protocol-defined criteria for a responder was a score of 1 (very much improved) or 2 (much improved) on the scale at endpoint. A non-responder was defined as a score of ≥ 3 at endpoint. The proportion of responders based on the CGI global improvement item is presented in Table 35. At the treatment cycle 3 LOCF endpoint 71/105 (67.6%) subjects in the paroxetine CR 25mg group and 66/116 (56.9%) subjects in the paroxetine CR 12.5mg group were classed as responders compared to 50/116 (43.1%) subjects in the placebo group.

Table 35 Summary of the Percentage of Subjects Responding on the CGI Global Improvement Item (Score of 1 or 2) (ITT Population)

	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	N	%	n	N	%	n	N	%
TC 1 OC	60	96	62.5	57	101	56.4	46	105	43.8
TC 2 OC	48	71	67.6	49	87	56.3	37	91	40.7
TC 3 OC	56	75	74.7	48	81	59.3	38	82	46.3
TC 3 LOCF Endpoint	71	105	67.6	66	116	56.9	50	116	43.1

Data Source: Section 13, [Table 13.37](#).

n = the number of subjects who responded; N = the total number of subjects for whom data is available;

TC = Treatment Cycle.

[Table 36](#) shows the odds ratio (95% CI) for responders on the CGI global improvement Item for the ITT population.

The odds of being a CGI responder on paroxetine CR 25mg relative to the odds of being a responder on placebo at treatment cycle 3 LOCF endpoint was 3.47 [95% CI (1.87, 6.43), $p < 0.001$] indicating a statistically significant benefit of paroxetine CR 25mg over placebo. The odds of being a CGI responder on paroxetine CR 12.5mg relative to the odds of being a responder on placebo at treatment cycle 3 LOCF endpoint was 1.97 [95% CI (1.11, 3.50), $p = 0.021$] indicating a statistically significant benefit of paroxetine CR 12.5mg over placebo.

The results of the treatment cycle 3 OC analysis were similar to the results of the treatment cycle 3 LOCF endpoint analysis. Statistically significant differences were observed in favor of the two paroxetine CR treatment groups over placebo.

Table 36 Summary of Logistic Regression for Percentage of Subjects Responding on the CGI Global Improvement Item Adjusted for Center Group and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons	Odds Ratio ¹	Pairwise Comparisons	
			95% CI for Odds Ratio	p-value
TC 3 OC	Parox CR 25mg vs placebo	4.65	2.16, 10.03	<0.001
	Parox CR 12.5mg vs placebo	1.99	1.00, 3.95	0.049
TC 3 LOCF Endpoint	Parox CR 25mg vs placebo	3.47	1.87, 6.43	<0.001
	Parox CR 12.5mg vs placebo	1.97	1.11, 3.50	0.021

Data Source: Section 13, [Table 13.38](#).

TC = Treatment Cycle

1. The odds ratio represents the odds of improving with paroxetine CR relative to placebo.

Section 16, [Figure 13.11](#) shows the odds ratio (95% CI) for responders, defined as a score of 1 or 2 on the CGI global improvement item.

7.2.11. Proportion of Responders on the PGE

The number (%) of subjects in each category of PGE at treatment cycles 1-3 is summarized for the ITT population in Section 13, [Table 13.42](#).

The protocol-defined response criteria was defined as a score of 1 (very much improved) or 2 (much improved) on the scale at endpoint. A non-responder was defined as a score of ≥ 3 at endpoint. The proportion of responders based on the PGE is presented in Table 37. At the treatment cycle 3 LOCF endpoint 49/102 (48.0%) subjects in the paroxetine CR 25mg group and 59/114 (51.8%) subjects in the paroxetine CR 12.5mg group were classed as responders compared to 33/115 (28.7%) subjects in the placebo group.

Table 37 Summary of the Percentage of Subjects Responding on the PGE Item (Score of 1 or 2) (ITT Population)

	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	N	%	n	N	%	n	N	%
TC 1 OC	48	89	53.9	44	95	46.3	39	105	37.1
TC 2 OC	36	70	51.4	41	82	50.0	22	87	25.3
TC 3 OC	41	75	54.7	42	77	54.5	25	81	30.9
TC 3 LOCF Endpoint	49	102	48.0	59	114	51.8	33	115	28.7

Data Source: Section 13, [Table 13.40](#).

n = the number of subjects who responded; N = the total number of subjects for whom data is available;

TC = Treatment Cycle.

[Table 38](#) shows the odds ratio (95% CI) for responders on the PGE for the ITT population.

The odds of being a PGE responder on paroxetine CR 25mg relative to the odds of being a responder on placebo at treatment cycle 3 LOCF endpoint was 2.67 [95% CI (1.44, 4.94), $p=0.002$] indicating a statistically significant benefit of paroxetine CR 25mg over placebo. The odds of being a PGE responder on paroxetine CR 12.5mg relative to the odds of being a responder on placebo at treatment cycle 3 LOCF endpoint was 3.07 [95% CI (1.69, 5.58), $p<0.001$] indicating a statistically significant benefit of paroxetine CR 12.5mg over placebo.

The results of the treatment cycle 3 OC analysis were similar to the results of the treatment cycle 3 LOCF endpoint analysis. Statistically significant differences were observed in favor of the two paroxetine CR treatment groups over placebo.

Table 38 Summary of Logistic Regression for Percentage of Subjects Responding on the PGE Adjusted for Center Group and Age (ITT Population)

Change from Baseline to:	Treatment Comparisons	Odds Ratio ¹	Pairwise Comparisons	
			95% CI for Odds Ratio	p-value
TC 3 OC	Parox CR 25mg vs placebo	3.49	1.67, 7.30	<0.001
	Parox CR 12.5mg vs placebo	3.21	1.55, 6.62	0.002
TC 3 LOCF Endpoint	Parox CR 25mg vs placebo	2.67	1.44, 4.94	0.002
	Parox CR 12.5mg vs placebo	3.07	1.69, 5.58	<0.001

Data Source: Section 13, [Table 13.41](#).

TC = Treatment Cycle

1. The odds ratio represents the odds of improving with paroxetine CR relative to placebo.

Section 16, [Figure 13.12](#) shows the odds ratio (95% CI) for responders, defined as a score of 1 or 2 on the PGE.

7.3. Other Efficacy Results

7.3.1. Change from Baseline in Individual VAS Item Scores

Summary statistics for baseline and change from baseline in luteal phase individual VAS item scores (irritability, tension, depressed mood, affective lability, decreased interest, difficulty concentrating, lack of energy, change in appetite, change in sleep pattern, feeling out of control, physical symptoms) are presented for the ITT population in Section 13, [Table 13.16](#), [Table 13.17](#), [Table 13.18](#), [Table 13.19](#), [Table 13.20](#), [Table 13.21](#), [Table 13.22](#), [Table 13.23](#), [Table 13.24](#), [Table 13.25](#) and [Table 13.26](#). The mean baseline luteal phase individual VAS item scores were similar for the treatment groups. At the end of treatment cycle 3, the means for all individual VAS item scores were reduced for each treatment group, with both paroxetine CR treatment groups showing larger reductions than the placebo group.

The mean change from baseline (± 2 s.e.) in the 11 individual VAS Item Scores is shown in Section 16, [Figure 13.7.2.1](#), [Figure 13.7.2.2](#), [Figure 13.7.2.3](#), [Figure 13.7.2.4](#),

Figure 13.7.2.5, Figure 13.7.2.6, Figure 13.7.2.7, Figure 13.7.2.8, Figure 13.7.2.9, Figure 13.7.2.10 and Figure 13.7.2.7.11.

7.3.2. PESM

The number and percentage of subjects in each category of the PESM questionnaire are presented for the subset of the ITT population who responded to the questionnaire in Table 39.

Of those who responded, a total of 69/114 (60.5%) subjects in the paroxetine CR 25mg group and 73/128 (57.0%) subjects in the paroxetine CR 12.5mg group stated that they would take study medication again compared to 62/119 (52.1%) subjects in the placebo group. The main reason for not taking study medication again was side effects in the paroxetine CR 25mg group and lack of efficacy in the paroxetine CR 12.5mg and placebo groups.

Table 39 Number (%) of Subjects in Each Category of the PESM Questionnaire (ITT Population)

Subject Evaluation	Treatment Group					
	Parox CR 25mg N =114		Parox CR 12.5mg N =128		Placebo N =119	
Total	114	(100.0)	128	(100.0)	119	(100.0)
Yes	69	(60.5)	73	(57.0)	62	(52.1)
No	28	(24.6)	32	(25.0)	45	(37.8)
Lack of Efficacy	11	(39.3)	23	(71.9)	41	(91.1)
Side Effects	16	(57.1)	9	(28.1)	2	(4.4)
Other	1	(3.6)	0		2	(4.4)
Not Sure	17	(14.9)	23	(18.0)	12	(10.1)
Lack of Efficacy	7	(41.2)	15	(65.2)	6	(50.0)
Side Effects	3	(17.6)	2	(8.7)	2	(16.7)
Anti-medication ¹	1	(5.9)	1	(4.3)	0	
Other	6	(35.3)	5	(21.7)	4	(33.3)

Data Source: Section 13, [Table 13.46](#).

Percentages for the number of subjects responding yes, no or not sure to the question 'Would you take this medication again?' are based on the total number of respondents.

Percentages for the reason (i.e. lack of efficacy, side effects etc.) are based on the number of subjects who responded no or not sure.

1. A dislike of taking tablets.

7.4. Efficacy Conclusions

- For the primary efficacy variable, change from baseline in mean luteal phase VAS-Mood score at the treatment cycle 3 LOCF endpoint, a statistically significant difference was demonstrated in favor of paroxetine CR 25mg and 12.5mg versus placebo [paroxetine CR 25mg: adjusted mean difference = -10.79mm, 95% CI

(-16.46, -5.12), $p < 0.001$; paroxetine CR 12.5mg: adjusted mean difference = -7.66mm, 95% CI (-13.25, -2.08), $p = 0.007$].

- There were no statistically significant differences between the paroxetine CR treatment groups and placebo for the change from baseline in mean luteal phase VAS physical symptoms score at the treatment cycle 3 LOCF endpoint, although the results were numerically in favor of the paroxetine CR groups [paroxetine CR 25mg: adjusted mean difference = -5.28mm, 95% CI (-12.26, 1.69), $p = 0.137$; paroxetine CR 12.5mg: adjusted mean difference = -6.57mm, 95% CI (-13.42, 0.29), $p = 0.060$].
- Statistically significant differences were demonstrated in favor of both paroxetine CR doses versus placebo in the mean change from baseline in VAS total score ((Regulatory requested variable), at treatment cycle 3 LOCF endpoint [paroxetine CR 25mg: adjusted mean difference = -77.82mm, 95% CI (-133.47, -22.16), $p = 0.006$; paroxetine CR 12.5mg: adjusted mean difference = -73.13mm, 95% CI (-127.91, -18.36), $p = 0.009$].
- Of the remaining endpoints, statistically significant differences were observed in favor of both paroxetine CR doses versus placebo in the majority of subject rated secondary efficacy variables. These were the change from baseline in AUC daily luteal phase VAS-Mood score, SDS total score, SDS work item and SDS family/home item (only for paroxetine CR 25mg). The odds of being a responder as defined by a 50% reduction from baseline in mean luteal phase VAS-Mood score, a mean luteal phase VAS-Mood score $\leq$ baseline follicular phase VAS-Mood score, or a score of 1 or 2 on the PGE scale at endpoint, showed a statistically significant difference in favor of paroxetine CR 25mg and paroxetine CR 12.5mg versus placebo at the treatment cycle 3 LOCF endpoint. No statistically significant differences were observed for the SDS social/leisure item, but the differences observed were numerically in favor of both paroxetine CR doses versus placebo.
- For the clinician rated endpoints, the odds of being a responder on the CGI global improvement item showed a statistically significant difference in favor of both paroxetine CR doses versus placebo. Statistically significant differences were also observed in favor of paroxetine CR 25mg versus placebo in the change from baseline in CGI severity of illness item, and change from baseline in PMTS-O total score. No statistically significant differences were observed between paroxetine CR 12.5mg and placebo in these two endpoints.
- Whilst there was evidence that both paroxetine CR treatments were superior to placebo for the majority of the efficacy variables, the magnitude of the response was greater in the paroxetine CR 25mg group than in the paroxetine CR 12.5mg group.
- Results from the treatment cycle 3 OC analyses generally supported the results of the treatment cycle 3 LOCF endpoint analyses.

The efficacy results from this study demonstrate that paroxetine CR 25mg and 12.5mg are both effective for the treatment of female outpatients with PMDD, and that the response of subjects who received paroxetine CR 25mg is usually greater than the response seen with paroxetine CR 12.5mg.

8. QUALITY OF LIFE AND EMPLOYMENT STATUS

This section presents the analyses of the quality of life and employment status data. These analyses were conducted using the ITT population.

8.1. Change from Baseline in EuroQol VAS Score

Summary statistics for baseline and change from baseline in EuroQol VAS for the ITT population are presented in Table 40. At baseline, the mean EuroQol VAS scores were comparable across treatment groups with a range of 52.2 to 54.2mm. At the end of treatment cycle 3 the mean change from baseline in EuroQol VAS scores was 22.0mm (s.d. 32.88) in the paroxetine CR 25mg group and 22.9mm (s.d. 30.59) in the paroxetine CR 12.5mg group compared to 20.7mm (s.d. 32.66) in the placebo group.

Table 40 Summary Statistics for Baseline and Change from Baseline in EuroQol VAS (ITT Population)

Visit	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Baseline: N =	86	110	102
Mean (s.d.)	54.1 (31.59)	52.2 (30.35)	54.2 (30.77)
Median	65.0	42.0	50.0
Range	0 to 100	0 to 100	2 to 100
End of Treatment Cycle 1: N =	71	88	92
Mean (s.d.)	20.3 (31.10)	17.8 (35.09)	13.2 (31.49)
Median	10.0	10.5	5.0
Range	-75 to 85	-99 to 90	-75 to 80
End of Treatment Cycle 2: N =	54	75	76
Mean (s.d.)	19.4 (34.46)	23.8 (29.96)	12.0 (32.37)
Median	10.0	11.0	5.0
Range	-81 to 91	-40 to 98	-85 to 83
End of Treatment Cycle 3: N =	54	69	69
Mean (s.d.)	22.0 (32.88)	22.9 (30.59)	20.7 (32.66)
Median	10.0	20.0	15.0
Range	-37 to 95	-71 to 80	-71 to 95

Data Source: Section 14, [Table 14.3](#).

Only subjects with baseline assessments are included.

A summary of analysis of the adjusted mean change from baseline in EuroQol VAS adjusted for center group, baseline score, age, and employment status, for the ITT population is presented in [Table 41](#). At the treatment cycle 3 LOCF endpoint, a statistically significant difference was observed for the paroxetine CR 25mg treatment group versus placebo [adjusted mean difference = 8.31mm, 95% CI (1.19, 15.43), $p=0.022$], and although the paroxetine CR 12.5mg group showed numerical superiority over placebo treatment, the difference was not statistically significant.

For the OC analysis, there were no statistically significant differences, but both paroxetine CR treatments were numerically superior to placebo.

Table 41 Summary and Analysis of Adjusted Mean Change from Baseline in EuroQol VAS Adjusted for Center Group, Baseline Score, Age and Employment Status (ITT Population)

Change from Baseline to:	Treatment Comparisons (Group 1 vs Group 2)	Pairwise Comparisons							
		n ¹	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2	Treatment Difference ²	95% CI for Treatment Difference	p-value for Treatment Difference
TC 3 OC	Parox CR 25mg vs placebo	191	23.64	3.21	16.74	3.06	6.91	-0.96, 14.77	0.085
	Parox CR 12.5mg vs placebo	191	20.32	2.98	16.74	3.06	3.58	-3.76, 10.92	0.337
TC 3 LOCF Endpt	Parox CR 25mg vs placebo	272	21.64	2.95	13.33	2.77	8.31	1.19, 15.43	0.022
	Parox CR 12.5mg vs placebo	272	17.19	2.73	13.33	2.77	3.86	-2.80, 10.52	0.254

Data Source: Section 14, [Table 14.1](#) and [Table 14.2](#).

TC = Treatment Cycle; Endpt = Endpoint.

1. n= number used in analysis.
2. Difference in adjusted least square means are shown.

8.2. Change from Baseline in the Weighted EQ-5D Health Profile Score (EQ-5D Utility Score)

Summary statistics for baseline and change from baseline for EQ-5D utility score for the ITT population is presented in Table 42. At baseline, mean EQ-5D utility scores were similar across treatment groups with a range of 0.650 to 0.693.

Improvement, as measured by increased utility scores, was seen in all treatment groups at the end of treatment cycle 3, with both paroxetine CR treatment groups showing slightly larger changes from baseline than placebo. The mean change from baseline in utility scores at the end of treatment cycle 3 was 0.179 (s.d. 0.331) in the paroxetine CR 25mg group, 0.195 (s.d. 0.304) in the paroxetine CR 12.5mg group, and 0.163 (s.d. 0.303) in the placebo group.

Table 42 Summary Statistics for Baseline, Treatment Cycle 3 and Change from Baseline for EQ-5D Utility Score (ITT Population)

Visit	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Baseline: N =	84	111	104
Mean (s.d.)	0.693 (0.324)	0.650 (0.323)	0.670 (0.328)
Median	0.796	0.689	0.725
Range	-0.221 to 1.000	-0.077 to 1.000	-0.181 to 1.000
End of Treatment Cycle 3: N =	74	76	80
Mean (s.d.)	0.848 (0.238)	0.859 (0.173)	0.805 (0.225)
Median	1.000	0.848	0.796
Range	-0.066 to 1.000	0.101 to 1.000	0.030 to 1.000
Change from Baseline: N =	53	69	69
Mean (s.d.)	0.179 (0.331)	0.195 (0.304)	0.163 (0.303)
Median	0.152	0.107	0.036
Range	-0.564 to 1.221	-0.624 to 0.843	-0.590 to 0.972

Data Source: Section 14, [Table 14.5](#).

A positive change from baseline indicates an improvement in the subjects EQ-5D utility score.

8.3. EQ-5D Health Profiles at Baseline and Treatment Cycle 3

The number and percentage of subjects reporting at least some level of difficulty is shown in [Table 43](#) by category of EQ-5D health profile at baseline and end of treatment cycle 3 for the ITT population. At baseline, the distribution of responses on the EQ-5D were generally similar across all treatment groups for all 5 categories. The percentage of subjects reporting any problem at baseline was greatest in the categories for anxiety/depression, pain/discomfort, and usual activities. At treatment cycle 3 OC the percentage of subjects with reports of problems were reduced for each treatment group for almost all categories. The most notable reductions were seen in the categories where the most problems were reported at baseline (i.e. anxiety/depression, pain/discomfort, usual activities), and for these problems the reductions for both paroxetine CR treatment groups were larger than for the placebo group.

Table 43 Summary of EQ-5D Health Profile at Baseline and End of Treatment Cycle 3 by Treatment Group. Proportions of Subjects with a Problem (ITT Population)

Problem	Treatment Groups					
	Parox CR 25mg		Parox CR 12.5mg		Placebo	
	Baseline n/N (%)	End TC 3 n/N (%)	Baseline n/N (%)	End TC 3 n/N (%)	Baseline n/N (%)	End TC 3 n/N (%)
Anxiety/Depression	50/86 (58.1)	19/75 (25.3)	73/111 (65.8)	20/76 (26.3)	63/104 (60.6)	30/80 (37.5)
Mobility	11/86 (12.8)	4/75 (5.3)	9/111 (8.1)	6/77 (7.8)	14/104 (13.5)	8/81 (9.9)
Pain/Discomfort	46/84 (54.8)	25/75 (33.3)	72/111 (64.9)	33/76 (43.4)	59/104 (56.7)	40/81 (49.4)
Self Care	3/86 (3.5)	2/75 (2.7)	1/111 (0.9)	1/77 (1.3)	4/104 (3.8)	3/81 (3.7)
Usual Activities	31/86 (36.0)	12/74 (16.2)	46/111 (41.4)	15/76 (19.7)	40/104 (38.5)	23/81 (28.4)

Data Source: Section 14, [Table 14.4](#).

Note: Results expressed as n/N (%), where n = number of subjects with a problem, N = total number of subjects assessed for that parameter at that timepoint and (%) = n/N expressed as a %.

TC = Treatment Cycle.

Section 16, [Figure 14.1](#) and [Figure 14.2](#) show the distribution of EQ-5D health profile items at baseline and treatment cycle 3 respectively.

8.4. ISCO-88

The ISCO-88 captures 10 major employment classifications. The number and proportion of subjects in each category of the ISCO-88 at baseline is presented for the ITT population in Table 44. The majority of subjects with a current occupation categorized themselves as “professional”, “technician or associate professional”, “clerk”, and “service/shop/sales worker”. The distribution of occupations was generally similar across the treatment groups.

Table 44 **Number (%) of Subjects in Each Category of the ISCO-88 (ITT Population)**

Occupation	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Legislator, Senior Official or Manager	4 (3.4)	4 (3.1)	3 (2.5)
Professional	28 (24.1)	28 (21.5)	33 (27.5)
Technician or Associate Professional	26 (22.4)	36 (27.7)	24 (20.0)
Clerk	19 (16.4)	21 (16.2)	30 (25.0)
Service/Shop/Sales Worker	14 (12.1)	18 (13.8)	16 (13.3)
Skilled (Agricultural/Fishery)	1 (0.9)	0	3 (2.5)
Craft and Related Trades Worker (e.g., miner, builder)	1 (0.9)	2 (1.5)	0
Machine Operator/Assembler	2 (1.7)	5 (3.8)	1 (0.8)
Military	0	1 (0.8)	0
Elementary Occupation	1 (0.9)	1 (0.8)	0
Not Applicable	20 (17.2)	14 (10.8)	10 (8.3)

Data Source: Section 14, [Table 14.6](#).

8.5. Overall Work Productivity Score from the WPAI

The number of subjects in each category of the WPAI employed/unemployed question for the ITT population is presented in Section 14, [Table 14.7](#). A total of 251/300 (83.7%) subjects were employed at baseline, with slightly lower proportions in both paroxetine CR treatment groups compared with placebo (paroxetine CR 25mg: 81.4%; paroxetine CR 12.5mg: 82.7%; placebo: 86.5%). The proportions of employed subjects in the paroxetine CR 12.5mg and placebo groups were maintained at treatment cycles 1, 2 and 3, but reduced slightly in the paroxetine CR 25mg group to 55/74 (74.3%) at treatment cycle 3.

Summary statistics of the number of hours missed from work for health reasons, hours missed from work for other reasons, and the number of hours worked, are presented for the ITT population in Section 14, [Table 14.8](#), [Table 14.9](#) and [Table 14.10](#), respectively. The number of hours missed from work for health and other reasons were low but variable, and no marked differences were observed between the treatment groups. The mean number of hours worked at baseline was comparable across the treatment groups

with a range of 27.6 to 28.8. There was no notable change over the course of the study in the mean number of hours worked.

A summary of the number and percentage of subjects with health problems affecting work productivity and regular daily activities for the ITT population is provided in Table 45. At baseline the proportions of subjects with health problems affecting work productivity or daily activities were similar across the treatment groups with ranges of 88.4 to 89.4% and 93.6 to 96.2% respectively. The proportion of subjects reporting health problems affecting work productivity and regular daily activities was reduced in all treatment groups at the end of treatment cycle 3. For work activities and regular daily activities, the paroxetine CR 25mg treatment group showed the greatest reduction, with the paroxetine CR 12.5mg group showing the smallest change for work activities, and the placebo group showing the smallest change for daily activities.

Table 45 Proportions of Subjects with Health Problems Affecting Work Productivity and Regular Daily Activities from the WPAI (ITT Population)

	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	N	%	n	N	%	n	N	%
Health Problems Affecting Work Productivity¹									
Baseline	59	66	89.4	77	87	88.5	76	86	88.4
End of TC 1	47	66	71.2	62	80	77.5	66	85	77.6
End of TC 2	33	52	63.5	53	71	74.6	55	73	75.3
End of TC 3	32	53	60.4	46	60	76.7	44	63	69.8
Health Problems Affecting Regular Daily Activities¹									
Baseline	81	86	94.2	102	109	93.6	100	104	96.2
End of TC 1	66	88	75.0	85	100	85.0	92	105	87.6
End of TC 2	53	70	75.7	70	85	82.4	76	88	86.4
End of TC 3	55	75	73.3	61	77	79.2	64	80	80.0

Data Source: Section 14, [Table 14.11](#) and [Table 14.12](#).

TC = Treatment Cycle.

- The results are shown as the number of subjects with a response of 1 or more (n), expressed as a percentage of the total number of subjects at that timepoint (N).

8.6. Quality of Life and Employment Status Conclusions

- For the change from baseline in EuroQol VAS, a statistically significant difference was demonstrated in favor of paroxetine CR 25mg versus placebo at the treatment cycle 3 LOCF endpoint [adjusted mean difference = 8.31mm, 95% CI (1.19, 15.43), $p=0.022$], and the paroxetine CR 12.5mg group showed numerical, but not statistically significant, superiority over placebo treatment. For the OC analysis at treatment cycle 3, there were no statistically significant differences, but both paroxetine CR treatments were numerically superior to placebo.

- Improvement, as measured by increased EQ-5D utility scores, was seen in all treatment groups at the end of treatment cycle 3 with both paroxetine CR treatment groups showing slightly larger changes from baseline than placebo. At the end of treatment cycle 3 the percentage of subjects reporting problems was reduced for each treatment group for all categories of the EQ-5D health profile. The most notable reductions compared with baseline were seen in anxiety/depression, pain/discomfort and usual activities, and for these problems the reductions for both paroxetine CR treatment groups were larger than for the placebo group. This is based on a subset of subjects who completed treatment cycle 3.
- The proportion of subjects reporting health problems affecting work productivity and regular daily activities was reduced in all treatment groups at the end of treatment cycle 3. For work activities and regular daily activities, the paroxetine CR 25mg treatment group showed the greatest reduction, with the paroxetine CR 12.5mg group showing the smallest change for work activities, and the placebo group showing the smallest change for daily activities.

9. SAFETY RESULTS

This section describes the safety data for the ITT population. The safety data analyzed include AEs, laboratory data, and vital signs. Safety data are presented for the pre-treatment, treatment and follow-up phases.

9.1. Extent of Exposure

Table 46 shows the exposure of each subject to paroxetine CR or placebo by treatment group, as well as descriptive statistics (means, standard deviation, range and total exposure in years) for overall duration of exposure.

For the ITT population, the range of exposure to double-blind study medication was 1 to 88 days with over 81% of subjects in each treatment group being exposed to at least 29 days of study medication. The mean number of days exposure to study medication was slightly lower in the paroxetine CR 25mg treatment group compared to the paroxetine CR 12.5mg and placebo groups, paroxetine CR 25mg group: 36.5 days (s.d. 12.83); paroxetine CR 12.5mg: 38.6 days (s.d. 12.85); placebo: 40.8 days (s.d. 8.82), and this was also true for the total exposure in years, paroxetine CR 25mg group: 11.6 years; paroxetine CR 12.5mg: 13.8 years; placebo: 13.4 years.

Table 46 **Number (%) of Subjects Exposed to Each Dosage of Paroxetine CR and Placebo by Time Intervals and Mean Treatment Duration (ITT Population)**

	Treatment Group					
	Parox CR 25mg N = 116		Parox CR 12.5mg N = 130		Placebo N = 120	
Study Drug Exposure: Days						
1-7	7	(6.0)	5	(3.8)	1	(0.8)
8-14	9	(7.8)	4	(3.1)	1	(0.8)
15-21	3	(2.6)	8	(6.2)	3	(2.5)
22-28	2	(1.7)	5	(3.8)	6	(5.0)
29-44	62	(53.4)	69	(53.1)	73	(60.8)
45-60	33	(28.4)	37	(28.5)	34	(28.3)
≥61	0		2	(1.5)	2	(1.7)
Mean duration (s.d.)	36.5 (12.83)		38.6 (12.85)		40.8 (8.82)	
Median	41.0		41.0		42.0	
Range	4-53		1-88		7-65	
Total exposure: years	11.6		13.8		13.4	

Data Source: Section 15, [Table 15.34](#).

For each subject exposure was the last treatment date minus the first treatment date plus 1 for each of the individual treatment cycles, since the treatment was intermittent.

9.2. Adverse Events

9.2.1. Pre-treatment Adverse Events

Summaries of AEs occurring during the screening phase by body system and preferred term for the screening-only population and randomized non-ITT population are provided in Section 15, [Table 15.1](#) and [Table 15.2](#) respectively.

A summary of AEs occurring during the screening phase prior to randomization to double-blind study medication for the ITT population is presented in Section 15, [Table 15.3](#). A total of 96/366 (26.2%) subjects reported AEs occurring prior to the first dose of double-blind study medication. The most commonly reported AEs ($\geq 3\%$) were headache (25/366 subjects, 6.8%), infection (14/366, 3.8%) and respiratory disorder (12/366, 3.3%).

9.2.2. Treatment Emergent Adverse Events

Summaries of all emergent AEs occurring during the treatment phase (i.e., occurring during the interval from first to last dose of randomized medication) by body system and preferred term are provided in Section 15, [Table 15.4](#) (by body system and preferred term) and Section 15, [Table 15.5](#) (by preferred term in descending order for those events occurring in 1% or more of the population) for the ITT population. [Table 47](#) presents a summary of the most frequently reported ($\geq 5\%$ in any treatment group) AEs occurring during the treatment phase in descending order of frequency.

Overall, 89/116 (76.7%) subjects in the paroxetine CR 25mg group, 88/130 (67.7%) subjects in the paroxetine CR 12.5mg group and 68/120 (56.7%) subjects in the placebo group, reported emergent AEs during the treatment phase. The majority of AEs were related to the nervous system, body as a whole, and digestive system.

In the paroxetine CR 25mg treatment group, nausea was the most frequently reported treatment emergent AE [27/116 (23.3%)], followed by asthenia [22/116 (19.0%)]. For the paroxetine CR 12.5mg treatment group the most frequently reported treatment emergent AEs were nausea, headache and asthenia [all 16/130 (12.3%)], followed by insomnia [13/130 (10.0%)], and for the placebo treatment group the most frequently reported treatment emergent AE was headache [17/120 (14.2%)], followed by respiratory disorder [13/120 (10.8%)]. For the majority of paroxetine CR subjects who experienced nausea the time to first occurrence was within the first seven days of starting treatment (Section 15, [Table 15.20](#)).

Commonly reported treatment emergent AEs ($\geq 5\%$ in either paroxetine CR group), which occurred at an incidence at least twice that of placebo were nausea, asthenia, libido decreased, sweating, diarrhea, dizziness, tremor, insomnia and sinusitis (Section 15, [Supplementary Table 15.1](#)).

There appeared to be a dose dependent relationship in the treatment emergent AEs reported, with more treatment emergent AEs being reported overall in the paroxetine CR 25mg group [89/116 (76.7%)] than in the paroxetine CR 12.5mg group [88/130 (67.7%)].

Furthermore, the majority of the most frequently reported treatment emergent AEs ($\geq 5\%$ in any treatment group) had a higher incidence in the paroxetine CR 25mg group than in the paroxetine CR 12.5mg group. Exceptions were respiratory disorder, insomnia and sinusitis.

Table 47 **Number (%) of Subjects with the most Frequently Reported ($\geq 5\%$ in Any Treatment Group) Treatment Emergent Adverse Events (ITT Population)**

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Total Subjects with at least one AE	89 (76.7)	88 (67.7)	68 (56.7)
Nausea	27 (23.3)	16 (12.3)	2 (1.7)
Asthenia	22 (19.0)	16 (12.3)	5 (4.2)
Headache	18 (15.5)	16 (12.3)	17 (14.2)
Libido Decreased	15 (12.9)	7 (5.4)	7 (5.8)
Infection	10 (8.6)	5 (3.8)	8 (6.7)
Sweating	10 (8.6)	4 (3.1)	1 (0.8)
Diarrhea	8 (6.9)	7 (5.4)	0
Dizziness	8 (6.9)	7 (5.4)	3 (2.5)
Tremor	7 (6.0)	4 (3.1)	0
Respiratory Disorder	5 (4.3)	9 (6.9)	13 (10.8)
Insomnia	4 (3.4)	13 (10.0)	3 (2.5)
Sinusitis	3 (2.6)	7 (5.4)	2 (1.7)

Data Source: Section 15, [Table 15.4](#) and [Table 15.5](#).

9.2.3. Treatment Emergent Adverse Events by Severity

Summaries of AEs occurring during the treatment phase by severity are presented in Section 15, [Table 15.10](#) (by body system and preferred term) and Section 15, [Table 15.11](#) (by preferred term in descending order for those events occurring in 1% or more of the population). In addition, a summary of AEs occurring during the treatment phase by maximum severity is presented by body system and preferred term in Section 15, [Table 15.22](#).

The majority of AEs, regardless of treatment group, were rated as mild or moderate in intensity. [Table 48](#) presents a summary of the most frequent ($\geq 2\%$ in any treatment group) severe AEs occurring during the treatment phase. Severe AEs were more common in the paroxetine CR 25mg [29/116 subjects (25.0%)] and 12.5mg groups [26/130 subjects (20.0%)] compared to the placebo group [17/120 subjects (14.2%)].

Libido decreased was the most frequently reported severe AE in the paroxetine CR 25mg treatment group [6/116 (5.2%)], asthenia was the most frequently reported severe AE in the paroxetine CR 12.5mg treatment group [4/130 (3.1%)] and headache was the most frequently reported severe AE in the placebo treatment group [4/120 (3.3%)].

Table 48 **Number (%) of Subjects with the most Frequently Reported ($\geq 2\%$ in Any Treatment Group) Severe Adverse Events Occurring During the Treatment Phase (ITT Population)**

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Total Subjects with at least one severe AE	29 (25.0)	26 (20.0)	17 (14.2)
Libido Decreased	6 (5.2)	3 (2.3)	1 (0.8)
Nausea	5 (4.3)	3 (2.3)	0
Sweating	5 (4.3)	1 (0.8)	1 (0.8)
Asthenia	4 (3.4)	4 (3.1)	0
Headache	3 (2.6)	3 (2.3)	4 (3.3)
Infection	2 (1.7)	1 (0.8)	3 (2.5)
Migraine	0	0	3 (2.5)
Trauma	0	0	3 (2.5)

Data Source: Section 15, [Table 15.10](#) and [Table 15.11](#).

9.2.4. Treatment Emergent Adverse Events by Relationship to Treatment

Summaries of AEs that were judged to be related or possibly related to study medication occurring during the treatment phase are presented in Section 15, [Table 15.14](#) (by body system and preferred term) and Section 15, [Table 15.15](#) (by preferred term in descending order for those events occurring in 1% or more of the population). [Table 49](#) presents a summary of the most frequent ($\geq 5\%$ in any treatment group) AEs occurring during the treatment phase that were judged by the investigator to be related or possibly related to study medication in descending order of frequency.

The incidence of AEs considered by investigators to be related or possibly related to study medication was higher in the paroxetine CR groups compared to the placebo group: 69/116 (59.5%) subjects in the paroxetine CR 25mg group, 56/130 (43.1%) subjects in the paroxetine CR 12.5mg group, and 25/120 (20.8%) subjects in the placebo group.

In the paroxetine CR 25mg treatment group, nausea was the most frequently reported treatment emergent AE thought to be related or possibly related to study medication [25/116 (21.6%)], followed by asthenia [19/116 (16.4%)]. For the paroxetine CR 12.5mg treatment group the most frequently reported related or possibly related AE was asthenia [15/130 (11.5%)], followed by nausea [13/130 (10.0%)], and for the placebo treatment group the most frequently reported related or possibly related AE were headache and libido decreased [both 6/120 (5.0%)], followed by asthenia [4/120 (3.3%)].

Table 49 **Number (%) of Subjects with the most Frequently Reported ($\geq 5\%$ in Any Treatment Group) Related or Possibly Related Adverse Events Occurring During the Treatment Phase (ITT Population)**

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Total Subjects with at least one related or possibly related AE	69 (59.5)	56 (43.1)	25 (20.8)
Nausea	25 (21.6)	13 (10.0)	2 (1.7)
Asthenia	19 (16.4)	15 (11.5)	4 (3.3)
Libido Decreased	15 (12.9)	7 (5.4)	6 (5.0)
Sweating	9 (7.8)	4 (3.1)	1 (0.8)
Dizziness	8 (6.9)	6 (4.6)	2 (1.7)
Headache	8 (6.9)	8 (6.2)	6 (5.0)
Tremor	7 (6.0)	4 (3.1)	0
Diarrhea	6 (5.2)	6 (4.6)	0
Insomnia	2 (1.7)	10 (7.7)	2 (1.7)

Data Source: Section 15, [Table 15.14](#) and [Table 15.15](#).

9.2.5. Treatment Emergent Adverse Events by Time of First Occurrence

Summaries of AEs occurring during the treatment phase by time of first occurrence are presented in Section 15, [Table 15.20](#) (by body system and preferred term) and Section 15, [Table 15.21](#) (by preferred term in descending order for those events occurring in 1% or more of the population).

[Table 50](#) provides an overview of the time of first occurrence for the five most frequently reported AEs within each treatment group (or >5 where the incidences are equal). The study treatment period was divided into intervals of one week segments during the first month, then one month and then any remaining days. A subject with an AE must have taken at least one dose of study medication at any point in the interval to be included. For the most frequently reported AEs for the paroxetine treatment groups ($\geq 12\%$ incidence for both paroxetine CR treatment groups), nausea, asthenia and headache, the time to first occurrence was generally during Days 1 to 7, although this was less marked for headache. For the placebo treatment group, AEs were more evenly distributed throughout the study period.

Table 50 **Number of Subjects with the Most Frequently Reported Treatment Emergent Adverse Events by Time of First Occurrence Based on Verbatim Term (ITT Population)**

Treatment Group AE Preferred Term	Day of First Occurrence						Total
	1-7 days	8-14 days	15-21 days	22-28 days	29-60 days	≥ 61 days	
Parox CR 25mg¹: N=	65	18	16	5	35	8	89
Nausea	23	0	0	0	4	0	27
Asthenia	18	2	1	0	3	0	22
Headache	6	3	2	1	4	2	18
Libido Decreased	12	1	0	2	0	0	15
Infection	3	0	4	0	3	0	10
Sweating	7	0	2	0	0	1	10
Parox CR 12.5mg: N=	48	12	12	9	37	12	88
Nausea	11	2	1	0	2	0	16
Asthenia	10	3	0	0	3	0	16
Headache	7	2	0	2	4	1	16
Insomnia	9	1	0	0	3	0	13
Respiratory Disorder	3	1	0	0	4	1	9
Placebo²: N=	21	17	9	8	42	9	68
Headache	3	5	2	1	4	2	17
Respiratory Disorder	2	0	1	1	9	0	13
Infection	1	1	0	1	3	2	8
Libido Decreased	3	1	0	0	3	0	7
Asthenia	2	0	1	1	1	0	5
Back Pain	0	1	1	0	2	1	5
Pharyngitis	1	0	0	0	4	0	5

Data Source: Section 15, [Table 15.20](#) and [Table 15.21](#).

N = Number of subjects who experienced at least one AE during the specified interval (not all of equal length).

Note: Although the data are time to first occurrence of an event, since different verbatim terms may code to the same preferred term, the same event may appear more than once for a particular subject. Since the total column is the number of subjects with at least one AE of the specified type, the total number of events may exceed the total number of subjects. For example, this applies to asthenia for the paroxetine CR 25mg treatment group; total subjects are 22, but the total events are 24. Each AE is assigned to an interval based on the onset date.

1. There are six AEs for the paroxetine CR 25mg treatment group because infection and sweating had the same incidence.
2. There are seven AEs for the placebo treatment group because asthenia, back pain and pharyngitis had the same incidence.

9.2.6. Adverse Events by Time of Occurrence Relating to Treatment Periods

Section 15, [Supplementary Table 15.8](#) details the number of subjects with AEs by time of occurrence based on six “on medication” and “off medication” periods during, and following, the three treatment cycles, by severity and for all severities combined. An overview of this data (all severities combined) for the most frequently reported AEs (≥5% in any treatment group in any of the periods) is shown in [Table 51](#). The AEs are ordered based on the paroxetine CR 25mg treatment group for “on medication” treatment cycle 1, and all AEs for paroxetine CR treatment groups with an incidence of ≥5% and at least twice the incidence for placebo in the same treatment period are in bold.

For each of the three treatment groups, the overall incidence of AEs was higher in each of the "on study medication" time windows compared to the following "off study medication" time windows.

The overall incidence of AEs occurring during the "on study medication" time windows for both of the paroxetine CR treatment groups was highest in the first treatment cycle (paroxetine CR 25mg: 61.2%; paroxetine CR 12.5mg: 43.8%), reducing to a range of 29 to 36% during the "on study medication" time windows associated with treatment cycles 2 and 3. During the "on study medication" time window during treatment cycle 1 for the paroxetine CR 25mg group, seven AEs (nausea, asthenia, libido decreased, sweating, diarrhea, dizziness, and tremor) occurred at an incidence of $\geq 5\%$ and at least twice that of placebo. This reduced down to two AEs (nausea and asthenia) and three AEs (nausea, asthenia and libido decreased) during the "on study medication" time windows during treatment cycles 2 and 3 respectively. For the paroxetine CR 12.5mg treatment group, three AEs (nausea, asthenia and insomnia) occurred at an incidence of $\geq 5\%$ and at least twice that of placebo, during the "on study medication" time window during treatment cycle 1, reducing to one AE (asthenia) and zero AEs during the "on study medication" time windows during treatment cycles 2 and 3 respectively.

For the "off study medication" periods, the incidence of AEs for both paroxetine CR groups was more consistent over the three cycles at between 16 and 21%. For the "off study medication" periods, the incidence of AEs for the placebo group ranged from 11 to 16%. During the "off study medication" periods, in the paroxetine CR treatment groups there was just one AE that occurred at an incidence of $\geq 5\%$ and at least twice that of placebo (infection, paroxetine CR 25mg group).

Table 51 **Number (%) of Subjects with the Most Frequently Reported ($\geq 5\%$ in Any Treatment Group at Any Treatment Period) AEs by Time of Occurrence Based on “On Medication” and “Off Medication” Treatment Periods. All Severities Combined (ITT Population)**

Treatment Group AE Preferred Term	Treatment Period					
	On Med During TC1	Off Med Following TC1	On Med During TC2	Off Med Following TC2	On Med During TC3	Off Med Following TC3
Parox CR 25mg: N=	116	116	100	100	93	93
Total ¹	71 (61.2)	24 (20.7)	31 (31.0)	21 (21.0)	33 (35.5)	19 (20.4)
Nausea	23 (19.8)	0	8 (8.0)	1 (1.0)	5 (5.4)	1 (1.1)
Asthenia	20 (17.2)	2 (1.7)	7 (7.0)	1 (1.0)	8 (8.6)	2 (2.2)
Headache	12 (10.3)	4 (3.4)	5 (5.0)	5 (5.0)	8 (8.6)	3 (3.2)
Libido Decreased	12 (10.3)	0	5 (5.0)	0	5 (5.4)	0
Sweating	8 (6.9)	1 (0.9)	4 (4.0)	0	2 (2.2)	0
Diarrhea	7 (6.0)	0	1 (1.0)	1 (1.0)	1 (1.1)	0
Dizziness	6 (5.2)	1 (0.9)	2 (2.0)	0	2 (2.2)	0
Tremor	6 (5.2)	0	3 (3.0)	0	3 (3.2)	0
Infection	3 (2.6)	6 (5.2)	1 (1.0)	1 (1.0)	0	2 (2.2)
Insomnia	3 (2.6)	0	0	1 (1.0)	0	1 (1.1)
Parox CR 12.5mg: N=	130	130	118	118	109	109
Total ¹	57 (43.8)	22 (16.9)	41 (34.7)	19 (16.1)	32 (29.4)	23 (21.1)
Nausea	14 (10.8)	1 (0.8)	4 (3.4)	1 (0.8)	2 (1.8)	1 (0.9)
Asthenia	13 (10.0)	0	6 (5.1)	1 (0.8)	4 (3.7)	1 (0.9)
Headache	9 (6.9)	5 (3.8)	8 (6.8)	5 (4.2)	5 (4.6)	3 (2.8)
Libido decreased	5 (3.8)	0	3 (2.5)	1 (0.8)	3 (2.8)	0
Sweating	3 (2.3)	0	1 (0.8)	0	1 (0.9)	0
Diarrhea	5 (3.8)	0	2 (1.7)	0	2 (1.8)	0
Dizziness	5 (3.8)	0	0	2 (1.7)	0	0
Tremor	4 (3.1)	0	1 (0.8)	0	0	0
Infection	1 (0.8)	1 (0.8)	1 (0.8)	1 (0.8)	1 (0.9)	2 (1.8)
Insomnia	10 (7.7)	0	4 (3.4)	1 (0.8)	2 (1.8)	3 (2.8)
Placebo: N=	120	120	114	114	107	107
Total ¹	37 (30.8)	13 (10.8)	33 (28.9)	18 (15.8)	30 (28.0)	15 (14.0)
Nausea	2 (1.7)	0	0	0	0	0
Asthenia	3 (2.5)	1 (0.8)	0	0	1 (0.9)	0
Headache	9 (7.5)	4 (3.3)	10 (8.8)	3 (2.6)	6 (5.6)	2 (1.9)
Libido Decreased	4 (3.3)	0	3 (2.6)	0	1 (0.9)	0
Sweating	0	0	1 (0.9)	0	0	0
Diarrhea	0	0	0	0	0	1 (0.9)
Dizziness	1 (0.8)	0	0	1 (0.9)	1 (0.9)	0
Tremor	0	0	0	0	0	0
Infection	2 (1.7)	0	1 (0.9)	1 (0.9)	5 (4.7)	2 (1.9)
Insomnia	0	0	1 (0.9)	1 (0.9)	2 (1.9)	0

Data Source: Section 15, [Supplementary Table 15.8](#).

TC = Treatment cycle; Med = Medication; N = Number of subjects who took at least one dose of study medication in the specified interval, and the AE percentages are based on this number.

Note: All AEs for paroxetine CR treatment groups with an incidence of $\geq 5\%$ and at least twice the incidence for placebo in the same treatment period are in bold.

1. Total is the total number of subjects who reported one or more AEs during the specified interval.

9.2.7. Follow-up Emergent Adverse Events

Summaries of all AEs emergent during the follow-up phase are provided in Section 15, [Table 15.6](#) (by body system and preferred term) and Section 15, [Table 15.7](#) (by preferred term in descending order for those events occurring in 1% or more of the population).

Table 52 presents a summary of the most frequently reported ($\geq 1\%$ in any treatment group) AEs occurring during the follow-up phase in descending order of frequency. The overall incidence of AEs emergent during the follow-up phase was low.

AEs during the follow-up phase were more prevalent in the paroxetine CR groups than the placebo group [19/116 (16.4%) subjects in the paroxetine CR 25mg group, 29/129 (22.5%) subjects in the paroxetine CR 12.5mg group and 15/120 (12.5%) subjects in the placebo group]. The most frequently reported AEs during the follow-up phase were infection, for subjects randomized to paroxetine CR 25mg, headache, for subjects randomized to paroxetine CR 12.5mg, and anemia for subjects randomized to placebo.

Table 52 Number (%) of Subjects with the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Adverse Events Occurring During the Follow-up Phase (ITT Population)

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 129 ¹	Placebo N = 120
Total Subjects with at least one AE	19 (16.4)	29 (22.5)	15 (12.5)
Infection	3 (2.6)	2 (1.6)	2 (1.7)
Asthenia	2 (1.7)	1 (0.8)	0
Headache	2 (1.7)	5 (3.9)	2 (1.7)
Anemia	1 (0.9)	0	3 (2.5)
Depression	1 (0.9)	3 (2.3)	1 (0.8)
Insomnia	1 (0.9)	2 (1.6)	0
Respiratory Disorder	1 (0.9)	2 (1.6)	1 (0.8)
Breast Pain	0	2 (1.6)	0
Hypertension	0	2 (1.6)	0
Palpitation	0	2 (1.6)	0
Trauma	0	2 (1.6)	0

Data Source: Section 15, [Table 15.6](#) and [Table 15.7](#).

1. One subject in the paroxetine CR 12.5mg treatment group did not satisfy the criteria to be included in the follow-up denominator (see Section 5.8.6.4).

9.2.8. Follow-up Emergent Adverse Events by Severity

Summaries of AEs emergent during the follow-up phase by severity are presented in Section 15, [Table 15.12](#) (by body system and preferred term) and Section 15, [Table 15.13](#) (by preferred term in descending order for those events occurring in 1% or more of the population). In addition, a summary of AEs occurring during the follow-up phase by maximum severity is presented by body system and preferred term in Section 15, [Table 15.23](#).

The majority of emergent follow-up phase AEs, regardless of treatment group, were rated by investigators as mild or moderate. Table 53 presents a summary of severe AEs with an incidence of $\geq 1\%$ occurring during the follow-up phase. The most frequently reported severe AE for subjects who had received paroxetine CR 25mg was infection [2/116 (1.7%)], and for paroxetine CR 12.5mg, depression [2/129 (1.6%)]. No severe AEs with an incidence of $\geq 1\%$ were reported for subjects who had received placebo.

Table 53 **Number (%) of Subjects with the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Severe Adverse Events Occurring During the Follow-up Phase (ITT Population)**

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 129 ¹	Placebo N = 120
Total Subjects with at least one severe AE	6 (5.2)	7 (5.4)	3 (2.5)
Infection	2 (1.7)	1 (0.8)	1 (0.8)
Depression	0	2 (1.6)	0

Data Source: Section 15, [Table 15.12](#) and [Table 15.13](#).

1. One subject in the paroxetine CR 12.5mg treatment group did not satisfy the criteria to be included in the follow-up denominator (see Section 5.8.6.4).

9.2.9. Follow-up Emergent Adverse Events by Relationship to Treatment

Summaries of AEs emergent during the follow-up phase that were judged by the investigator to be related or possibly related to double-blind study medication are presented in Section 15, [Table 15.16](#) (by body system and preferred term) and Section 15, [Table 15.17](#) (by preferred term in descending order for those events occurring in 1% or more of the population).

The majority of AEs occurring during the follow-up phase were considered unrelated to study medication. [Table 54](#) presents a summary of the most frequently reported ($\geq 1\%$ in any treatment group) AEs occurring during the follow-up phase that were judged to be related or possibly related to study medication in descending order of frequency. No AEs with an incidence of $\geq 1\%$ were reported for subjects receiving paroxetine CR 25mg and placebo. The most frequently reported AEs for subjects receiving paroxetine CR 12.5mg were headache [3/129 (2.3%)] and palpitation [2/129 (1.6%)].

Table 54 **Number (%) of Subjects with the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Related or Possibly Related Adverse Events Occurring During the Follow-up Phase (ITT Population)**

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 129 ¹	Placebo N = 120
Total Subjects with at least one related or possibly related AE	5 (4.3)	8 (6.2)	1 (0.8)
Headache	0	3 (2.3)	0
Palpitation	0	2 (1.6)	0

Data Source: Section 15, [Table 15.16](#) and [Table 15.17](#).

1. One subject in the paroxetine CR 12.5mg treatment group did not satisfy the criteria to be included in the follow-up denominator (see Section 5.8.6.4).

9.3. Serious Adverse Events

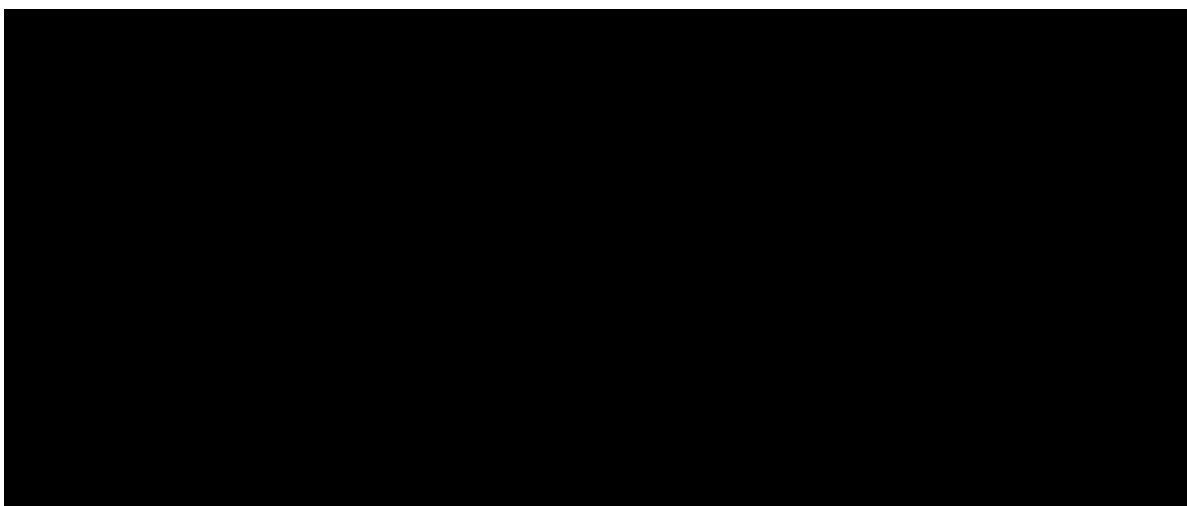
9.3.1. Fatal Events

No deaths occurred during the course of this study, including the 30-day period following the last dose of study medication.

9.3.2. Non-Fatal Events

Summaries of serious non-fatal AEs occurring at any time during the study are presented in Section 15, [Table 15.8](#) (by body system and preferred term) and Section 15, [Table 15.9](#) (by preferred term in descending order for those events occurring in 1% or more of the population).

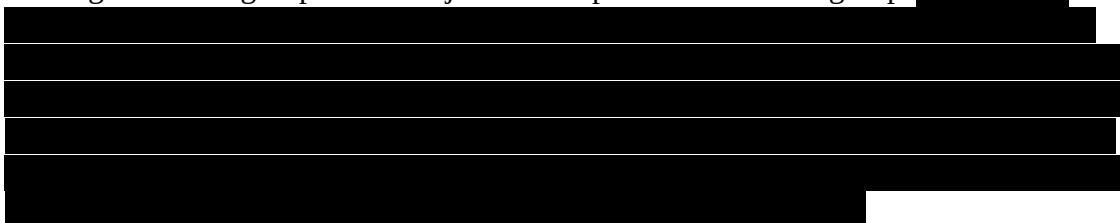
A listing of subjects with non-fatal SAEs is provided in [Table 55](#).

Table 55 Listing of Subjects with Non-fatal Serious Adverse Events


NA = Not applicable; subject never received randomized study medication.

1. Days relative to start of randomized study medication (days relative to stop of randomized study medication).

Seven subjects reported treatment or follow-up phase emergent non-fatal SAEs, 2 subjects in the paroxetine CR 25mg treatment group, 3 subjects in the paroxetine CR 12.5mg treatment group and 2 subjects in the placebo treatment group.



Treatment with single-blind study medication was stopped due to this event, and the patient was not randomized to receive double-blind study medication.

Full narratives for subjects with non-fatal SAEs are provided in Section 15, [Table 15.36](#). There may be minor discrepancies in the details of the SAEs included in the clinical narratives compared with the safety tabulations, because the data come from two different databases and have been collected at different points in time. However, it is considered that these differences, if any, are minor in nature and do not change the overall clinical significance or understanding of the SAEs. The Operating Companies Experience Accession and Notification System (OCEANS) was used for the reporting of SAEs.

9.4. Adverse Events Leading to Withdrawal from the Study

[Table 56](#) presents a summary of the most frequently reported ($\geq 1\%$ in any treatment group) AEs with an action of drug stopped which led to withdrawal from the study in descending order of frequency.

A total of 34/366 (9.3%) subjects withdrew from the study because of an AE. The number of subjects withdrawn because of an AE was higher in the paroxetine CR 25mg group [16/116 (13.8%) subjects] and paroxetine CR 12.5mg group [13/130 (10.0%)] compared to the placebo group [5/120 (4.2%) subjects] (Section 15, [Table 15.18](#)). Narratives for subjects with AEs leading to discontinuation are provided in Section 15, [Table 15.37](#).

The most frequently occurring AE which led to withdrawal from the study for subjects receiving paroxetine CR 25mg was nausea [4/116 (3.4%)], and for paroxetine CR 12.5mg-treated subjects was insomnia [4/130 (3.1%)]. For subjects receiving placebo, no AE leading to withdrawal from the study occurred in more than one subject.

Table 56 Summary of the most Frequently Reported ($\geq 1\%$ in Any Treatment Group) Adverse Events by Subjects Who Withdrew from the Study Due to an Adverse Event. Number (%) of Subjects (ITT Population)

AE Preferred Term	Treatment Group		
	Parox CR 25mg N = 116	Parox CR 12.5mg N = 130	Placebo N = 120
Total Subjects with at least one AE	16 (13.8)	13 (10.0)	5 (4.2)
Nausea	4 (3.4)	3 (2.3)	0
Dizziness	3 (2.6)	1 (0.8)	0
Insomnia	2 (1.7)	4 (3.1)	0
Tremor	2 (1.7)	1 (0.8)	0
Asthenia	1 (0.9)	2 (1.5)	0

Data Source: Section 15, [Table 15.18](#) and [Table 15.19](#).

9.5. Pregnancies

No subject had a positive serum beta-HCG pregnancy test during the treatment or follow-up phases of the study (Section 15, [Table 15.31](#)). [REDACTED]

9.6. Clinical Laboratory Evaluations

9.6.1. Laboratory Values Over Time

Section 15, [Table 15.33](#) presents summary statistics for baseline and change from baseline to “endpoint” (last available value on treatment or during the follow-up i.e., within 14 days of the last study dose) for each of the laboratory parameters monitored during the study. Baseline mean laboratory values were comparable across treatment groups. Changes from baseline to endpoint were generally small and of no clinical relevance, and were well balanced across the treatment groups.

Baseline, endpoint and follow-up laboratory values were categorized as high and of clinical concern, above normal range, within normal range, below normal range and below normal range and of clinical concern. Section 15, [Table 15.30](#) presents the number and percentage of subjects with transitions in laboratory values per parameter (i.e., subjects whose laboratory value changed category) from baseline to endpoint. The transitions were generally comparable between treatment groups.

9.6.2. Laboratory Abnormalities of Potential Clinical Concern

The sponsor-defined criteria for laboratory values of clinical concern are described in Section 5.8.6.5 and shown in Section 15, [Table 15.29](#). Individual case narratives for subjects with laboratory values of potential clinical concern are provided in Section 15, [Table 15.38](#).

No subjects had one or more laboratory values meeting the sponsor's predefined values of potential clinical concern during the treatment phase. Eight subjects had one or more laboratory values meeting the sponsor's predefined values of potential clinical concern during the follow-up phase (Section 15, [Table 15.27](#)). One subject was in the paroxetine CR 25mg treatment group (eosinophils, high), 4 in the paroxetine CR 12.5mg treatment group (eosinophils, high in 2 subjects; white blood cell count, low in 2 subjects) and 3 in the placebo treated group (hematocrit, low; ALAT, high; eosinophils, high). Note: Although Section 15, [Table 15.27](#) does not differentiate between treatment and follow-up phases, subjects' visit dates were compared with their medication stop dates to obtain this by visit information.

[REDACTED]

[REDACTED] This was moderate liver function test abnormal which was considered by the investigator to be probably unrelated to study medication. The value had returned to within the normal range at the post follow-up visit.

9.7. Vital Signs

9.7.1. Vital Signs Over Time

[Table 57](#) presents a summary of mean blood pressure (diastolic and systolic), and pulse rate at baseline and change from baseline by visit. The mean baseline values for vital sign parameters were comparable between treatment groups, and mean changes from baseline were small and generally comparable between treatment groups.

Table 57 Summary Statistics for Baseline and Change from Baseline for Vital Signs by Visit (ITT Population)

Vital Signs Parameter ¹	Treatment Group								
	Parox CR 25mg			Parox CR 12.5mg			Placebo		
	n	Mean	s.d.	n	Mean	s.d.	n	Mean	s.d.
Diastolic BP (mm Hg)									
Baseline	116	75.8	9.47	130	74.2	9.90	120	74.0	9.17
Treatment Cycle 1	97	-0.7	7.18	118	0.0	7.10	115	0.5	8.26
Treatment Cycle 2	92	-1.3	8.22	105	-1.5	7.91	98	1.3	8.78
Treatment Cycle 3	3	4.7	9.87	3	-1.7	7.64	5	0.4	8.96
Follow-up	102	-1.1	9.12	112	-0.2	8.15	109	-0.2	9.57
Endpoint	112	-1.1	9.11	124	-0.3	8.29	118	0.2	9.52
Systolic BP (mm Hg)									
Baseline	116	118.0	13.83	130	116.4	13.37	120	117.3	11.60
Treatment Cycle 1	97	-0.9	10.69	118	0.0	10.43	115	-0.2	9.59
Treatment Cycle 2	92	-1.9	12.47	105	-1.2	13.12	98	-0.8	9.92
Treatment Cycle 3	3	3.7	6.03	3	-6.3	7.09	5	-0.6	13.18
Follow-up	102	-2.3	12.29	112	1.4	10.78	109	-1.7	10.05
Endpoint	112	-2.3	12.30	124	0.5	10.99	118	-1.1	10.24
Pulse Rate (bpm)									
Baseline	116	70.7	9.22	130	70.4	8.93	120	69.0	8.88
Treatment Cycle 1	97	-1.3	7.94	118	-0.3	7.80	115	1.7	8.86
Treatment Cycle 2	92	-1.1	8.32	105	-0.6	7.38	98	0.7	7.75
Treatment Cycle 3	3	7.0	14.11	3	-2.3	2.08	5	-1.2	9.55
Follow-up	102	0.1	8.96	112	-0.1	9.08	109	1.4	8.48
Endpoint	112	0.5	8.82	124	-0.2	8.82	118	1.0	8.52

Data Source: Section 15, [Table 15.24](#).

Endpoint was the last reading during the randomized treatment phase or in the 14 day follow-up.

1. All vital signs parameters were taken in the sitting position.

Baseline, endpoint and follow-up vital signs values were categorized as above normal range, below normal range, within normal range, significant increase from baseline, and significant decrease from baseline. Section 15, [Table 15.26](#) presents the number and percentage of subjects with transitions in vital sign values (i.e., subjects whose vital sign value changed category) from baseline to endpoint. The number of transitions was small and transitions were generally comparable between treatment groups.

9.7.2. Vital Signs Abnormalities of Potential Clinical Concern

Two subjects had one or more vital signs measurement meeting the sponsor's predetermined potential clinical concern criteria (Section 5.8.6.5) during the study (Section 15, [Table 15.25](#)). [REDACTED]

[REDACTED] All later sitting blood pressure values for these subjects were within the normal range.

9.8. Drug-Drug Interactions

A potential for concomitant medication-paroxetine CR interaction was explored by examining the treatment emergent AEs reported in subjects who were taking selected concomitant medication compared to the AEs reported for subjects who were not taking concomitant medications (see [Table 58](#)). The comparison was limited to the following concomitant medications: acetylsalicylic acid, caffeine, ibuprofen, loratadine and paracetamol, which were the most frequently used medications excluding vitamins. The overall incidence of AEs in subjects taking concomitant medications was similar or slightly higher than the incidence among subjects not taking concomitant medication for all three treatment groups. There were a few examples where an AE was noticeably more prevalent in subjects receiving a concomitant medication. In some cases this was true for all three treatment groups, and in some cases it was likely that the AE had been treated with the concomitant medication. Although the number of subjects taking certain medications was very small (the number of subjects in three of the on concomitant medication groups ranged from 1-10), there does not appear to be any clinically significant association between incidence of AEs and the use of concomitant medications.

Table 58 Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in the Either Paroxetine CR Group) by Whether they were Receiving/Not Receiving Commonly Administered Concomitant Medications (ITT Population)

AE Preferred Term	Paroxetine CR 25mg N = 116		Treatment Group Paroxetine CR 12.5mg N = 130		Placebo N = 120	
	Yes	No	Yes	No	Yes	No
Acetylsalicylic Acid						
Total subjects receiving/not receiving conmed: N	3	113	10	120	9	111
Total subjects with a least 1 AE	2 (66.7)	87 (77.0)	7 (70.0)	81 (67.5)	8 (88.9)	60 (54.1)
Allergic Reaction	0	1 (0.9)	2 (20.0)	0	0	3 (2.7)
Asthenia	0	22 (19.5)	0	16 (13.3)	0	5 (4.5)
Headache	0	18 (15.9)	3 (30.0)	13 (10.8)	4 (44.4)	13 (11.7)
Trauma	0	2 (1.8)	1 (10.0)	2 (1.7)	0	4 (3.6)
Migraine	0	0	1 (10.0)	0	1 (11.1)	2 (1.8)
Myocardial Infarction	0	0	1 (10.0)	0	0	0
Tachycardia	1 (33.3)	0	0	0	0	0
Decreased Appetite	0	4 (3.5)	1 (10.0)	0	0	0
Dry Mouth	0	3 (2.7)	1 (10.0)	2 (1.7)	0	1 (0.9)
Dyspepsia	1 (33.3)	2 (1.8)	0	2 (1.7)	0	2 (1.8)
Nausea	0	27 (23.9)	2 (20.0)	14 (11.7)	0	2 (1.8)
Tooth Disorder	1 (33.3)	0	0	1 (0.8)	0	2 (1.8)
Myalgia	1 (33.3)	0	0	2 (1.7)	0	3 (2.7)
Dizziness	0	8 (7.1)	1 (10.0)	6 (5.0)	0	3 (2.7)
Insomnia	0	4 (3.5)	2 (20.0)	11 (9.2)	0	3 (2.7)
Libido Decreased	1 (33.3)	14 (12.4)	0	7 (5.8)	1 (11.1)	6 (5.4)
Nervousness	0	1 (0.9)	1 (10.0)	5 (4.2)	0	2 (1.8)
Tremor	0	7 (6.2)	2 (20.0)	2 (1.7)	0	0
Respiratory Disorder	0	5 (4.4)	2 (20.0)	7 (5.8)	4 (44.4)	9 (8.1)
Maculopapular Rash	0	0	1 (10.0)	0	0	0
Ear Disorder	0	0	1 (10.0)	0	0	0
Dysmenorrhea	1 (33.3)	3 (2.7)	0	4 (3.3)	2 (22.2)	2 (1.8)
Menstrual Disorder	1 (33.3)	1 (0.9)	0	1 (0.8)	0	0
Caffeine						
Total subjects receiving/not receiving conmed: N	2	114	5	125	5	115
Total subjects with a least 1 AE	2 (100.0)	87 (76.3)	2 (40.0)	86 (68.8)	5 (100.0)	63 (54.8)
Allergic Reaction	0	1 (0.9)	1 (20.0)	1 (0.8)	0	3 (2.6)
Asthenia	0	22 (19.3)	0	16 (12.8)	0	5 (4.3)
Headache	0	18 (15.8)	1 (20.0)	15 (12.0)	2 (40.0)	15 (13.0)
Migraine	0	0	1 (20.0)	0	0	3 (2.6)
Nausea	1 (50.0)	26 (22.8)	2 (40.0)	14 (11.2)	0	2 (1.7)
Tooth Disorder	1 (50.0)	0	0	1 (0.8)	0	2 (1.7)
Myalgia	1 (50.0)	0	0	2 (1.6)	0	3 (2.6)
Dizziness	0	8 (7.0)	1 (20.0)	6 (4.8)	0	3 (2.6)
Insomnia	0	4 (3.5)	0	13 (10.4)	0	3 (2.6)
Libido Decreased	1 (50.0)	14 (12.3)	0	7 (5.6)	1 (20.0)	6 (5.2)
Dysmenorrhea	1 (50.0)	3 (2.6)	0	4 (3.2)	2 (40.0)	2 (1.7)

Continued

Table 58 **Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in the Either Paroxetine CR Group) by Whether they were Receiving/Not Receiving Commonly Administered Concomitant Medications (ITT Population) (Continued)**

AE Preferred Term	Paroxetine CR 25mg N = 116		Treatment Group Paroxetine CR 12.5mg N = 130		Placebo N = 120	
	Yes	No	Yes	No	Yes	No
Ibuprofen						
Total subjects receiving/not receiving conmed: N	26	90	33	97	24	96
Total subjects with a least 1 AE	26 (100.0)	63 (70.0)	29 (87.9)	59 (60.8)	22 (91.7)	46 (47.9)
Asthenia	9 (34.6)	13 (14.4)	7 (21.2)	9 (9.3)	0	5 (5.2)
Headache	9 (34.6)	9 (10.0)	6 (18.2)	10 (10.3)	7 (29.2)	10 (10.4)
Infection	3 (11.5)	7 (7.8)	2 (6.1)	3 (3.1)	4 (16.7)	4 (4.2)
Diarrhea	4 (15.4)	4 (4.4)	0	7 (7.2)	0	0
Nausea	7 (26.9)	20 (22.2)	5 (15.2)	11 (11.3)	0	2 (2.1)
Insomnia	2 (7.7)	2 (2.2)	4 (12.1)	9 (9.3)	0	3 (3.1)
Libido Decreased	4 (15.4)	11 (12.2)	3 (9.1)	4 (4.1)	2 (8.3)	5 (5.2)
Pharyngitis	3 (11.5)	0	0	0	1 (4.2)	4 (4.2)
Dysmenorrhea	3 (11.5)	1 (1.1)	3 (9.1)	1 (1.0)	2 (8.3)	2 (2.1)
Loratadine						
Total subjects receiving/not receiving conmed: N	6	110	3	127	1	119
Total subjects with a least 1 AE	5 (83.3)	84 (76.4)	3 (100.0)	85 (66.9)	1 (100.0)	67 (56.3)
Allergic Reaction	0	1 (0.9)	1 (33.3)	1 (0.8)	0	3 (2.5)
Asthenia	4 (66.7)	18 (16.4)	0	16 (12.6)	0	5 (4.2)
Fever	1 (16.7)	1 (0.9)	0	0	0	1 (0.8)
Headache	1 (16.7)	17 (15.5)	1 (33.3)	15 (11.8)	0	17 (14.3)
Infection	1 (16.7)	9 (8.2)	0	5 (3.9)	0	8 (6.7)
Pain	1 (16.7)	1 (0.9)	0	2 (1.6)	0	2 (1.7)
Trauma	0	2 (1.8)	1 (33.3)	2 (1.6)	0	4 (3.4)
Decreased Appetite	1 (16.7)	3 (2.7)	0	1 (0.8)	0	0
Diarrhea	2 (33.3)	6 (5.5)	1 (33.3)	6 (4.7)	0	0
Increased Appetite	1 (16.7)	0	0	0	0	1 (0.8)
Nausea	3 (50.0)	24 (21.8)	0	16 (12.6)	0	2 (1.7)
Alcohol Abuse	1 (16.7)	0	0	0	0	0
Hypesthesia	1 (16.7)	1 (0.9)	0	0	0	0
Insomnia	0	4 (3.6)	0	13 (10.2)	0	3 (2.5)
Libido Decreased	1 (16.7)	14 (12.7)	0	7 (5.5)	0	7 (5.9)
Tremor	2 (33.3)	5 (4.5)	0	4 (3.1)	0	0
Bronchitis	1 (16.7)	0	0	3 (2.4)	0	0
Pharyngitis	2 (33.3)	1 (0.9)	0	0	0	5 (4.2)
Respiratory Disorder	1 (16.7)	4 (3.6)	0	9 (7.1)	0	13 (10.9)
Sinusitis	0	3 (2.7)	2 (66.7)	5 (3.9)	0	2 (1.7)
Sweating	1 (16.7)	9 (8.2)	0	4 (3.1)	0	1 (0.8)
Ear Disorder	0	0	1 (33.3)	0	0	0
Otitis Media	0	0	1 (33.3)	0	0	2 (1.7)
Female Genital Disorders	1 (16.7)	2 (1.8)	0	2 (1.6)	0	0

Continued

Table 58 Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in the Either Paroxetine CR Group) by Whether they were Receiving/Not Receiving Commonly Administered Concomitant Medications (ITT Population) (Continued)

AE Preferred Term	Paroxetine CR 25mg N = 116		Treatment Group Paroxetine CR 12.5mg N = 130		Placebo N = 120	
	Yes	No	Yes	No	Yes	No
Paracetamol						
Total subjects receiving/not receiving conmed: N	30	86	26	104	40	80
Total subjects with a least 1 AE	28 (93.3)	61 (70.9)	24 (92.3)	64 (61.5)	30 (75.0)	38 (47.5)
Asthenia	9 (30.0)	13 (15.1)	5 (19.2)	11 (10.6)	1 (2.5)	4 (5.0)
Headache	9 (30.0)	9 (10.5)	7 (26.9)	9 (8.7)	13 (32.5)	4 (5.0)
Infection	5 (16.7)	5 (5.8)	2 (7.7)	3 (2.9)	5 (12.5)	3 (3.8)
Diarrhea	5 (16.7)	3 (3.5)	3 (11.5)	4 (3.8)	0	0
Nausea	11 (36.7)	16 (18.6)	8 (30.8)	8 (7.7)	1 (2.5)	1 (1.3)
Dizziness	2 (6.7)	6 (7.0)	3 (11.5)	4 (3.8)	2 (5.0)	1 (1.3)
Insomnia	2 (6.7)	2 (2.3)	1 (3.8)	12 (11.5)	3 (7.5)	0
Libido Decreased	7 (23.3)	8 (9.3)	1 (3.8)	6 (5.8)	4 (10.0)	3 (3.8)
Tremor	3 (10.0)	4 (4.7)	1 (3.8)	3 (2.9)	0	0
Sweating	4 (13.3)	6 (7.0)	1 (3.8)	3 (2.9)	1 (2.5)	0
Dysmenorrhea	4 (13.3)	0	2 (7.7)	2 (1.9)	2 (5.0)	2 (2.5)

Data Source: Section 15, [Supplementary Table 15.2](#).

Conmed = Concomitant medication.

9.9. Drug-Disease Interactions

A potential for disease-paroxetine CR interaction was explored by examining the treatment emergent AEs reported in subjects who had a particular active medical condition on entry to the study compared to the AEs reported for subjects who did not have this condition (see [Table 59](#)). The comparison was limited to the following conditions: allergy NEC, female genital disorder other, headache, migraine and allergic rhinitis, which were the most frequent active conditions on entry to the study excluding contraceptive management. In most cases, the incidence of AEs in subjects with one of the active medical conditions was similar or higher than the incidence among subjects without that condition for all three treatment groups. The number of subjects in three of the active condition groups was small (4-16 subjects), making it difficult to draw any firm conclusions for individual AEs, but overall, there does not appear to be any clinically significant association between incidence of AEs and the selected medical conditions.

Table 59 **Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in Either Paroxetine Group) by Selected Active Medical History Conditions (ITT Population)**

AE Preferred Term	Paroxetine CR 25mg N = 116		Treatment Group Paroxetine CR 12.5mg N = 130		Placebo N = 120	
	Yes	No	Yes	No	Yes	No
Allergy, NEC						
Total subjects with/without condition: N	4	112	6	124	5	115
Total subjects with a least 1 AE	2 (50.0)	87 (77.7)	6 (100.0)	82 (66.1)	2 (40.0)	66 (57.4)
Asthenia	0	22 (19.6)	1 (16.7)	15 (12.1)	0	5 (4.3)
Flu Syndrome	0	1 (0.9)	1 (16.7)	0	0	0
Headache	1 (25.0)	17 (15.2)	2 (33.3)	14 (11.3)	0	17 (14.8)
Neoplasm	0	1 (0.9)	1 (16.7)	0	0	0
Pain	0	2 (1.8)	1 (16.7)	1 (0.8)	1 (20.0)	1 (0.9)
Hypertension	0	0	1 (16.7)	0	0	0
Constipation	0	3 (2.7)	1 (16.7)	0	0	1 (0.9)
Diarrhea	1 (25.0)	7 (6.3)	0	7 (5.6)	0	0
Dysphagia	0	0	1 (16.7)	1 (0.8)	0	0
Nausea	0	27 (24.1)	1 (16.7)	15 (12.1)	0	2 (1.7)
Generalized Edema	0	1 (0.9)	1 (16.7)	1 (0.8)	0	1 (0.9)
Dizziness	0	8 (7.1)	1 (16.7)	6 (4.8)	0	3 (2.6)
Insomnia	0	4 (3.6)	0	13 (10.5)	0	3 (2.6)
Libido Decreased	0	15 (13.4)	0	7 (5.6)	0	7 (6.1)
Somnolence	1 (25.0)	4 (3.6)	0	3 (2.4)	0	1 (0.9)
Respiratory Disorder	0	5 (4.5)	2 (33.3)	7 (5.6)	0	13 (11.3)
Sweating	0	10 (8.9)	1 (16.7)	3 (2.4)	0	1 (0.9)
Taste Perversion	0	0	1 (16.7)	0	0	0
Female Genital Disorder, Other						
Total subjects with/without condition: N	28	88	34	96	25	95
Total subjects with a least 1 AE	23 (82.1)	66 (75.0)	28 (82.4)	60 (62.5)	18 (72.0)	50 (52.6)
Asthenia	8 (28.6)	14 (15.9)	7 (20.6)	9 (9.4)	0	5 (5.3)
Headache	5 (17.9)	13 (14.8)	7 (20.6)	9 (9.4)	3 (12.0)	14 (14.7)
Infection	3 (10.7)	7 (8.0)	2 (5.9)	3 (3.1)	3 (12.0)	5 (5.3)
Diarrhea	4 (14.3)	4 (4.5)	2 (5.9)	5 (5.2)	0	0
Nausea	11 (39.3)	16 (18.2)	4 (11.8)	12 (12.5)	0	2 (2.1)
Dizziness	3 (10.7)	5 (5.7)	2 (5.9)	5 (5.2)	3 (12.0)	0
Insomnia	2 (7.1)	2 (2.3)	2 (5.9)	11 (11.5)	1 (4.0)	2 (2.1)
Libido Decreased	5 (17.9)	10 (11.4)	2 (5.9)	5 (5.2)	3 (12.0)	4 (4.2)
Tremor	3 (10.7)	4 (4.5)	1 (2.9)	3 (3.1)	0	0
Sweating	3 (10.7)	7 (8.0)	0	4 (4.2)	0	1 (1.1)

Continued

Table 59 **Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in Either Paroxetine Group) by Selected Active Medical History Conditions (ITT Population) (Continued)**

AE Preferred Term	Paroxetine CR 25mg N = 116		Treatment Group Paroxetine CR 12.5mg N = 130		Placebo N = 120	
	Yes	No	Yes	No	Yes	No
Headache						
Total subjects with/without condition: N	40	76	39	91	36	84
Total subjects with a least 1 AE	34 (85.0)	55 (72.4)	27 (69.2)	61 (67.0)	25 (69.4)	43 (51.2)
Asthenia	10 (25.0)	12 (15.8)	3 (7.7)	13 (14.3)	1 (2.8)	4 (4.8)
Headache	6 (15.0)	12 (15.8)	4 (10.3)	12 (13.2)	2 (5.6)	15 (17.9)
Infection	1 (2.5)	9 (11.8)	4 (10.3)	1 (1.1)	1 (2.8)	7 (8.3)
Diarrhea	5 (12.5)	3 (3.9)	3 (7.7)	4 (4.4)	0	0
Nausea	11 (27.5)	16 (21.1)	6 (15.4)	10 (11.0)	0	2 (2.4)
Dizziness	3 (7.5)	5 (6.6)	4 (10.3)	3 (3.3)	3 (8.3)	0
Insomnia	2 (5.0)	2 (2.6)	2 (5.1)	11 (12.1)	1 (2.8)	2 (2.4)
Libido Decreased	5 (12.5)	10 (13.2)	1 (2.6)	6 (6.6)	2 (5.6)	5 (6.0)
Tremor	5 (12.5)	2 (2.6)	1 (2.6)	3 (3.3)	0	0
Sweating	2 (5.0)	8 (10.5)	1 (2.6)	3 (3.3)	0	1 (1.2)
Migraine						
Total subjects with/without condition: N	12	104	9	121	10	110
Total subjects with a least 1 AE	9 (75.0)	80 (76.9)	5 (55.6)	83 (68.6)	5 (50.0)	63 (57.3)
Allergic Reaction	0	1 (1.0)	1 (11.1)	1 (0.8)	0	3 (2.7)
Asthenia	1 (8.3)	21 (20.2)	1 (11.1)	15 (12.4)	0	5 (4.5)
Headache	0	18 (17.3)	2 (22.2)	14 (11.6)	2 (20.0)	15 (13.6)
Migraine	0	0	1 (11.1)	0	1 (10.0)	2 (1.8)
Dry Mouth	2 (16.7)	1 (1.0)	0	3 (2.5)	0	1 (0.9)
Dysphagia	0	0	1 (11.1)	1 (0.8)	0	0
Nausea	5 (41.7)	22 (21.2)	1 (11.1)	15 (12.4)	0	2 (1.8)
Concentration Impaired	0	1 (1.0)	1 (11.1)	1 (0.8)	0	0
Dizziness	1 (8.3)	7 (6.7)	2 (22.2)	5 (4.1)	1 (10.0)	2 (1.8)
Insomnia	0	4 (3.8)	1 (11.1)	12 (9.9)	0	3 (2.7)
Libido Decreased	1 (8.3)	14 (13.5)	0	7 (5.8)	2 (20.0)	5 (4.5)
Somnolence	1 (8.3)	4 (3.8)	1 (11.1)	2 (1.7)	0	1 (0.9)
Tremor	0	7 (6.7)	1 (11.1)	3 (2.5)	0	0
Amenorrhea	0	0	1 (11.1)	0	0	1 (0.9)
Female Genital Disorders	0	3 (2.9)	1 (11.1)	1 (0.8)	0	0

Continued

Table 59 Number (%) of Subjects with Frequently Occurring Treatment Emergent AEs ($\geq 10\%$ in Either Paroxetine Group) by Selected Active Medical History Conditions (ITT Population) (Continued)

AE Preferred Term	Paroxetine CR 25mg N = 116		Treatment Group Paroxetine CR 12.5mg N = 130		Placebo N = 120	
	Yes	No	Yes	No	Yes	No
Allergic Rhinitis						
Total subjects with/without condition: N	16	100	7	123	9	111
Total subjects with a least 1 AE	13 (81.3)	76 (76.0)	4 (57.1)	84 (68.3)	8 (88.9)	60 (54.1)
Allergic Reaction	1 (6.3)	0	1 (14.3)	1 (0.8)	1 (11.1)	2 (1.8)
Asthenia	5 (31.3)	17 (17.0)	0	16 (13.0)	0	5 (4.5)
Headache	2 (12.5)	16 (16.0)	1 (14.3)	15 (12.2)	2 (22.2)	15 (13.5)
Infection	2 (12.5)	8 (8.0)	0	5 (4.1)	0	8 (7.2)
Trauma	0	2 (2.0)	1 (14.3)	2 (1.6)	1 (11.1)	3 (2.7)
Decreased Appetite	2 (12.5)	2 (2.0)	0	1 (0.8)	0	0
Diarrhea	1 (6.3)	7 (7.0)	2 (28.6)	5 (4.1)	0	0
Flatulence	0	0	1 (14.3)	0	1 (11.1)	0
Nausea	7 (43.8)	20 (20.0)	0	16 (13.0)	0	2 (1.8)
Concentration Impaired	0	1 (1.0)	1 (14.3)	1 (0.8)	0	0
Insomnia	0	4 (4.0)	0	13 (10.6)	1 (11.1)	2 (1.8)
Libido Decreased	3 (18.8)	12 (12.0)	2 (28.6)	5 (4.1)	1 (11.1)	6 (5.4)
Somnolence	0	5 (5.0)	1 (14.3)	2 (1.6)	0	1 (0.9)
Tremor	2 (12.5)	5 (5.0)	0	4 (3.3)	0	0
Asthma	0	0	1 (14.3)	0	0	0
Yawn	0	0	1 (14.3)	1 (0.8)	0	0
Eczema	0	0	1 (14.3)	0	0	0
Ear Disorder	0	0	1 (14.3)	0	0	0
Female Genital Disorders	1 (6.3)	2 (2.0)	1 (14.3)	1 (0.8)	0	0

Data Source: Section 15, [Supplementary Table 15.3](#).

9.10. Comparative AE Summaries

9.10.1. Paroxetine CR Intermittent Versus Continuous Dosing in PMDD

For the treatment emergent AE comparison, data from four treatment regimens were used: intermittent paroxetine CR, consisting of combined data from the paroxetine CR 25mg and 12.5mg treatment groups from the present PMDD study; intermittent placebo, from the present PMDD study; continuous paroxetine CR, consisting of the combined paroxetine CR 25mg and 12.5mg treatment groups from PMDD studies 677, 688 and 689; continuous placebo, consisting of the combined data from PMDD studies 677, 688 and 689. In the same way, follow-up AE data was compared using these four treatment regimens.

A comparison of the most frequent ($\geq 5\%$ in either paroxetine treatment regimen) treatment emergent AEs for paroxetine CR in the treatment of PMDD using intermittent treatment and continuous dosing is shown in [Table 60](#). The relative incidences of AEs for intermittent treatment with paroxetine CR and placebo were similar, but slightly lower, than for continuous treatment. For each paroxetine treatment regimen the 5 most common

AEs are shown in bold. Four of the 5 most common AEs for paroxetine CR intermittent treatment are also common for continuous paroxetine CR treatment, and the incidences of these common AEs and the remaining AEs in Table 60 are, in most cases, similar for the two treatment regimens. The exceptions are somnolence and female genital disorders, where the relative incidence for continuous treatment was approximately 3 times that for intermittent treatment.

Table 60 **Comparative Summary of Treatment Emergent AEs for Paroxetine CR Intermittent and Continuous Dosing in PMDD. Number (%) of Subjects with Frequently Occurring AEs ($\geq 5\%$ in Either Paroxetine CR Group) (ITT Population)**

AE Preferred Term	Intermittent Dosing		Continuous Dosing ¹	
	Paroxetine CR N = 246	Placebo N = 120	Paroxetine CR N = 681	Placebo N = 349
Total Subjects with at least 1 AE	177 (72.0)	68 (56.7)	518 (76.1)	215 (61.6)
Nausea	43 (17.5)	2 (1.7)	118 (17.3)	23 (6.6)
Asthenia	38 (15.4)	5 (4.2)	118 (17.3)	20 (5.7)
Headache	34 (13.8)	17 (14.2)	103 (15.1)	42 (12.0)
Libido Decreased	22 (8.9)	7 (5.8)	78 (11.5)	17 (4.9)
Insomnia	17 (6.9)	3 (2.5)	54 (7.9)	7 (2.0)
Diarrhea	15 (6.1)	0	38 (5.6)	7 (2.0)
Dizziness	15 (6.1)	3 (2.5)	46 (6.8)	12 (3.4)
Infection	15 (6.1)	8 (6.7)	42 (6.2)	15 (4.3)
Respiratory Disorder	14 (5.7)	13 (10.8)	38 (5.6)	28 (8.0)
Sweating	14 (5.7)	1 (0.8)	45 (6.6)	3 (0.9)
Somnolence	8 (3.3)	1 (0.8)	62 (9.1)	6 (1.7)
Female Genital Disorders	5 (2.0)	0	53 (7.8)	4 (1.1)

Data Source: Section 15, [Supplementary Table 15.5](#).

Note: For each paroxetine treatment regimen the 5 most common AEs are shown in bold.

1. PMDD continuous treatment studies 677, 688 and 689.

Section 15, [Supplementary Table 15.7](#) details treatment emergent AEs which were unique to intermittent paroxetine CR treatment compared to continuous paroxetine CR treatment in patients with major depressive disorder, panic disorder and PMDD. There were 9 AEs, moniliasis, shock, myocardial infarction, pulmonary embolus, colitis, maculopapular rash, breast atrophy, leukorrhea and puncture site reaction, and all only occurred in one subject each.

A comparison of the most frequent ($\geq 1\%$ in either paroxetine treatment regime) follow-up phase emergent AEs for paroxetine CR in the treatment of PMDD following intermittent treatment and continuous dosing is shown in [Table 61](#). The overall incidence of follow-up AEs following intermittent treatment with paroxetine CR was slightly lower than following continuous paroxetine CR treatment. The incidences for the two placebo treatment groups were similar. For each paroxetine treatment regime the 3 most common AEs are shown in bold. Although the proportions are generally low, only one of the three most common AEs for paroxetine CR intermittent treatment is common for continuous paroxetine CR treatment (headache). The most notable exception was dizziness, which was experienced by 8% of continuous treatment paroxetine CR subjects and no intermittently treated subjects. However, there are a number of other AEs where the incidence for continuous paroxetine CR treatment is 3 or more times higher than for

intermittent treatment. Only one AE had a 3 or more times higher incidence for intermittent paroxetine CR treatment compared to continuous, this was depression.

Table 61 **Comparative Summary of Follow-up Phase Emergent AEs for Paroxetine CR Intermittent and Continuous Dosing in PMDD. Number (%) of Subjects with Frequently Occurring AEs ($\geq 1\%$ in Either Paroxetine CR Group) (ITT Population)**

AE Preferred Term	Intermittent Dosing		Continuous Dosing ¹	
	Paroxetine CR N = 245	Placebo N = 120	Paroxetine CR ² N = 289	Placebo N = 168
Total Subjects with at least 1 AE	48 (19.6)	15 (12.5)	72 (24.9)	21 (12.5)
Headache	7 (2.9)	2 (1.7)	9 (3.1)	5 (3.0)
Infection	5 (2.0)	2 (1.7)	5 (1.7)	0
Depression	4 (1.6)	1 (0.8)	1 (0.3)	0
Asthenia	3 (1.2)	0	5 (1.7)	3 (1.8)
Insomnia	3 (1.2)	0	2 (0.7)	1 (0.6)
Respiratory Disorder	3 (1.2)	1 (0.8)	2 (0.7)	2 (1.2)
Nausea	2 (0.8)	0	7 (2.4)	1 (0.6)
Emotional Lability	1 (0.4)	0	4 (1.4)	0
Menstrual Disorder	1 (0.4)	0	5 (1.7)	0
Vertigo	1 (0.4)	0	3 (1.0)	0
Anxiety	0	0	5 (1.7)	0
Diarrhea	0	1 (0.8)	3 (1.0)	0
Dizziness	0	0	23 (8.0)	0
Nervousness	0	0	7 (2.4)	0
Unintended Pregnancy	0	0	3 (1.0)	1 (0.6)

Data Source: Section 15, [Supplementary Table 15.6](#).

Note: For each paroxetine treatment regimen the 3 most common AEs are shown in bold. Four AEs are shown in bold for the paroxetine CR continuous treatment regimen because nausea and nervousness had the same incidence.

1. PMDD continuous treatment studies 677, 688 and 689.

9.11. Safety Conclusions

- For the ITT population, the range of exposure to double-blind study medication was 1 to 88 days with over 81% of subjects in each treatment group being exposed to at least 29 days of study medication.
- The safety results of this study indicate that paroxetine CR (25mg/day or 12.5mg/day) is generally well-tolerated when administered on an intermittent basis during the luteal phase of the menstrual cycle to female outpatients with PMDD according to DSM-IV criteria A to D, over a period of up to 3 menstrual cycles.
- Overall, 89/116 (76.7%) subjects in the paroxetine CR 25mg group and 88/130 (67.7%) subjects in the paroxetine CR 12.5mg group reported AEs during the treatment phase compared to 68/120 (56.7%) in the placebo group. Commonly reported treatment emergent AEs ($\geq 5\%$ in either paroxetine CR group), which occurred at an incidence at least twice that of placebo were nausea, asthenia, libido decreased, sweating, diarrhea, dizziness, tremor, insomnia and sinusitis. The majority of treatment emergent AEs in the paroxetine CR groups were rated as mild or moderate in severity. Overall, 69/116 (59.5%) subjects in the paroxetine CR 25mg group and 56/130 (43.1%) subjects in the paroxetine CR 12.5mg group reported AEs

judged related or possibly related to study medication compared to 25/120 (20.8%) in the placebo group.

- For the most frequently reported treatment emergent AEs for the paroxetine treatment groups ($\geq 12\%$ incidence for both paroxetine CR treatment groups), nausea, asthenia and headache, the time to first occurrence was generally during Days 1 to 7, although this was less marked for headache.
- The overall incidence of AEs occurring during the "on study medication" time windows for both of the paroxetine CR treatment groups was highest in the first treatment cycle (paroxetine CR 25mg: 61.2%; paroxetine CR 12.5mg: 43.8%), reducing to a range of 29 to 36% during the "on study medication" time windows associated with treatment cycles 2 and 3. After the first treatment cycle, the incidences of AEs for both paroxetine CR treatment groups during each half of the cycle were similar to those for placebo-treated subjects.
- Follow-up phase emergent AEs were less frequent overall, than those reported during the treatment phase and were more prevalent in the paroxetine CR groups than the placebo group.
- No deaths occurred during the treatment phase or follow-up phase. Seven subjects reported non-fatal serious AEs during the treatment or follow-up phases: 2 subjects in the paroxetine CR 25mg treatment group, anaphylactoid reaction and abortion; 3 subjects in the paroxetine CR 12.5mg treatment group, depression with emotional lability, pulmonary embolus, and emotional lability; 2 subjects in the placebo treatment group, trauma (2 subjects). One subject reported a non-fatal serious AE five days prior to receiving paroxetine CR 12.5mg, unintended pregnancy.
- The number of subjects withdrawn because of an AE was higher in the paroxetine CR 25mg [16/116 (13.8%) subjects] and 12.5mg groups [13/130 (10.0%) subjects] compared to the placebo group [5/120 (4.2%) subjects].
- Subject vital signs and laboratory data showed no clinically meaningful changes associated with the use of paroxetine CR in subjects with PMDD.
- An examination of the relationship between common concomitant medications or medical history on the incidence of AEs, did not suggest any clinically significant association.
- A comparison of AEs for subjects receiving intermittent paroxetine CR in the present study and subjects receiving continuous paroxetine CR for PMDD showed similarities in the overall incidence and general profile for treatment emergent AEs. However for follow-up AEs, the present study had a slightly lower overall incidence, and the incidence for some particular AEs (e.g., dizziness) was noticeably lower.

10. DISCUSSION AND CONCLUSIONS

10.1. Discussion

The results of this multicenter, randomized, double-blind, placebo-controlled, study indicate that intermittent dosing with paroxetine CR was generally well tolerated and provided effective benefit when administered to women with DSM-IV defined PMDD. The treatment effect of paroxetine CR 25mg and 12.5mg versus placebo was statistically significant for the primary efficacy variable and the majority of the secondary variables. The estimated differences for paroxetine CR 25mg were usually larger than those for paroxetine CR 12.5mg.

This study was well conducted and enrolled an appropriate population for assessment of efficacy and safety (i.e. women of child-bearing potential who were determined to have PMDD according to DSM-IV criteria A to D). The protocol defined a single primary outcome measure, change from baseline in mean luteal phase VAS-Mood score at the treatment cycle 3 LOCF endpoint, and a number of secondary efficacy measures which included further assessments of VAS-Mood response in addition to instruments which assessed changes in functional impairment. Appropriate statistical methods were used to analyze these efficacy variables. Primary inferences were based on the treatment cycle 3 LOCF endpoint. Robustness of the main analyses was assessed by additionally examining the treatment cycle 3 OC dataset.

A higher proportion of paroxetine CR treated subjects were withdrawn from the study compared with the placebo group [paroxetine CR 25mg: 29/116 (25.0%); paroxetine CR 12.5mg: 26/130 (20.0%); placebo: 19/120 (15.8%)]. The primary reason for early withdrawal in both of the paroxetine CR groups was “Adverse Event”, paroxetine CR 25mg: 16/116 (13.8%); paroxetine CR 12.5mg: 13/130 (10.0%). The primary reason for early withdrawal in the placebo group was “Lack of Efficacy”, 6/120 (5.0%).

For the primary endpoint, change from baseline in mean luteal phase VAS-Mood score at the treatment cycle 3 LOCF endpoint, a statistically significant difference was demonstrated in favor of paroxetine CR 25mg and 12.5mg versus placebo [paroxetine CR 25mg: adjusted mean difference = -10.79mm, 95% CI (-16.46, -5.12), $p < 0.001$; paroxetine CR 12.5mg: adjusted mean difference = -7.66mm, 95% CI (-13.25, -2.08), $p = 0.007$]. The results of the treatment cycle 3 OC analysis supported these results, with statistically significant differences in favor of the paroxetine CR treatment groups.

All of the secondary efficacy variables, including the Regulatory requested variable (VAS total score), showed differences in favor of both paroxetine CR treatments versus placebo at the treatment cycle 3 LOCF endpoint, and these differences were statistically significant for the majority of these variables, including the VAS total score. These secondary efficacy results were generally supported by the treatment cycle 3 OC analyses. The secondary efficacy variables included various assessments of VAS-Mood scores, VAS physical symptoms scores, VAS total score, all individual SDS item scores (as well as the total SDS score), and global responses of subjects to treatment according

to both investigator (CGI severity of illness, CGI global improvement, PMTS-O) and subject assessment (PGE).

Subjects also showed improvements during the study as measured by a number of Quality of Life assessments, EuroQol VAS, EQ-5D health profile and utility score, and WPAI. Results of the analysis for the change from baseline in EuroQol VAS at the treatment cycle 3 LOCF endpoint showed a statistically significant difference in favor of paroxetine CR 25mg versus placebo, and the paroxetine CR 12.5mg group showed numerical superiority over placebo treatment, but this was not statistically significant.

The improvements observed on the VAS-Mood scale, taken in conjunction with the improvements observed on the majority of secondary efficacy measures and the Regulatory requested variable, clearly demonstrated a clinical benefit for PMDD subjects treated with intermittent paroxetine CR 25mg and 12.5mg. These included various physician-rated global assessments of efficacy (CGI severity of illness, CGI global improvement), and subject-rated improvements in family/home (SDS item). Alternative scales such as the PMTS-O, used specifically for PMDD, also supported the findings of the primary efficacy measure.

In this study, 89/116 (76.7%) subjects in the paroxetine CR 25mg group, 88/130 (67.7%) subjects in the paroxetine CR 12.5mg group, and 68/120 (56.7%) in the placebo group reported AEs during the treatment phase. The majority of AEs reported by subjects taking intermittent paroxetine CR were related to the nervous system, body as a whole, and digestive system. Commonly reported treatment emergent AEs ($\geq 5\%$ in either paroxetine CR group), which occurred at an incidence at least twice that of placebo were nausea, asthenia, libido decreased, sweating, diarrhea, dizziness, tremor, insomnia and sinusitis. The majority of treatment emergent AEs in the paroxetine CR groups were rated by investigators as mild or moderate in severity, and related or possibly related to study medication.

For the most frequently reported treatment emergent AEs for the paroxetine treatment groups, nausea, asthenia and headache, the time to first occurrence was generally during Days 1 to 7, although this was less marked for headache.

Follow-up phase AEs were less frequent overall, than those reported during the treatment phase, but were more prevalent in the paroxetine CR groups than the placebo group. The majority of follow-up emergent AEs in the paroxetine CR groups were rated by investigators as mild or moderate in intensity and unrelated or probably unrelated to study medication.

The overall incidence of AEs occurring during the "on study medication" time windows for both of the paroxetine CR treatment groups was highest in the first treatment cycle (paroxetine CR 25mg: 61.2%; paroxetine CR 12.5mg: 43.8%), reducing to a range of 29 to 36% during the "on study medication" time windows associated with treatment cycles 2 and 3. After the first treatment cycle, the incidences of AEs for both paroxetine CR treatment groups during each half of the cycle were similar to those for placebo-treated subjects.

The profile of treatment emergent AEs observed in the present intermittent paroxetine CR study was, in general, comparable with those reported for subjects taking continuous paroxetine IR for major depressive disorder, panic disorder, obsessive compulsive disorder, social anxiety disorder, generalized anxiety disorder, and post traumatic stress disorder; and subjects taking continuous paroxetine CR for major depressive disorder and panic disorder ([GlaxoSmithKline Document Number \[BRL-029060/RSD-1014BX/2 \]](#)). A comparison of treatment emergent AEs for subjects receiving intermittent paroxetine CR in the present study and subjects receiving continuous paroxetine CR for PMDD showed similarities in the overall incidence and general profile of AEs. However, for follow-up AEs, the present study had a slightly lower overall incidence, and the incidence for some particular AEs was noticeably lower. An examination of the effect of common concomitant medications or medical history on the incidence of treatment emergent AEs in the present study did not suggest any clinically significant association.

There were no treatment phase or follow-up phase deaths. Seven subjects reported non-fatal serious AEs during the treatment or follow-up phases, 2 subjects in the paroxetine CR 25mg treatment group, 3 subjects in the paroxetine CR 12.5mg treatment group and 2 subjects in the placebo treatment group. One subject reported a non-fatal serious AE five days prior to receiving paroxetine CR 12.5mg (unintended pregnancy). All but one of the SAEs (related anaphylactoid reaction for a subject receiving paroxetine CR 25mg) were considered to be probably unrelated or unrelated to study medication, but the SAEs for two of the subjects were considered to be possibly or probably associated with protocol design or procedures.

The number of subjects withdrawn because of an AE was higher in the paroxetine CR 25mg [16/116 (13.8%) subjects] and 12.5mg groups [13/130 (10.0%) subjects] compared to the placebo group [5/120 (4.2%) subjects].

Subject vital sign and laboratory data showed no clinically meaningful changes associated with the use of paroxetine CR in subjects with PMDD. The number of subjects with laboratory and vital sign values of potential clinical concern was low.

10.2. Conclusions

- The results of this study have demonstrated that intermittent paroxetine CR provides effective benefit in the treatment of females with PMDD. Paroxetine CR 25mg and 12.5mg were statistically superior to placebo for the primary efficacy variable, change from baseline in mean luteal phase VAS-Mood score at the treatment cycle 3 LOCF endpoint, and the majority of the secondary efficacy parameters.
- While paroxetine CR 12.5mg was shown to be statistically superior to placebo for the primary and the majority of the secondary efficacy variables at the treatment cycle 3 LOCF endpoint, the estimated differences for paroxetine CR 12.5mg were usually smaller than for paroxetine CR 25mg.
- Intermittent paroxetine CR was generally well tolerated, and the nature of the AEs observed in subjects with PMDD taking paroxetine CR (25mg and 12.5mg) was, in general, comparable to those reported in other psychiatric disorders for which

paroxetine CR is approved. The paroxetine CR 12.5mg treatment group experienced slightly fewer AEs than the paroxetine CR 25mg group.

11. REFERENCES

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12. DATA SOURCE TABLES: STUDY POPULATION

	Page
Table 12.1 Number (%) of Subjects by Study Status and Population All Subjects	153
Table 12.2 Number (%) of Subjects by Study Status and Population by Country All Subjects	154
Table 12.3 Number (%) of Subjects with Protocol Violations Leading to Exclusion from the Per Protocol Analysis Intention-to-Treat Population . .	160
Table 12.4 Number (%) of Subjects with Protocol Deviations Included in the Per Protocol Analysis Per Protocol Population	161
Table 12.5 Number (%) of Subjects who were Withdrawn Pre-Randomisation by the Reason for Withdrawal Screening Only Population	162
Table 12.6 Number (%) of Randomised Subjects who Completed the Study or were Withdrawn by the Reason for Withdrawal Intention-to-Treat Population	163
Table 12.7 Number (%) of Randomised Subjects who Completed the Study or were Withdrawn by the Reason for Withdrawal Per Protocol Population	164
Table 12.8 Number (%) of Subjects Remaining/Withdrawing from the Study at each Visit Intention-to-Treat Population	165
Table 12.9 Cumulative Number (%) of Randomised Subjects Withdrawn During the Study by Reason for Withdrawal Intention-to-Treat Population	166
Table 12.10 Number (%) of Subjects Randomised and Completed at each Centre by Country Intention-to-Treat Population	168
Table 12.11 Number (%) of Subjects by Race and Age Group Screening Only Population	177
Table 12.12 Number (%) of Subjects by Race and Age Group Intention-to-Treat Population	178
Table 12.13 Number (%) of Subjects by Race and Age Group Per Protocol Population	179
Table 12.14 Summary Statistics for Age Screening Only Population	180
Table 12.15 Summary Statistics for Age, Height, Weight and Body Mass Index (BMI) at Study Entry Randomised (non-ITT) Population	181
Table 12.16 Summary Statistics for Age, Height, Weight and Body Mass Index (BMI) at Study Entry Intention-to-Treat Population	182
Table 12.17 Summary Statistics for Age, Height, Weight and Body Mass Index (BMI) at Study Entry Per Protocol Population	183
Table 12.18 Significant Medical / Surgical History and Physical Examination Prior and Active Conditions Ordered by Body System and Preferred Term Screening Only Population	184
Table 12.19 Significant Medical / Surgical History and Physical Examination Prior and Active Conditions Ordered by Body System and Preferred Term Randomised (non-ITT) Population	199

Table 12.20 Significant Medical / Surgical History and Physical Examination Prior Conditions Ordered by Body System and Preferred Term Intention-to-Treat Population.	201
Table 12.21 Significant Medical / Surgical History and Physical Examination Prior Conditions by Preferred Term Ordered in Decreasing Frequency Intention-to-Treat Population.	213
Table 12.22 Significant Medical / Surgical History and Physical Examination Active Conditions Ordered by Body System and Preferred Term Intention-to-Treat Population.	223
Table 12.23 Significant Medical / Surgical History and Physical Examination Active Conditions by Preferred Term Ordered in Decreasing Frequency Intention-to-Treat Population.	232
Table 12.24 Number (%) of Subjects with other Psychiatric Disorders (from full psychiatric history and MINI interview) Intention-to-Treat Population .	239
Table 12.25 Relationship to Onset of PMDD Symptoms by Category Intention-to-Treat Population.	240
Table 12.26 Summary Statistics for Persistency of PMDD, Age at Onset of PMDD Symptoms and Duration of PMDD Symptoms Intention-to-Treat Population	241
Table 12.27 Obstetrics and Gynaecological History by Treatment Group Intention-to-Treat Population.	242
Table 12.28 Number (%) of Subjects by Previous Treatment for PMDD Intention-to-Treat Population.	243
Table 12.29 Summary Statistics for MADRS Total Score at Screening Intention-to-Treat Population.	246
Table 12.30 Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term Screening Only Population	247
Table 12.31 Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term Randomised (non-ITT) Population	258
Table 12.32 Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term Intention-to-Treat Population	260
Table 12.33 Number (%) of Subjects with Prior Medication by Preferred Term Ordered by Decreasing Frequency Intention-to-Treat Population. .	271
Table 12.34 Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term Treatment Phase Intention-to-Treat Population	285
Table 12.35 Number (%) of Subjects with Concomitant Medication by Preferred Term Ordered by Decreasing Frequency Treatment Phase Intention-to-Treat Population.	296
Table 12.36 Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase Intention-to-Treat Population	310
Table 12.37 Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase Ordered by Decreasing Frequency Intention-to-Treat Population.	318
Table 12.38 Number (%) of Subjects by Study Medication Capsule Compliance by Menstrual Cycle Intention-to-Treat Population	328

Table 12.39 Number (%) of Subjects by Study Medication Compliance for Interruption in Study drug and Adherence to taking medication during the luteal phase, and Overall Compliance by Menstrual Cycle Intention-to-Treat Population.	329

Table 12.1

Number (%) of Subjects by Study Status and Population
All Subjects

Status	No Therapy Dispensed (N=1242)	Paroxetine CR 25 mg (N=119)	Treatment Group Paroxetine CR 12.5 mg (N=131)	Placebo (N=123)	Total (N=1615)
Screened	1242 (100.0%)	119 (100.0%)	131 (100.0%)	123 (100.0%)	1615 (100.0%)
Screening Failures	797 (64.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	797 (49.3%)
Run in Failures	445 (35.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	445 (27.6%)
Randomised	0 (0.0%)	119 (100.0%)	131 (100.0%)	123 (100.0%)	373 (23.1%)
Completed *	0 (0.0%)	87 (73.1%)	104 (79.4%)	101 (82.1%)	292 (18.1%)
Early Withdrawal +	1242 (100.0%)	32 (26.9%)	27 (20.6%)	22 (17.9%)	1323 (81.9%)
Intention to Treat Population	0 (0.0%)	116 (97.5%)	130 (99.2%)	120 (97.6%)	366 (22.7%)
Per Protocol Population	0 (0.0%)	74 (62.2%)	99 (75.6%)	96 (78.0%)	269 (16.7%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.2

Number (%) of Subjects by Study Status and Population by Country
All Subjects

----- Country=Finland (5 centre(s)) -----						
Status	No Therapy Dispensed (N=163)	Paroxetine CR 25 mg (N=12)	Treatment Group Paroxetine CR 12.5 mg (N=11)	Placebo (N=11)	Total (N=197)	
Screened	163 (100.0%)	12 (100.0%)	11 (100.0%)	11 (100.0%)	197 (100.0%)	
Screening Failures	115 (70.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	115 (58.4%)	
Run in Failures	48 (29.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	48 (24.4%)	
Randomised	0 (0.0%)	12 (100.0%)	11 (100.0%)	11 (100.0%)	34 (17.3%)	
Completed *	0 (0.0%)	8 (66.7%)	8 (72.7%)	7 (63.6%)	23 (11.7%)	
Early Withdrawal +	163 (100.0%)	4 (33.3%)	3 (27.3%)	4 (36.4%)	174 (88.3%)	
Intention to Treat Population	0 (0.0%)	12 (100.0%)	11 (100.0%)	10 (90.9%)	33 (16.8%)	
Per Protocol Population	0 (0.0%)	8 (66.7%)	9 (81.8%)	8 (72.7%)	25 (12.7%)	

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.2

Number (%) of Subjects by Study Status and Population by Country
All Subjects

----- Country=Germany (5 centre(s)) -----

Status	No Therapy Dispensed (N=64)	Paroxetine CR 25 mg (N=19)	Treatment Group Paroxetine CR 12.5 mg (N=22)	Placebo (N=21)	Total (N=126)
Screened	64 (100.0%)	19 (100.0%)	22 (100.0%)	21 (100.0%)	126 (100.0%)
Screening Failures	39 (60.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	39 (31.0%)
Run in Failures	25 (39.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	25 (19.8%)
Randomised	0 (0.0%)	19 (100.0%)	22 (100.0%)	21 (100.0%)	62 (49.2%)
Completed *	0 (0.0%)	15 (78.9%)	18 (81.8%)	20 (95.2%)	53 (42.1%)
Early Withdrawal +	64 (100.0%)	4 (21.1%)	4 (18.2%)	1 (4.8%)	73 (57.9%)
Intention to Treat Population	0 (0.0%)	19 (100.0%)	21 (95.5%)	21 (100.0%)	61 (48.4%)
Per Protocol Population	0 (0.0%)	11 (57.9%)	18 (81.8%)	18 (85.7%)	47 (37.3%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.2

Number (%) of Subjects by Study Status and Population by Country
All Subjects

----- Country=Netherlands (7 centre(s)) -----

Status	No Therapy Dispensed (N=175)	Paroxetine CR 25 mg (N=19)	Treatment Group Paroxetine CR 12.5 mg (N=23)	Placebo (N=21)	Total (N=238)
Screened	175 (100.0%)	19 (100.0%)	23 (100.0%)	21 (100.0%)	238 (100.0%)
Screening Failures	105 (60.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	105 (44.1%)
Run in Failures	70 (40.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	70 (29.4%)
Randomised	0 (0.0%)	19 (100.0%)	23 (100.0%)	21 (100.0%)	63 (26.5%)
Completed *	0 (0.0%)	15 (78.9%)	19 (82.6%)	17 (81.0%)	51 (21.4%)
Early Withdrawal +	175 (100.0%)	4 (21.1%)	4 (17.4%)	4 (19.0%)	187 (78.6%)
Intention to Treat Population	0 (0.0%)	19 (100.0%)	23 (100.0%)	21 (100.0%)	63 (26.5%)
Per Protocol Population	0 (0.0%)	13 (68.4%)	19 (82.6%)	16 (76.2%)	48 (20.2%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.2

Number (%) of Subjects by Study Status and Population by Country
All Subjects

----- Country=Norway (6 centre(s)) -----

Status	No Therapy Dispensed (N=86)	Paroxetine CR 25 mg (N=8)	Treatment Group Paroxetine CR 12.5 mg (N=8)	Placebo (N=7)	Total (N=109)
Screened	86 (100.0%)	8 (100.0%)	8 (100.0%)	7 (100.0%)	109 (100.0%)
Screening Failures	50 (58.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	50 (45.9%)
Run in Failures	36 (41.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	36 (33.0%)
Randomised	0 (0.0%)	8 (100.0%)	8 (100.0%)	7 (100.0%)	23 (21.1%)
Completed *	0 (0.0%)	5 (62.5%)	5 (62.5%)	5 (71.4%)	15 (13.8%)
Early Withdrawal +	86 (100.0%)	3 (37.5%)	3 (37.5%)	2 (28.6%)	94 (86.2%)
Intention to Treat Population	0 (0.0%)	8 (100.0%)	8 (100.0%)	6 (85.7%)	22 (20.2%)
Per Protocol Population	0 (0.0%)	4 (50.0%)	7 (87.5%)	4 (57.1%)	15 (13.8%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.2

Number (%) of Subjects by Study Status and Population by Country
All Subjects

----- Country=Sweden (11 centre(s)) -----

Status	No Therapy Dispensed (N=319)	Paroxetine CR 25 mg (N=35)	Treatment Group Paroxetine CR 12.5 mg (N=36)	Placebo (N=36)	Total (N=426)
Screened	319 (100.0%)	35 (100.0%)	36 (100.0%)	36 (100.0%)	426 (100.0%)
Screening Failures	188 (58.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	188 (44.1%)
Run in Failures	131 (41.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	131 (30.8%)
Randomised	0 (0.0%)	35 (100.0%)	36 (100.0%)	36 (100.0%)	107 (25.1%)
Completed *	0 (0.0%)	27 (77.1%)	33 (91.7%)	33 (91.7%)	93 (21.8%)
Early Withdrawal +	319 (100.0%)	8 (22.9%)	3 (8.3%)	3 (8.3%)	333 (78.2%)
Intention to Treat Population	0 (0.0%)	35 (100.0%)	36 (100.0%)	36 (100.0%)	107 (25.1%)
Per Protocol Population	0 (0.0%)	24 (68.6%)	24 (66.7%)	30 (83.3%)	78 (18.3%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.2

Number (%) of Subjects by Study Status and Population by Country
All Subjects

----- Country=United States of America (19 centre(s)) -----						
Status	No Therapy Dispensed (N=435)	Paroxetine CR 25 mg (N=26)	Treatment Group Paroxetine CR 12.5 mg (N=31)	Placebo (N=27)	Total (N=519)	
Screened	435 (100.0%)	26 (100.0%)	31 (100.0%)	27 (100.0%)	519 (100.0%)	
Screening Failures	300 (69.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	300 (57.8%)	
Run in Failures	135 (31.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	135 (26.0%)	
Randomised	0 (0.0%)	26 (100.0%)	31 (100.0%)	27 (100.0%)	84 (16.2%)	
Completed *	0 (0.0%)	17 (65.4%)	21 (67.7%)	19 (70.4%)	57 (11.0%)	
Early Withdrawal +	435 (100.0%)	9 (34.6%)	10 (32.3%)	8 (29.6%)	462 (89.0%)	
Intention to Treat Population	0 (0.0%)	23 (88.5%)	31 (100.0%)	26 (96.3%)	80 (15.4%)	
Per Protocol Population	0 (0.0%)	14 (53.8%)	22 (71.0%)	20 (74.1%)	56 (10.8%)	

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 No Therapy Dispensed Subjects are not Randomised and have No Randomised Therapy Dispensed
 Per Protocol Population is the Intention to Treat population excluding subjects with protocol violations
 The ITT population for each efficacy analysis will differ due to the number of subjects who are eligible for each endpoint

Table 12.3

Number (%) of Subjects with Protocol Violations Leading to Exclusion from the Per Protocol Analysis
Intention-to-Treat Population

	Treatment Group				
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)	
Total Number of Subjects with at least one Protocol Violation*	42 (36.2%)	31 (23.8%)	24 (20.0%)	97 (26.5%)	
Total Number of Subjects with no Protocol Violations	74 (63.8%)	99 (76.2%)	96 (80.0%)	269 (73.5%)	
History of Axis I disorder (other than specific phobias) within 6 months prior to screening	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
Ongoing Medication which may effect PMDD symptomatology	6 (5.2%)	1 (0.8%)	5 (4.2%)	12 (3.3%)	
Pregnant or lactating women	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)	
Study medication non-compliance	29 (25.0%)	26 (20.0%)	17 (14.2%)	72 (19.7%)	
Insufficient 'on-offness' of premenstrual symptoms^	11 (9.5%)	5 (3.8%)	4 (3.3%)	20 (5.5%)	
Hormonal contraception use	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)	

* A Subject can have more than one protocol violation leading to exclusion

^ Based on percentage and luteal phase compliance and interruption in study drug criteria

Table 12.4

Number (%) of Subjects with Protocol Deviations Included in the Per Protocol Analysis
Per Protocol Population

	Treatment Group			
	Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)	Total (N=269)

Total Number of Subjects with at least one Protocol Deviation*	0 (0.0%)	2 (2.0%)	2 (2.1%)	4 (1.5%)
Severe, clinically significant, concurrent disease	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.4%)
Outside permitted age range	0 (0.0%)	1 (1.0%)	2 (2.1%)	3 (1.1%)

* A Subject may have more than one protocol deviation

Table 12.5

Number (%) of Subjects who were Withdrawn Pre-Randomisation by the Reason for Withdrawal
Screening Only Population

Reason for Pre-Randomisation Withdrawal*	Treatment Group No Therapy Dispensed (N=1242)
Baseline Adverse Event **	3 (0.2%)
Does not meet Inclusion/Exclusion Criteria	754 (60.7%)
Protocol Deviation (including Non-Compliance)	133 (10.7%)
Lost to Follow-up	134 (10.8%)
Other Reason	218 (17.6%)
Total Withdrawn	1242 (100.0%)

* Reason based on Subject Continuation/Withdrawal eCRF response

** Including death as an outcome

Table 12.6

Number (%) of Randomised Subjects who Completed the Study or were Withdrawn by the Reason for Withdrawal
Intention-to-Treat Population

Reason for Study Conclusion	Treatment Group			Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Completed Study *	87 (75.0%)	104 (80.0%)	101 (84.2%)	292 (79.8%)
Total Withdrawn +	29 (25.0%)	26 (20.0%)	19 (15.8%)	74 (20.2%)
- Adverse Event **	16 (13.8%)	13 (10.0%)	5 (4.2%)	34 (9.3%)
- Lack of Efficacy	2 (1.7%)	2 (1.5%)	6 (5.0%)	10 (2.7%)
- Protocol Deviation ++	2 (1.7%)	4 (3.1%)	2 (1.7%)	8 (2.2%)
- Lost to Follow-up	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
- Other Reason	2 (1.7%)	3 (2.3%)	2 (1.7%)	7 (1.9%)
- Programmatically Assigned ^	4 (3.4%)	3 (2.3%)	4 (3.3%)	11 (3.0%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 Under withdrawn the first five categories are based on the Continuation/Withdrawal eCRF response
 ** Including death as an outcome
 ++Including non-compliance
 ^ Investigator tick-box states subject completed the study but the subject didn't complete Treatment Cycle 3 on study medication

Table 12.7

Number (%) of Randomised Subjects who Completed the Study or were Withdrawn by the Reason for Withdrawal
Per Protocol Population

Reason for Study Conclusion	Treatment Group			Total (N=269)
	Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)	
Completed Study *	65 (87.8%)	88 (88.9%)	82 (85.4%)	235 (87.4%)
Total Withdrawn +	9 (12.2%)	11 (11.1%)	14 (14.6%)	34 (12.6%)
- Adverse Event **	3 (4.1%)	4 (4.0%)	2 (2.1%)	9 (3.3%)
- Lack of Efficacy	2 (2.7%)	1 (1.0%)	6 (6.3%)	9 (3.3%)
- Protocol Deviation ++	0 (0.0%)	2 (2.0%)	0 (0.0%)	2 (0.7%)
- Lost to Follow-up	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
- Other Reason	1 (1.4%)	1 (1.0%)	2 (2.1%)	4 (1.5%)
- Programmatically Assigned ^	3 (4.1%)	3 (3.0%)	4 (4.2%)	10 (3.7%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
 +Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication
 Under withdrawn the first five categories are based on the Continuation/Withdrawal eCRF response
 ** Including death as an outcome
 ++Including non-compliance
 ^ Investigator tick-box states subject completed the study but the subject didn't complete Treatment Cycle 3 on study medication

Table 12.8

Number (%) of Subjects Remaining/Withdrawing from the Study at each Visit
Intention-to-Treat Population

Visit	Status	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Treatment Cycle 1	Withdrawn	15 (12.9%)	10 (7.7%)	3 (2.5%)	28 (7.7%)
	Remaining in Study	101 (87.1%)	120 (92.3%)	117 (97.5%)	338 (92.3%)
Treatment Cycle 2	Withdrawn	5 (4.3%)	10 (7.7%)	9 (7.5%)	24 (6.6%)
	Remaining in Study	96 (82.8%)	110 (84.6%)	108 (90.0%)	314 (85.8%)
Treatment Cycle 3	Withdrawn	9 (7.8%)	6 (4.6%)	7 (5.8%)	22 (6.0%)
	Remaining in Study	87 (75.0%)	104 (80.0%)	101 (84.2%)	292 (79.8%)

Withdrawn=Investigator tick-box states subject did not complete the study or did not complete Treatment Cycle 3 on study medication
 Remaining in Study=Subjects last dose of study medication was after the end of the given treatment cycle,
 or the investigator tick-box states Subject completed the study whereby the subject is assigned as remaining in study
 up to and including Treatment Cycle 3

Table 12.9

Cumulative Number (%) of Randomised Subjects Withdrawn During the Study by Reason for Withdrawal
Intention-to-Treat Population

	Treatment Group																							
	Paroxetine CR 25 mg (N = 116)								Paroxetine CR 12.5 mg (N = 130)								Placebo (N = 120)							
	AE	%	LE	%	Other	%	Total	%	AE	%	LE	%	Other	%	Total	%	AE	%	LE	%	Other	%	Total	%
Cycle																								
Treatment																								
Cycle 1	11	9.5	1	0.9	3	2.6	15	12.9	7	5.4	1	0.8	2	1.5	10	7.7	1	0.8	2	1.7	0	0.0	3	2.5
Treatment																								
Cycle 2	14	12.1	1	0.9	5	4.3	20	17.2	12	9.2	1	0.8	7	5.4	20	15.4	4	3.3	4	3.3	4	3.3	12	10.0
Treatment																								
Cycle 3	16	13.8	2	1.7	11	9.5	29	25.0	13	10.0	2	1.5	11	8.5	26	20.0	5	4.2	6	5.0	8	6.7	19	15.8

(Continued)

Withdrawn=Investigator tick-box states subject did not complete the study or did not complete Treatment Cycle 3 on study medication
 AE=Adverse Event, LE=Lack of Efficacy, and Other includes Protocol Deviation, Lost to Follow-up and Other reason based on the eCRF
 In addition, those assigned programmatically as withdrawals are in this Other category

Table 12.9

Cumulative Number (%) of Randomised Subjects Withdrawn During the Study by Reason for Withdrawal
Intention-to-Treat Population

	Treatment Group							
	Total (N = 366)							
	AE	%	LE	%	Other	%	Total	%
Cycle								
Treatment								
Cycle 1	19	5.2	4	1.1	5	1.4	28	7.7
Treatment								
Cycle 2	30	8.2	6	1.6	16	4.4	52	14.2
Treatment								
Cycle 3	34	9.3	10	2.7	30	8.2	74	20.2

Withdrawn=Investigator tick-box states subject did not complete the study or did not complete Treatment Cycle 3 on study medication
 AE=Adverse Event, LE=Lack of Efficacy, and Other includes Protocol Deviation, Lost to Follow-up and Other reason based on the eCRF
 In addition, those assigned programmatically as withdrawals are in this Other category

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : Finland

Centre	Investigator	Status	Treatment Group			
			Paroxetine CR 25 mg (N=12)	Paroxetine CR 12.5 mg (N=11)	Placebo (N=10)	Total (N=33)
168		Randomised	2 (16.7%)	2 (18.2%)	2 (20.0%)	6 (18.2%)
		Completed*	2 (16.7%)	0 (0.0%)	2 (20.0%)	4 (12.1%)
		Early Withdrawal+	0 (0.0%)	2 (18.2%)	0 (0.0%)	2 (6.1%)
		Randomised	2 (16.7%)	2 (18.2%)	1 (10.0%)	5 (15.2%)
		Completed*	1 (8.3%)	2 (18.2%)	1 (10.0%)	4 (12.1%)
		Early Withdrawal+	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (3.0%)
		Randomised	2 (16.7%)	1 (9.1%)	1 (10.0%)	4 (12.1%)
		Completed*	1 (8.3%)	1 (9.1%)	0 (0.0%)	2 (6.1%)
		Early Withdrawal+	1 (8.3%)	0 (0.0%)	1 (10.0%)	2 (6.1%)
		Randomised	4 (33.3%)	3 (27.3%)	4 (40.0%)	11 (33.3%)
		Completed*	3 (25.0%)	3 (27.3%)	3 (30.0%)	9 (27.3%)
		Early Withdrawal+	1 (8.3%)	0 (0.0%)	1 (10.0%)	2 (6.1%)
		Randomised	2 (16.7%)	3 (27.3%)	2 (20.0%)	7 (21.2%)
		Completed*	1 (8.3%)	2 (18.2%)	1 (10.0%)	4 (12.1%)
		Early Withdrawal+	1 (8.3%)	1 (9.1%)	1 (10.0%)	3 (9.1%)

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* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : Germany

Centre	Investigator	Status	Treatment Group				Total (N=61)
			Paroxetine CR 25 mg (N=19)	Paroxetine CR 12.5 mg (N=21)	Placebo (N=21)		
		Randomised	4 (21.1%)	4 (19.0%)	4 (19.0%)		12 (19.7%)
		Completed*	4 (21.1%)	3 (14.3%)	4 (19.0%)		11 (18.0%)
		Early Withdrawal+	0 (0.0%)	1 (4.8%)	0 (0.0%)		1 (1.6%)
		Randomised	0 (0.0%)	2 (9.5%)	1 (4.8%)		3 (4.9%)
		Completed*	0 (0.0%)	2 (9.5%)	1 (4.8%)		3 (4.9%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	7 (36.8%)	7 (33.3%)	7 (33.3%)		21 (34.4%)
		Completed*	5 (26.3%)	6 (28.6%)	7 (33.3%)		18 (29.5%)
		Early Withdrawal+	2 (10.5%)	1 (4.8%)	0 (0.0%)		3 (4.9%)
		Randomised	3 (15.8%)	3 (14.3%)	4 (19.0%)		10 (16.4%)
		Completed*	2 (10.5%)	2 (9.5%)	3 (14.3%)		7 (11.5%)
		Early Withdrawal+	1 (5.3%)	1 (4.8%)	1 (4.8%)		3 (4.9%)
		Randomised	5 (26.3%)	5 (23.8%)	5 (23.8%)		15 (24.6%)
		Completed*	4 (21.1%)	5 (23.8%)	5 (23.8%)		14 (23.0%)
		Early Withdrawal+	1 (5.3%)	0 (0.0%)	0 (0.0%)		1 (1.6%)

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* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : Netherlands

Centre	Investigator	Status	Treatment Group				Total (N=63)
			Paroxetine CR 25 mg (N=19)	Paroxetine CR 12.5 mg (N=23)	Placebo (N=21)		
		Randomised	3 (15.8%)	4 (17.4%)	4 (19.0%)		11 (17.5%)
		Completed*	2 (10.5%)	3 (13.0%)	3 (14.3%)		8 (12.7%)
		Early Withdrawal+	1 (5.3%)	1 (4.3%)	1 (4.8%)		3 (4.8%)
		Randomised	3 (15.8%)	4 (17.4%)	4 (19.0%)		11 (17.5%)
		Completed*	3 (15.8%)	2 (8.7%)	3 (14.3%)		8 (12.7%)
		Early Withdrawal+	0 (0.0%)	2 (8.7%)	1 (4.8%)		3 (4.8%)
		Randomised	2 (10.5%)	2 (8.7%)	2 (9.5%)		6 (9.5%)
		Completed*	1 (5.3%)	2 (8.7%)	2 (9.5%)		5 (7.9%)
		Early Withdrawal+	1 (5.3%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
		Randomised	1 (5.3%)	2 (8.7%)	2 (9.5%)		5 (7.9%)
		Completed*	1 (5.3%)	2 (8.7%)	1 (4.8%)		4 (6.3%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	1 (4.8%)		1 (1.6%)
		Randomised	1 (5.3%)	1 (4.3%)	0 (0.0%)		2 (3.2%)
		Completed*	1 (5.3%)	1 (4.3%)	0 (0.0%)		2 (3.2%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	5 (26.3%)	6 (26.1%)	6 (28.6%)		17 (27.0%)
		Completed*	4 (21.1%)	5 (21.7%)	6 (28.6%)		15 (23.8%)
		Early Withdrawal+	1 (5.3%)	1 (4.3%)	0 (0.0%)		2 (3.2%)
		Randomised	4 (21.1%)	4 (17.4%)	3 (14.3%)		11 (17.5%)
		Completed*	3 (15.8%)	4 (17.4%)	2 (9.5%)		9 (14.3%)
		Early Withdrawal+	1 (5.3%)	0 (0.0%)	1 (4.8%)		2 (3.2%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : Norway

Centre	Investigator	Status	Treatment Group				Total (N=22)
			Paroxetine CR 25 mg (N=8)	Paroxetine CR 12.5 mg (N=8)	Placebo (N=6)		
		Randomised	1 (12.5%)	1 (12.5%)	0 (0.0%)		2 (9.1%)
		Completed*	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Early Withdrawal+	1 (12.5%)	1 (12.5%)	0 (0.0%)		2 (9.1%)
		Randomised	2 (25.0%)	2 (25.0%)	2 (33.3%)		6 (27.3%)
		Completed*	0 (0.0%)	2 (25.0%)	2 (33.3%)		4 (18.2%)
		Early Withdrawal+	2 (25.0%)	0 (0.0%)	0 (0.0%)		2 (9.1%)
		Randomised	2 (25.0%)	1 (12.5%)	2 (33.3%)		5 (22.7%)
		Completed*	2 (25.0%)	1 (12.5%)	1 (16.7%)		4 (18.2%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	1 (16.7%)		1 (4.5%)
		Randomised	2 (25.0%)	2 (25.0%)	2 (33.3%)		6 (27.3%)
		Completed*	2 (25.0%)	2 (25.0%)	2 (33.3%)		6 (27.3%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	0 (0.0%)	2 (25.0%)	0 (0.0%)		2 (9.1%)
		Completed*	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Early Withdrawal+	0 (0.0%)	2 (25.0%)	0 (0.0%)		2 (9.1%)
		Randomised	1 (12.5%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
		Completed*	1 (12.5%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Completed*	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : Sweden

Centre	Investigator	Status	Treatment Group				Total (N=107)
			Paroxetine CR 25 mg (N=35)	Paroxetine CR 12.5 mg (N=36)	Placebo (N=36)		
		Randomised	2 (5.7%)	2 (5.6%)	2 (5.6%)		6 (5.6%)
		Completed*	2 (5.7%)	2 (5.6%)	2 (5.6%)		6 (5.6%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	7 (20.0%)	6 (16.7%)	6 (16.7%)		19 (17.8%)
		Completed*	4 (11.4%)	5 (13.9%)	4 (11.1%)		13 (12.1%)
		Early Withdrawal+	3 (8.6%)	1 (2.8%)	2 (5.6%)		6 (5.6%)
		Randomised	4 (11.4%)	3 (8.3%)	4 (11.1%)		11 (10.3%)
		Completed*	3 (8.6%)	3 (8.3%)	3 (8.3%)		9 (8.4%)
		Early Withdrawal+	1 (2.9%)	0 (0.0%)	1 (2.8%)		2 (1.9%)
		Randomised	6 (17.1%)	5 (13.9%)	4 (11.1%)		15 (14.0%)
		Completed*	6 (17.1%)	5 (13.9%)	4 (11.1%)		15 (14.0%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	1 (2.9%)	0 (0.0%)	2 (5.6%)		3 (2.8%)
		Completed*	0 (0.0%)	0 (0.0%)	2 (5.6%)		2 (1.9%)
		Early Withdrawal+	1 (2.9%)	0 (0.0%)	0 (0.0%)		1 (0.9%)
		Randomised	4 (11.4%)	5 (13.9%)	5 (13.9%)		14 (13.1%)
		Completed*	3 (8.6%)	5 (13.9%)	5 (13.9%)		13 (12.1%)
		Early Withdrawal+	1 (2.9%)	0 (0.0%)	0 (0.0%)		1 (0.9%)
		Randomised	7 (20.0%)	8 (22.2%)	7 (19.4%)		22 (20.6%)
		Completed*	6 (17.1%)	7 (19.4%)	7 (19.4%)		20 (18.7%)
		Early Withdrawal+	1 (2.9%)	1 (2.8%)	0 (0.0%)		2 (1.9%)
		Randomised	2 (5.7%)	1 (2.8%)	1 (2.8%)		4 (3.7%)
		Completed*	1 (2.9%)	1 (2.8%)	1 (2.8%)		3 (2.8%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : Sweden

Centre	Investigator	Status	Treatment Group				Total (N=107)
			Paroxetine CR 25 mg (N=35)	Paroxetine CR 12.5 mg (N=36)	Placebo (N=36)		
		Early Withdrawal+	1 (2.9%)	0 (0.0%)	0 (0.0%)		1 (0.9%)
		Randomised	0 (0.0%)	2 (5.6%)	1 (2.8%)		3 (2.8%)
		Completed*	0 (0.0%)	2 (5.6%)	1 (2.8%)		3 (2.8%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	2 (5.7%)	3 (8.3%)	3 (8.3%)		8 (7.5%)
		Completed*	2 (5.7%)	2 (5.6%)	3 (8.3%)		7 (6.5%)
		Early Withdrawal+	0 (0.0%)	1 (2.8%)	0 (0.0%)		1 (0.9%)
		Randomised	0 (0.0%)	1 (2.8%)	1 (2.8%)		2 (1.9%)
		Completed*	0 (0.0%)	1 (2.8%)	1 (2.8%)		2 (1.9%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : United States of America

Centre	Investigator	Status	Treatment Group			
			Paroxetine CR 25 mg (N=23)	Paroxetine CR 12.5 mg (N=31)	Placebo (N=26)	Total (N=80)
		Randomised	1 (4.3%)	1 (3.2%)	2 (7.7%)	4 (5.0%)
		Completed*	1 (4.3%)	1 (3.2%)	2 (7.7%)	4 (5.0%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
		Randomised	8 (34.8%)	7 (22.6%)	7 (26.9%)	22 (27.5%)
		Completed*	7 (30.4%)	4 (12.9%)	3 (11.5%)	14 (17.5%)
		Early Withdrawal+	1 (4.3%)	3 (9.7%)	4 (15.4%)	8 (10.0%)
		Randomised	1 (4.3%)	2 (6.5%)	2 (7.7%)	5 (6.3%)
		Completed*	0 (0.0%)	2 (6.5%)	2 (7.7%)	4 (5.0%)
		Early Withdrawal+	1 (4.3%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
		Randomised	2 (8.7%)	3 (9.7%)	1 (3.8%)	6 (7.5%)
		Completed*	1 (4.3%)	2 (6.5%)	1 (3.8%)	4 (5.0%)
		Early Withdrawal+	1 (4.3%)	1 (3.2%)	0 (0.0%)	2 (2.5%)
		Randomised	0 (0.0%)	1 (3.2%)	1 (3.8%)	2 (2.5%)
		Completed*	0 (0.0%)	1 (3.2%)	1 (3.8%)	2 (2.5%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
		Randomised	2 (8.7%)	2 (6.5%)	1 (3.8%)	5 (6.3%)
		Completed*	1 (4.3%)	1 (3.2%)	1 (3.8%)	3 (3.8%)
		Early Withdrawal+	1 (4.3%)	1 (3.2%)	0 (0.0%)	2 (2.5%)
		Randomised	2 (8.7%)	1 (3.2%)	2 (7.7%)	5 (6.3%)
		Completed*	2 (8.7%)	1 (3.2%)	2 (7.7%)	5 (6.3%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
		Randomised	0 (0.0%)	1 (3.2%)	1 (3.8%)	2 (2.5%)
		Completed*	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (1.3%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : United States of America

Centre	Investigator	Status	Treatment Group				Total (N=80)
			Paroxetine CR 25 mg (N=23)	Paroxetine CR 12.5 mg (N=31)	Placebo (N=26)		
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	1 (3.8%)		1 (1.3%)
		Randomised	2 (8.7%)	2 (6.5%)	2 (7.7%)		6 (7.5%)
		Completed*	2 (8.7%)	1 (3.2%)	2 (7.7%)		5 (6.3%)
		Early Withdrawal+	0 (0.0%)	1 (3.2%)	0 (0.0%)		1 (1.3%)
		Randomised	0 (0.0%)	2 (6.5%)	1 (3.8%)		3 (3.8%)
		Completed*	0 (0.0%)	0 (0.0%)	1 (3.8%)		1 (1.3%)
		Early Withdrawal+	0 (0.0%)	2 (6.5%)	0 (0.0%)		2 (2.5%)
		Randomised	1 (4.3%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
		Completed*	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Early Withdrawal+	1 (4.3%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
		Randomised	0 (0.0%)	0 (0.0%)	1 (3.8%)		1 (1.3%)
		Completed*	0 (0.0%)	0 (0.0%)	1 (3.8%)		1 (1.3%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	1 (4.3%)	1 (3.2%)	0 (0.0%)		2 (2.5%)
		Completed*	1 (4.3%)	1 (3.2%)	0 (0.0%)		2 (2.5%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	0 (0.0%)	1 (3.2%)	1 (3.8%)		2 (2.5%)
		Completed*	0 (0.0%)	0 (0.0%)	1 (3.8%)		1 (1.3%)
		Early Withdrawal+	0 (0.0%)	1 (3.2%)	0 (0.0%)		1 (1.3%)
		Randomised	1 (4.3%)	3 (9.7%)	1 (3.8%)		5 (6.3%)
		Completed*	1 (4.3%)	3 (9.7%)	0 (0.0%)		4 (5.0%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	1 (3.8%)		1 (1.3%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.10

Number (%) of Subjects Randomised and Completed at each Centre by Country
Intention-to-Treat Population

Country : United States of America

Centre	Investigator	Status	Treatment Group				Total (N=80)
			Paroxetine CR 25 mg (N=23)	Paroxetine CR 12.5 mg (N=31)	Placebo (N=26)		
		Randomised	1 (4.3%)	2 (6.5%)	2 (7.7%)		5 (6.3%)
		Completed*	0 (0.0%)	2 (6.5%)	2 (7.7%)		4 (5.0%)
		Early Withdrawal+	1 (4.3%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
		Randomised	0 (0.0%)	1 (3.2%)	0 (0.0%)		1 (1.3%)
		Completed*	0 (0.0%)	1 (3.2%)	0 (0.0%)		1 (1.3%)
		Early Withdrawal+	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
		Randomised	1 (4.3%)	1 (3.2%)	1 (3.8%)		3 (3.8%)
		Completed*	1 (4.3%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
		Early Withdrawal+	0 (0.0%)	1 (3.2%)	1 (3.8%)		2 (2.5%)

* Completed=Investigator tick-box states subject completed the study and subject completed Treatment Cycle 3 on study medication
+Withdrawn=Investigator tick-box states subject didn't complete the study or didn't complete Treatment Cycle 3 on study medication

Table 12.11

Number (%) of Subjects by Race and Age Group
Screening Only Population

		Treatment Group No Therapy Dispensed (N=1242)	
Race	White	1159	(93.3%)
	Black	52	(4.2%)
	Oriental	8	(0.6%)
	Other	23	(1.9%)
Age Group	18-25	67	(5.4%)
	26-35	381	(30.7%)
	>=36	794	(63.9%)

Table 12.12

Number (%) of Subjects by Race and Age Group
Intention-to-Treat Population

		Paroxetine CR 25 mg (N=116)		Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)		Total (N=366)	
Race	White	116	(100.0%)	125	(96.2%)	118	(98.3%)	359	(98.1%)
	Black	0	(0.0%)	3	(2.3%)	1	(0.8%)	4	(1.1%)
	Oriental	0	(0.0%)	1	(0.8%)	1	(0.8%)	2	(0.5%)
	Other	0	(0.0%)	1	(0.8%)	0	(0.0%)	1	(0.3%)
Age Group	18-25	5	(4.3%)	10	(7.7%)	2	(1.7%)	17	(4.6%)
	26-35	31	(26.7%)	45	(34.6%)	44	(36.7%)	120	(32.8%)
	>=36	80	(69.0%)	75	(57.7%)	74	(61.7%)	229	(62.6%)

Table 12.13

Number (%) of Subjects by Race and Age Group
Per Protocol Population

		Paroxetine CR 25 mg (N=74)		Paroxetine CR 12.5 mg (N=99)		Placebo (N=96)		Total (N=269)	
Race	White	74	(100.0%)	95	(96.0%)	94	(97.9%)	263	(97.8%)
	Black	0	(0.0%)	2	(2.0%)	1	(1.0%)	3	(1.1%)
	Oriental	0	(0.0%)	1	(1.0%)	1	(1.0%)	2	(0.7%)
	Other	0	(0.0%)	1	(1.0%)	0	(0.0%)	1	(0.4%)
Age Group	18-25	4	(5.4%)	6	(6.1%)	2	(2.1%)	12	(4.5%)
	26-35	21	(28.4%)	34	(34.3%)	34	(35.4%)	89	(33.1%)
	>=36	49	(66.2%)	59	(59.6%)	60	(62.5%)	168	(62.5%)

Table 12.14

Summary Statistics for Age
Screening Only Population

		Treatment Group No Therapy Dispensed (N=1242)

Age (years)	N	1242
	MEAN	36.7
	STD	5.81
	MEDIAN	38.0
	MINIMUM	18.0
	MAXIMUM	46.0

Table 12.15

Summary Statistics for Age, Height, Weight and Body Mass Index (BMI) at Study Entry
Randomised (non-ITT) Population

		Treatment Group			
		Paroxetine CR 25 mg (N=3)	Paroxetine CR 12.5 mg (N=1)	Placebo (N=3)	Total (N=7)
Age (years)	N	3	1	3	7
	MEAN	38.7	41.0	30.3	35.4
	STD	3.06		2.08	5.29
	MEDIAN	38.0	41.0	31.0	36.0
	MINIMUM	36.0	41.0	28.0	28.0
	MAXIMUM	42.0	41.0	32.0	42.0
Height (cm)	N	3	1	3	7
	MEAN	164.3	165.0	162.5	163.6
	STD	6.01		6.87	5.38
	MEDIAN	167.6	165.0	164.0	165.0
	MINIMUM	157.4	165.0	155.0	155.0
	MAXIMUM	168.0	165.0	168.5	168.5
Weight (kg)	N	3	1	3	7
	MEAN	64.3	60.0	72.4	67.2
	STD	11.34		11.14	10.50
	MEDIAN	60.0	60.0	70.0	62.6
	MINIMUM	55.8	60.0	62.6	55.8
	MAXIMUM	77.2	60.0	84.5	84.5
BMI (kg/m ²)	N	3	1	3	7
	MEAN	24.1	22.0	27.3	25.2
	STD	6.16		2.17	4.32
	MEDIAN	21.3	22.0	26.1	26.0
	MINIMUM	19.9	22.0	26.0	19.9
	MAXIMUM	31.2	22.0	29.8	31.2

Table 12.16

Summary Statistics for Age, Height, Weight and Body Mass Index (BMI) at Study Entry
Intention-to-Treat Population

		Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
Age (years)	N	116	130	120	366
	MEAN	37.2	35.9	36.9	36.6
	STD	5.39	6.01	5.51	5.67
	MEDIAN	38.0	36.0	37.5	37.5
	MINIMUM	19.0	20.0	22.0	19.0
	MAXIMUM	46.0	46.0	46.0	46.0
Height (cm)	N	116	130	120	366
	MEAN	165.4	166.0	166.8	166.1
	STD	6.71	6.13	6.62	6.49
	MEDIAN	165.0	166.0	167.3	166.0
	MINIMUM	147.3	149.9	152.4	147.3
	MAXIMUM	186.0	183.0	181.0	186.0
Weight (kg)	N	115	130	120	365
	MEAN	66.0	68.7	68.7	67.9
	STD	11.19	13.88	13.01	12.82
	MEDIAN	65.0	66.0	65.8	65.6
	MINIMUM	45.0	47.5	50.0	45.0
	MAXIMUM	99.5	132.9	114.0	132.9
BMI (kg/m ²)	N	115	130	120	365
	MEAN	24.1	24.9	24.7	24.6
	STD	3.44	4.49	4.75	4.29
	MEDIAN	23.9	23.9	23.4	23.7
	MINIMUM	17.1	18.0	17.9	17.1
	MAXIMUM	34.4	44.7	44.7	44.7

Table 12.17

Summary Statistics for Age, Height, Weight and Body Mass Index (BMI) at Study Entry
Per Protocol Population

		Treatment Group			
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)	Total (N=269)
Age (years)	N	74	99	96	269
	MEAN	36.8	36.3	37.0	36.7
	STD	5.50	5.97	5.43	5.64
	MEDIAN	38.0	37.0	38.0	38.0
	MINIMUM	19.0	20.0	22.0	19.0
	MAXIMUM	45.0	46.0	46.0	46.0
Height (cm)	N	74	99	96	269
	MEAN	164.9	165.9	166.6	165.9
	STD	6.51	6.42	6.70	6.56
	MEDIAN	165.0	165.1	166.5	165.1
	MINIMUM	151.0	149.9	152.4	149.9
	MAXIMUM	179.0	183.0	181.0	183.0
Weight (kg)	N	73	99	96	268
	MEAN	66.0	68.5	68.7	67.9
	STD	11.45	14.21	12.82	13.01
	MEDIAN	64.5	65.9	65.6	65.1
	MINIMUM	45.0	47.5	50.0	45.0
	MAXIMUM	99.5	132.9	113.9	132.9
BMI (kg/m ²)	N	73	99	96	268
	MEAN	24.2	24.9	24.8	24.7
	STD	3.56	4.58	4.78	4.40
	MEDIAN	23.9	24.3	23.7	23.9
	MINIMUM	17.1	18.0	17.9	17.1
	MAXIMUM	34.4	44.7	44.7	44.7

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
TOTAL	TOTAL	404	(32.5%)
ABDOMEN	TOTAL	36	(2.9%)
	HERNIA, ABDOMINAL	3	(0.2%)
	OPERATION, HERNIA REPAIR	4	(0.3%)
	OPERATION, OTHER	18	(1.4%)
	ABDOM PAIN, ABDOMINO-PELVIC	18	(1.4%)
ADNEXA	TOTAL	4	(0.3%)
	INFLAM PELVIC DIS	4	(0.3%)
ANUS	TOTAL	1	(0.1%)
	OPERATION, ANUS	1	(0.1%)
APPENDIX	TOTAL	34	(2.7%)
	APPENDICITIS	5	(0.4%)
	OPERATION, APPENDIX	32	(2.6%)
ARTERY	TOTAL	30	(2.4%)
	CEREBRAL ARTERY OCCLUSION	1	(0.1%)
	EMBOLISM/THROMBOSIS, PERIPH	1	(0.1%)
	MIGRAINE	28	(2.3%)
ARTICULAR	TOTAL	8	(0.6%)
	INTERVERTEB DISC, ABN	8	(0.6%)
BACK	TOTAL	24	(1.9%)
	BACK PAIN	24	(1.9%)
BILIARY TRACT	TOTAL	9	(0.7%)
	CHOLELITHIASIS	1	(0.1%)
	OPERATION, GB	9	(0.7%)
BILIRUBIN	TOTAL	4	(0.3%)
	JAUNDICE, UNSPEC	1	(0.1%)
	SERUM BILIRUBIN, INCREASED	3	(0.2%)
BLADDER	TOTAL	8	(0.6%)
	CYSTITIS	8	(0.6%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
BONE	TOTAL	16	(1.3%)
	BONE INFECT	1	(0.1%)
	FRACTURE, BONE UNSPEC	1	(0.1%)
	FRACTURE, LOWER LIMB	4	(0.3%)
	FRACTURE, NECK/TRUNK	1	(0.1%)
	FRACTURE, SKULL	1	(0.1%)
	FRACTURE, UPPER LIMB	3	(0.2%)
	JAW DIS	1	(0.1%)
	NEOPLASMS BENIGN	1	(0.1%)
	OPERATION, BONE/JOINT	7	(0.6%)
	RHEUMATIC DISORD	2	(0.2%)
BRAIN	TOTAL	13	(1.0%)
	BRAIN CONDIT, OTHER	1	(0.1%)
	INJURY, INTRACRANIAL	1	(0.1%)
	INSOMNIA	11	(0.9%)
BREAST	TOTAL	17	(1.4%)
	BREAST DISORD	3	(0.2%)
	MASS, BREAST	1	(0.1%)
	NEOPLASMS BENIGN	2	(0.2%)
	OPERATION, BREAST	14	(1.1%)
BREAST/MAMMARY GLAND	TOTAL	4	(0.3%)
	OPERATION, BREAST	4	(0.3%)
BRONCHUS	TOTAL	31	(2.5%)
	ASTHMA	25	(2.0%)
	BRONCHITIS, ACUTE	1	(0.1%)
	BRONCHITIS, CHRONIC	1	(0.1%)
	BRONCHITIS, OTHER	5	(0.4%)
BURSA	TOTAL	1	(0.1%)
	RHEUMATIC DISORD	1	(0.1%)
CAPILLARY	TOTAL	1	(0.1%)
	FLUSHING	1	(0.1%)
CARBOHYDRATE	TOTAL	2	(0.2%)
	CARBOHYDRATE DISORD	2	(0.2%)
CARDIOVASCULAR	TOTAL	17	(1.4%)
	HYPERTENSION	11	(0.9%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
CARDIOVASCULAR	HYPERTENSION/PREGNANCY	2	(0.2%)
	HYPOTENSION, OTHER	1	(0.1%)
	OPERATION, OTHER	1	(0.1%)
	ABDOM	1	(0.1%)
CARTILAGE	SYNCOPE AND COLLAPSE	2	(0.2%)
	TOTAL	2	(0.2%)
	DISLOCATION	1	(0.1%)
	JOINT, DERANGEMENT	1	(0.1%)
CAUSES OF INJURY	TOTAL	31	(2.5%)
	ADVERSE	4	(0.3%)
	EFF/ANALGESIC	1	(0.1%)
	ADVERSE	9	(0.7%)
	EFF/ANTI-INFECTION	1	(0.1%)
	ADVERSE	18	(1.4%)
	EFF/ANTIBIOTIC	1	(0.1%)
	ADVERSE EFF/BL	1	(0.1%)
	CONSTITUENT	1	(0.1%)
	ADVERSE EFF/HORMONE	2	(0.2%)
	ADVERSE EFF/OTHER	1	(0.1%)
	DRUG	1	(0.1%)
	ADVERSE	1	(0.1%)
	EFF/PSYCHOTROPICS	1	(0.1%)
	ADVERSE	1	(0.1%)
CEREBRAL CORTEX	EFF/SKIN, MUC MEMB	1	(0.1%)
	DRUG	1	(0.1%)
	POISONING	1	(0.1%)
CERVIX	TOTAL	1	(0.1%)
	EPILEPSY	1	(0.1%)
COAGULATION FACTORS	TOTAL	24	(1.9%)
	GENITAL FEMALE	12	(1.0%)
	DISORD, OTHER	1	(0.1%)
	OPERATION, FEM	15	(1.2%)
	GENITAL	1	(0.1%)
CONJUNCTIVA	PAP SMEAR, ABN	5	(0.4%)
	TOTAL	1	(0.1%)
	COAGULATION DEFECTS	1	(0.1%)
CONJUNCTIVA	TOTAL	3	(0.2%)
	CONJUNCTIVAL DISORD	3	(0.2%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
CORNEA	TOTAL	2	(0.2%)
	VISUAL DISTURB	2	(0.2%)
CRANIAL NERVE	TOTAL	1	(0.1%)
	PERIPH NERV SYST DISORD	1	(0.1%)
DIAGNOSTIC/THERAPEUTIC PROCS	TOTAL	10	(0.8%)
	EVALUATION, DX EXAM	3	(0.2%)
	PROCEDURE, EYE/EAR	2	(0.2%)
	PROCEDURES, OTHER	1	(0.1%)
	NONOPERATIVE RADIOLOGY, DIAGNOSTIC	3	(0.2%)
	THERAPY, REHAB	1	(0.1%)
DIGESTIVE	TOTAL	26	(2.1%)
	DIARRHEA	3	(0.2%)
	ENTERITIS/COLITIS	4	(0.3%)
	FLATULENCE	1	(0.1%)
	GASTRITIS/DUODENITIS	6	(0.5%)
	HEARTBURN	8	(0.6%)
	NAUSEA	1	(0.1%)
	NEOPLASMS, UNCERT BEHAV	1	(0.1%)
	OPERATION, STOMACH	1	(0.1%)
	STOMACH/DUODENUM DISORD	1	(0.1%)
	ULCER, PEPTIC, OTHER	1	(0.1%)
	VOMITING	1	(0.1%)
DUODENUM	TOTAL	1	(0.1%)
	ULCER, DUODENAL	1	(0.1%)
EAR/AUDITION, NOS	TOTAL	8	(0.6%)
	HEARING LOSS	5	(0.4%)
	TINNITUS	3	(0.2%)
ENZYME	TOTAL	1	(0.1%)
	TRANSAMINASE/LDH, ELEVATION	1	(0.1%)
ERYTHROCYTES	TOTAL	21	(1.7%)
	ANEMIA, HEMOLYT, HERED	1	(0.1%)
	ANEMIA, IRON DEFIC	3	(0.2%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
ERYTHROCYTES	ANEMIA, OTHER	15	(1.2%)
	ANEMIA, OTHER DEFIC	1	(0.1%)
	ANEMIA, PERNICIOUS	1	(0.1%)
ESOPHAGUS	TOTAL	4	(0.3%)
	ESOPHAGITIS	4	(0.3%)
EXTERNAL EAR	TOTAL	1	(0.1%)
	EAR/MASTOID DISORD	1	(0.1%)
	OPERATION, EAR	1	(0.1%)
EYE/VISION, NOS	TOTAL	5	(0.4%)
	EYE DISORD, OTHER	2	(0.2%)
	FOREIGN BODY EFF	1	(0.1%)
	OPERATION, EYE	1	(0.1%)
	VISUAL DISTURB	2	(0.2%)
EYELID	TOTAL	1	(0.1%)
	EYE DISORD, OTHER	1	(0.1%)
FACTORS INFLUENCING HEALTH	TOTAL	41	(3.3%)
	MANAGEMENT, CONTRACEPTIVE	35	(2.8%)
	MANAGEMENT, PROCREATIVE	1	(0.1%)
	NEED/OTHER	2	(0.2%)
	PROPHYLAXIS STATUS, POSTSURGICAL	4	(0.3%)
FALLOPIAN TUBE	TOTAL	57	(4.6%)
	OPERATION, FEM GENITAL	57	(4.6%)
FASCIA	TOTAL	1	(0.1%)
	SOFT TISSUE DISORD	1	(0.1%)
FEMALE REPRODUCTIVE	TOTAL	176	(14.2%)
	AMENORRHEA	1	(0.1%)
	GENITAL FEMALE DISORD, OTHER	125	(10.1%)
	INFERTILITY, FEMALE	4	(0.3%)
	MYCOSES	10	(0.8%)
	OPERATION, FEM GENITAL	11	(0.9%)
	PREGNANCY	8	(0.6%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
FEMALE REPRODUCTIVE	PREGNANCY, COMPLICATIONS	20	(1.6%)
	PROCEDURE, OBSTETRICAL	30	(2.4%)
	VAGINITIS	2	(0.2%)
FETUS	TOTAL	1	(0.1%)
	CONDITIONS, PERINATAL	1	(0.1%)
FLUID BALANCE	TOTAL	1	(0.1%)
	FLUID OVERLOAD	1	(0.1%)
GENERAL BODY OR SYS UNSPEC	TOTAL	4	(0.3%)
	MALAISE AND FATIGUE	2	(0.2%)
	PAIN, GENERAL	1	(0.1%)
	VIRAL INFECTION	1	(0.1%)
GENITOURINARY	TOTAL	19	(1.5%)
	GENITAL FEMALE	10	(0.8%)
	DISORD, OTHER		
	INFLAM PELVIC DIS	3	(0.2%)
	NEOPLASM, UNSPEC	1	(0.1%)
	URINARY TRACT	1	(0.1%)
	INFECT/PREGNANCY		
	VENEREAL DIS	1	(0.1%)
GLUCOSE	TOTAL	3	(0.2%)
	HYPOGLYCEMIA	1	(0.1%)
	PREGNANCY, COMPLICATIONS	2	(0.2%)
GUMS/PERIODONTIUM	TOTAL	4	(0.3%)
	PERIODONTAL DIS	2	(0.2%)
	TEETH DISORD	2	(0.2%)
HAIR	TOTAL	1	(0.1%)
	INFECT/PARASIT DIS, OTHER	1	(0.1%)
HEAD	TOTAL	158	(12.7%)
	HEADACHE	158	(12.7%)
HEART	TOTAL	12	(1.0%)
	ARRHYTHMIA	1	(0.1%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
HEART	CARDIAC MURMURS	5	(0.4%)
	HEART SOUNDS	1	(0.1%)
	PALPITATIONS	3	(0.2%)
	TACHYCARDIA, UNSPEC	3	(0.2%)
HEMATIC	TOTAL	2	(0.2%)
	COAGULATION DEFECTS	2	(0.2%)
INNER EAR	TOTAL	1	(0.1%)
	VESTIBULAR DISORD	1	(0.1%)
INTEGUMENTARY	TOTAL	1	(0.1%)
	VENEREAL DIS	1	(0.1%)
INTESTINES	TOTAL	1	(0.1%)
	INTEST MALABSORPTION	1	(0.1%)
JOINT	TOTAL	32	(2.6%)
	ARTHRITIS,	1	(0.1%)
	RHEUMATOID		
	ARTHROPATHY	5	(0.4%)
	CONG ANOM,	1	(0.1%)
	MUSCULOSKEL		
	DENTOFACIAL ANOM	1	(0.1%)
	DISLOCATION	1	(0.1%)
	JOINT DISORD, OTHER	2	(0.2%)
	JOINT, DERANGEMENT	5	(0.4%)
	OPERATION,	7	(0.6%)
	BONE/JOINT		
	OSTEOARTHRISIS	2	(0.2%)
	PAIN, JOINT	11	(0.9%)
KIDNEY	SPONDYLOPATHY,	2	(0.2%)
	INFLAM		
	TOTAL	7	(0.6%)
	CONG ANOM, GU	1	(0.1%)
	GLOMERULONEPHRITIS	2	(0.2%)
	KIDNEY INFECT	3	(0.2%)
LARGE INTESTINE	KIDNEY/URETER,	1	(0.1%)
	CALCULUS		
	TOTAL	18	(1.4%)
	CONSTIPATION	1	(0.1%)
	DIGESTIVE DISORD,	11	(0.9%)
	OTHER		
	ENTERITIS/COLITIS	2	(0.2%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
LARGE INTESTINE	INTEST DISORD, OTHER	2	(0.2%)
	OPERATION, INTEST	3	(0.2%)
	OPERATION, RECTUM/PERIRECT	1	(0.1%)
LARYNX	TOTAL	2	(0.2%)
	LARYNGITIS/TRACH, ACUTE	2	(0.2%)
LENS	TOTAL	3	(0.2%)
	VISUAL DISTURB	3	(0.2%)
LEUKOCYTES	TOTAL	4	(0.3%)
	EOSINOPHILIA	1	(0.1%)
	LEUKOPENIA	2	(0.2%)
	NEOPLASM MALIG, LYMPH/HEMAT	1	(0.1%)
LIGAMENT	TOTAL	1	(0.1%)
	OPERATION, BONE/JOINT	1	(0.1%)
	SPRAINS/STRAINS	1	(0.1%)
LIP	TOTAL	1	(0.1%)
	NEOPLASM MALIG, ORAL	1	(0.1%)
	OPERATION, NOSE/MOUTH	1	(0.1%)
LIPID	TOTAL	5	(0.4%)
	CHOLEST/TRIGLYCERIDE , ELEVATED	5	(0.4%)
LIVER	TOTAL	4	(0.3%)
	HEPATITIS	1	(0.1%)
	HEPATITIS, VIRAL	2	(0.2%)
	HEPATITS, VIRAL	1	(0.1%)
LOWER EXTREMITY	TOTAL	2	(0.2%)
	TRAUMA/INJURIES, UNSPEC	2	(0.2%)
LOWER PHARYNX	TOTAL	1	(0.1%)
	PAIN, THROAT	1	(0.1%)
LOWER URINARY TRACT	TOTAL	5	(0.4%)
	INCONTINENCE, STRESS	3	(0.2%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)
LOWER URINARY TRACT	INCONTINENCE, URINARY	1 (0.1%)
	OPERATION, OTHER URINARY	1 (0.1%)
LUNG	TOTAL	2 (0.2%)
	PNEUMONIA, OTHER	2 (0.2%)
METABOLIC/NUTRITIONAL/IMMUNE	TOTAL	12 (1.0%)
	BLOOD EXAM, ABN	1 (0.1%)
	OBESITY	10 (0.8%)
	WEIGHT LOSS	1 (0.1%)
MIDDLE EAR	TOTAL	8 (0.6%)
	EAR/MASTOID DISORD	1 (0.1%)
	OPERATION, EAR	3 (0.2%)
	OTITIS MEDIA	5 (0.4%)
MOUTH/OROPHARYNX	TOTAL	4 (0.3%)
	ORAL SOFT TISSUE DIS	1 (0.1%)
	TEETH DISORD	3 (0.2%)
MULTISYSTEMIC	TOTAL	23 (1.9%)
	ALLERGY, NEC	19 (1.5%)
	GENITAL FEMALE DISORD, OTHER	1 (0.1%)
	OPERATION, FEM GENITAL	1 (0.1%)
	PREGNANCY, COMPLICATIONS	1 (0.1%)
	VIRUS/CHLAMYD DIS, OTHER	2 (0.2%)
	TOTAL	9 (0.7%)
	CRAMP, LIMB	1 (0.1%)
MUSCLE	MYALGIA	4 (0.3%)
	SPASM, MUSCLE	4 (0.3%)
MUSCULAR/FASCIA	TOTAL	3 (0.2%)
	RHEUMATIC DISORD	2 (0.2%)
	SPRAINS/STRAINS	1 (0.1%)
MUSCULOSKELETAL	TOTAL	19 (1.5%)
	CONG ANOM, MUSCULOSKEL	1 (0.1%)
	DEFORMITY, ACQUIRED	1 (0.1%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
MUSCULOSKELETAL	JOINT DISORD, OTHER	3	(0.2%)
	OPERATION, BONE/JOINT	4	(0.3%)
	RHEUMATISM	1	(0.1%)
	SPRAINS/STRAINS	11	(0.9%)
MYOCARDIUM	TOTAL	1	(0.1%)
	MYOCARDITIS	1	(0.1%)
NAIL	TOTAL	1	(0.1%)
	MYCOSES	1	(0.1%)
NASOPHARYNX	TOTAL	30	(2.4%)
	NASOPHARYNGITIS, ACUTE	30	(2.4%)
NECK	TOTAL	5	(0.4%)
	CERVICAL DISORD, OTHER	1	(0.1%)
	PAIN, NECK	4	(0.3%)
NERVE	TOTAL	1	(0.1%)
	CERVICOBRACHIAL SYNDROME	1	(0.1%)
NERVOUS/SENSE ORGANS	TOTAL	2	(0.2%)
	DIZZINESS, POSTURAL	1	(0.1%)
	PARESTHESIA	1	(0.1%)
NON-ORGANIC	TOTAL	24	(1.9%)
	ANXIETY	2	(0.2%)
	DEPRESSION	16	(1.3%)
	MENTAL STATUS, IMPAIRED	1	(0.1%)
	NEUROSES	3	(0.2%)
	STRESS REACTION	2	(0.2%)
NOSE	TOTAL	57	(4.6%)
	EPISTAXIS	1	(0.1%)
	NASAL POLYPS	3	(0.2%)
	NASAL SEPTUM DEVIATED	1	(0.1%)
	OPERATION, NOSE/MOUTH	7	(0.6%)
	RHINITIS, ALLERGIC	46	(3.7%)
	RHINITIS,NOS	2	(0.2%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
ORGANIC	TOTAL	1	(0.1%)
	ALCOHOLIC DEPEND	1	(0.1%)
OVARY	TOTAL	12	(1.0%)
	GENITAL FEMALE DISORD, OTHER	8	(0.6%)
	OPERATION, FEM GENITAL	7	(0.6%)
PANCREAS/ENDOCRINE	TOTAL	3	(0.2%)
	DIABETES MELLITUS	2	(0.2%)
	HYPOGLYCEMIA	1	(0.1%)
PERITONEUM	TOTAL	1	(0.1%)
	PERITONEAL DISORD, OTHER	1	(0.1%)
PLATELETS	TOTAL	2	(0.2%)
	THROMBOCYTOPENIA	2	(0.2%)
PLEURA	TOTAL	1	(0.1%)
	OPERATION, RESP	1	(0.1%)
PSYCHOLOGICAL DISORDERS	TOTAL	6	(0.5%)
	NERVOUSNESS	1	(0.1%)
	PREGNANCY, COMPLICATIONS	4	(0.3%)
	TOBACCO USE	1	(0.1%)
REGION	TOTAL	7	(0.6%)
	PAIN, ABDOMINO-PELVIC	1	(0.1%)
	PAIN, LIMB	4	(0.3%)
	SWELLING/MASS, HEAD, NECK	2	(0.2%)
	TRAUMA/INJURIES, UNSPEC	1	(0.1%)
RESPIRATORY	TOTAL	23	(1.9%)
	COUGH	2	(0.2%)
	HYPERVENTILATION	1	(0.1%)
	INFLUENZA	19	(1.5%)
	RESP DIS, OTHER	1	(0.1%)
SALIVARY GLAND	TOTAL	1	(0.1%)
	DRY MOUTH	1	(0.1%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
SEBACEOUS GLAND	TOTAL	8	(0.6%)
	SKIN/SUBCUT DISORD, OTHER	8	(0.6%)
SHOULDER	TOTAL	3	(0.2%)
	RHEUMATIC DISORD	3	(0.2%)
SINUS	TOTAL	13	(1.0%)
	OPERATION, NOSE/MOUTH	2	(0.2%)
	SINUSITIS, CHRONIC	1	(0.1%)
	SINUSITIS, OTHER	3	(0.2%)
	SINUSITIS, NOS	7	(0.6%)
SKELETAL	TOTAL	2	(0.2%)
	BONE/CARTIL DISORD, OTHER	1	(0.1%)
	DENTOFACIAL ANOM	1	(0.1%)
SKIN	TOTAL	54	(4.3%)
	INFLAM SKIN/SUBCUT	36	(2.9%)
	MYCOSES	2	(0.2%)
	NEOPLASMS BENIGN	1	(0.1%)
	OPERATION, SKIN/SUBCUT	6	(0.5%)
	PRURITUS DISORD, UNSPEC	1	(0.1%)
	RASH/OTHER SKIN ERUPTION	2	(0.2%)
	SKIN/SUBCUT DISORD, OTHER	3	(0.2%)
	URTICARIA	6	(0.5%)
SPINAL CORD	TOTAL	1	(0.1%)
	OPERATION, CNS	1	(0.1%)
SPINAL NERVE	TOTAL	4	(0.3%)
	PERIPH NERV SYST DISORD	4	(0.3%)
STOMACH	TOTAL	7	(0.6%)
	DYSPEPSIA	5	(0.4%)
	OPERATION/STOMACH	1	(0.1%)
	ULCER, GASTRIC	1	(0.1%)
SWEAT GLAND	TOTAL	1	(0.1%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
SWEAT GLAND	HYPERHIDROSIS	1	(0.1%)
SYS UNSPEC	TOTAL	26	(2.1%)
	ALLERGIC REACTION, FOOD	9	(0.7%)
	BACT DIS, OTHER	1	(0.1%)
	EDEMA	3	(0.2%)
	GENITAL FEMALE DISORD, OTHER	1	(0.1%)
	INFECT/PARASIT DIS, OTHER	1	(0.1%)
	MYCOSES	2	(0.2%)
	OPERATION, HERNIA REPAIR	1	(0.1%)
	OPERATION, SOFT TISSUE	2	(0.2%)
	PROCEDURE, SURGERY UNSP	3	(0.2%)
	PSYCHOGENIC PHYSIOL DYSFUNC	1	(0.1%)
	VIRAL DIS/EXANTHEM	2	(0.2%)
TEETH	TOTAL	2	(0.2%)
	OPERATION, NOSE/MOUTH	2	(0.2%)
TENDON	TOTAL	2	(0.2%)
	OPERATION, MUSCLE/TENDON	2	(0.2%)
THORAX	TOTAL	7	(0.6%)
	NEOPLASMS BENIGN	2	(0.2%)
	PAIN UNSP, CHEST	1	(0.1%)
	PNEUMOTHORAX	4	(0.3%)
THYROID GLAND	TOTAL	30	(2.4%)
	GOITER	4	(0.3%)
	HYPERTHYROIDISM	1	(0.1%)
	HYPOTHYROIDISM	18	(1.4%)
	OPERATION, ENDOCR	2	(0.2%)
	THYROID DISORD, OTHER	3	(0.2%)
	THYROID FUNCTION, ABN	1	(0.1%)
	THYROIDITIS	1	(0.1%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
TONSILS/ADENOIDS	TOTAL	31	(2.5%)
	OPERATION, NOSE/MOUTH	31	(2.5%)
UPPER RESPIRATORY TRACT	TOTAL	23	(1.9%)
	CONGEN ANOM, HEAD/NECK	1	(0.1%)
	INFECTION, BACTERIAL	3	(0.2%)
	PHARYNGITIS, ACUTE	8	(0.6%)
	UPPER RESP DIS, OTHER	3	(0.2%)
	UPPER RESP DISORD, OTHER	2	(0.2%)
	UPPER RESP INFECT, ACUTE	7	(0.6%)
UPPER URINARY TRACT	TOTAL	1	(0.1%)
	OPERATION, KIDNEY	1	(0.1%)
URETER	TOTAL	1	(0.1%)
	CONG ANOM, GU	1	(0.1%)
	OPERATION, OTHER URINARY	1	(0.1%)
URETHRA	TOTAL	3	(0.2%)
	OPERATION, OTHER URINARY	1	(0.1%)
	URETHRAL DISORD	1	(0.1%)
	URETHRITIS	1	(0.1%)
URINARY TRACT	TOTAL	14	(1.1%)
	URINARY TRACT INFECTION	14	(1.1%)
UTERUS	TOTAL	12	(1.0%)
	GENITAL FEMALE DISORD, OTHER	2	(0.2%)
	INFLAM PELVIC DIS	2	(0.2%)
	NEOPLASMS BENIGN	3	(0.2%)
	OPERATION, FEM GENITAL	7	(0.6%)
VAGINA	TOTAL	7	(0.6%)
	GENITAL FEMALE DISORD, OTHER	2	(0.2%)

Table 12.18

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Treatment Group No Therapy Dispensed (N=1242)	
VAGINA	OPERATION, FEM GENITAL	5	(0.4%)
VALVE	TOTAL	2	(0.2%)
	MITRAL VALVE DISORD	1	(0.1%)
	VALVULAR HEART DISEASE, NOS	1	(0.1%)
VASCULAR	TOTAL	2	(0.2%)
	PULM EMBOLISM AND INFARCT	2	(0.2%)
VEIN	TOTAL	14	(1.1%)
	EMBOLISM/THROMBOSIS, VENOUS	2	(0.2%)
	HEMORRHOIDS	2	(0.2%)
	OPERATION, OTHER VESSELS	7	(0.6%)
	PHLEBITIS	1	(0.1%)
	PREGNANCY, COMPLICATIONS	1	(0.1%)
	VARICES	2	(0.2%)
VITAMINS/MINERALS	TOTAL	6	(0.5%)
	VITAMIN B DEFIC	3	(0.2%)
	VITAMIN DEFIC, OTHER	3	(0.2%)

Table 12.19

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Randomised (non-ITT) Population

Body System	Preferred Term	Treatment Group			Total (N=7)
		Paroxetine CR 25 mg (N=3)	Paroxetine CR 12.5 mg (N=1)	Placebo (N=3)	
TOTAL	TOTAL	3 (100.0%)	1 (100.0%)	2 (66.7%)	6 (85.7%)
ABDOMEN	TOTAL	2 (66.7%)	1 (100.0%)	0 (0.0%)	3 (42.9%)
	HERNIA, ABDOMINAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	PAIN, ABDOMINO-PELVIC	1 (33.3%)	1 (100.0%)	0 (0.0%)	2 (28.6%)
BRONCHUS	TOTAL	1 (33.3%)	1 (100.0%)	0 (0.0%)	2 (28.6%)
	ASTHMA	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (14.3%)
	BRONCHITIS, OTHER	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
CAUSES OF INJURY	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	ADVERSE EFF/PSYCHOTROPICS	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
FALLOPIAN TUBE	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	OPERATION, FEM GENITAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
FEMALE REPRODUCTIVE	TOTAL	3 (100.0%)	0 (0.0%)	0 (0.0%)	3 (42.9%)
	GENITAL FEMALE DISORD, OTHER	2 (66.7%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	PREGNANCY, COMPLICATIONS	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
GENERAL BODY OR SYS UNSPEC	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	PAIN, GENERAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
HEAD	TOTAL	2 (66.7%)	0 (0.0%)	1 (33.3%)	3 (42.9%)
	HEADACHE	2 (66.7%)	0 (0.0%)	1 (33.3%)	3 (42.9%)
MIDDLE EAR	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	OTITIS MEDIA	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
MULTISYSTEMIC	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	ALLERGY, NEC	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
NASOPHARYNX	TOTAL	2 (66.7%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	NASOPHARYNGITIS, ACUTE	2 (66.7%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
NERVOUS/SENSE ORGANS	TOTAL	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)

Table 12.19

Significant Medical / Surgical History and Physical Examination
Prior and Active Conditions Ordered by Body System and Preferred Term
Randomised (non-ITT) Population

Body System	Preferred Term	Treatment Group			Total (N=7)
		Paroxetine CR 25 mg (N=3)	Paroxetine CR 12.5 mg (N=1)	Placebo (N=3)	
NOSE	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	OPERATION, NOSE/MOUTH	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
OVARY	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	OPERATION, FEM GENITAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
RESPIRATORY	TOTAL	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	INFECTION, RESP	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
SEBACEOUS GLAND	TOTAL	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	SKIN/SUBCUT DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
SKIN	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	INFLAM SKIN/SUBCUT	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
URINARY TRACT	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	URINARY TRACT INFECTION	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	TOTAL	93 (80.2%)	103 (79.2%)	103 (85.8%)	299 (81.7%)	
ABDOMEN	TOTAL	8 (6.9%)	10 (7.7%)	11 (9.2%)	29 (7.9%)	
	HERNIA, ABDOMINAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	OPERATION, HERNIA REPAIR	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)	
	OPERATION, OTHER ABDOM	3 (2.6%)	3 (2.3%)	6 (5.0%)	12 (3.3%)	
	PAIN, ABDOMINO-PELVIC	5 (4.3%)	7 (5.4%)	4 (3.3%)	16 (4.4%)	
ADNEXA	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	INFLAM PELVIC DIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
APPENDIX	TOTAL	6 (5.2%)	12 (9.2%)	10 (8.3%)	28 (7.7%)	
	APPENDICITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	OPERATION, APPENDIX	6 (5.2%)	12 (9.2%)	9 (7.5%)	27 (7.4%)	
ARTERY	TOTAL	10 (8.6%)	10 (7.7%)	11 (9.2%)	31 (8.5%)	
	ARTERIAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	MIGRAINE	10 (8.6%)	9 (6.9%)	11 (9.2%)	30 (8.2%)	
ARTICULAR	TOTAL	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)	
	INTERVERTEB DISC, ABN	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)	
BACK	TOTAL	7 (6.0%)	5 (3.8%)	5 (4.2%)	17 (4.6%)	
	BACK PAIN	7 (6.0%)	5 (3.8%)	5 (4.2%)	17 (4.6%)	
BILIARY TRACT	TOTAL	3 (2.6%)	5 (3.8%)	5 (4.2%)	13 (3.6%)	
	CHOLELITHIASIS	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)	
	OPERATION, GB	3 (2.6%)	5 (3.8%)	5 (4.2%)	13 (3.6%)	
BLADDER	TOTAL	2 (1.7%)	4 (3.1%)	0 (0.0%)	6 (1.6%)	
	CYSTITIS	2 (1.7%)	4 (3.1%)	0 (0.0%)	6 (1.6%)	
BONE	TOTAL	2 (1.7%)	3 (2.3%)	5 (4.2%)	10 (2.7%)	
	BONE/CARTIL DISORD, OTHER	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)	
	FRACTURE, LOWER LIMB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	FRACTURE, UPPER LIMB	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)	
	JAW DIS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)	
	NEOPLASM MALIG, BONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
BONE	OPERATION, BONE/JOINT	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
BRAIN	TOTAL	1 (0.9%)	3 (2.3%)	2 (1.7%)	6 (1.6%)
	INSOMNIA	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
	VIRAL DIS/EXANTHEM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BREAST	TOTAL	7 (6.0%)	3 (2.3%)	3 (2.5%)	13 (3.6%)
	BREAST DISORD	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
	NEOPLASMS BENIGN	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	OPERATION, BREAST	4 (3.4%)	2 (1.5%)	3 (2.5%)	9 (2.5%)
BREAST/MAMMARY GLAND	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OPERATION, BREAST	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
BRONCHUS	TOTAL	6 (5.2%)	6 (4.6%)	6 (5.0%)	18 (4.9%)
	ASTHMA	5 (4.3%)	4 (3.1%)	5 (4.2%)	14 (3.8%)
	BRONCHITIS, ACUTE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	BRONCHITIS, CHRONIC	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	BRONCHITIS, OTHER	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
CARDIOVASCULAR	TOTAL	4 (3.4%)	2 (1.5%)	2 (1.7%)	8 (2.2%)
	BLOOD PRESSURE, DECREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYPERTENSION	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	HYPOTENSION, OTHER	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	SYNCOPE AND COLLAPSE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CAUSES OF INJURY	TOTAL	4 (3.4%)	9 (6.9%)	3 (2.5%)	16 (4.4%)
	ACCIDENT/MOTOR VEHICLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/ANALGESIC	0 (0.0%)	2 (1.5%)	2 (1.7%)	4 (1.1%)
	ADVERSE EFF/ANTI-INFECT	2 (1.7%)	4 (3.1%)	1 (0.8%)	7 (1.9%)
	ADVERSE EFF/ANTIBIOTIC	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
	ADVERSE EFF/HORMONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/OTHER DRUG	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/PSYCHOTROPICS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/SYST AGENT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SUICIDE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CENTRAL NERVOUS	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	CEREBRAL PALSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HEMORRHAGE, INTRACRANIAL OPERATION, CNS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
		0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CEREBRAL CORTEX	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	CONVULSIONS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	EPILEPSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CERVIX	TOTAL	7 (6.0%)	7 (5.4%)	12 (10.0%)	26 (7.1%)
	GENITAL FEMALE DISORD, OTHER OPERATION, FEM GENITAL	1 (0.9%)	6 (4.6%)	3 (2.5%)	10 (2.7%)
	PAP SMEAR, ABN	7 (6.0%)	2 (1.5%)	10 (8.3%)	19 (5.2%)
		1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
CONJUNCTIVA	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CONJUNCTIVAL DISORD	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CORNEA	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPERATION, EYE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CRANIAL NERVE	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	PERIPH NERV SYST DISORD	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
DIAGNOSTIC/THERAPEUT IC PROCS	TOTAL	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
	EVALUATION, DX EXAM	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	RADIOLOGY, DIAGNOSTIC	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
DIGESTIVE	TOTAL	6 (5.2%)	6 (4.6%)	6 (5.0%)	18 (4.9%)
	DIARRHEA	1 (0.9%)	2 (1.5%)	3 (2.5%)	6 (1.6%)
	ENTERITIS/COLITIS	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	FLATULENCE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	GASTRITIS/DUODENITIS	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
	HEARTBURN	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	NAUSEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	STOMACH/DUODENUM DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
		0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
EAR/AUDITION, NOS	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HEARING LOSS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ENZYME	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TRANSAMINASE/LDH, ELEVATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ERYTHROCYTES	TOTAL	1 (0.9%)	4 (3.1%)	6 (5.0%)	11 (3.0%)
	ANEMIA, IRON DEFIC	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	ANEMIA, OTHER	1 (0.9%)	4 (3.1%)	2 (1.7%)	7 (1.9%)
	ANEMIA, PERNICIOUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ARTHROPOD-BORNE DIS, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ESOPHAGUS	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ESOPHAGITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EXTERNAL EAR	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPERATION, EAR	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EXTRAOCULAR MUSCLES	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPERATION, EYE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EYE/VISION, NOS	TOTAL	2 (1.7%)	3 (2.3%)	2 (1.7%)	7 (1.9%)
	EYE DISORD, OTHER	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	OPERATION, EYE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	VISUAL DISTURB	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FACTORS INFLUENCING HEALTH	TOTAL	2 (1.7%)	5 (3.8%)	11 (9.2%)	18 (4.9%)
	MANAGEMENT, CONTRACEPTIVE	1 (0.9%)	5 (3.8%)	8 (6.7%)	14 (3.8%)
	MANAGEMENT, PROCREATIVE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NEED/OTHER PROPHYLAXIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PROCEDURES, REHAB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SUPERVISION/PREG	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FALLOPIAN TUBE	TOTAL	11 (9.5%)	17 (13.1%)	13 (10.8%)	41 (11.2%)
	OPERATION, FEM GENITAL	11 (9.5%)	17 (13.1%)	13 (10.8%)	41 (11.2%)
FEMALE REPRODUCTIVE	TOTAL	41 (35.3%)	43 (33.1%)	32 (26.7%)	116 (31.7%)
	AMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	GENITAL FEMALE DISORD, OTHER	27 (23.3%)	24 (18.5%)	18 (15.0%)	69 (18.9%)
	MYCOSES	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
FEMALE REPRODUCTIVE	OPERATION, FEM GENITAL	8 (6.9%)	3 (2.3%)	5 (4.2%)	16 (4.4%)
	PREGNANCY	3 (2.6%)	3 (2.3%)	1 (0.8%)	7 (1.9%)
	PREGNANCY, COMPLICATIONS	2 (1.7%)	5 (3.8%)	7 (5.8%)	14 (3.8%)
	PROCEDURE, OBSTETRICAL	5 (4.3%)	11 (8.5%)	6 (5.0%)	22 (6.0%)
	VAGINITIS	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
FETUS	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PREGNANCY, COMPLICATIONS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GENERAL BODY OR SYS UNSPEC	TOTAL	5 (4.3%)	5 (3.8%)	3 (2.5%)	13 (3.6%)
	MALAISE AND FATIGUE	3 (2.6%)	2 (1.5%)	0 (0.0%)	5 (1.4%)
	PAIN, GENERAL	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	PYREXIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VIRAL INFECTION	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	VIRUS/CHLAMYD DIS, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GENITOURINARY	TOTAL	4 (3.4%)	0 (0.0%)	1 (0.8%)	5 (1.4%)
	GENITAL FEMALE DISORD, OTHER	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	NEOPLASM, UNSPEC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	VIRAL DIS/EXANTHEM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
GLUCOSE	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	PREGNANCY, COMPLICATIONS	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
GUMS/PERIODONTIUM	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	OPERATION, NOSE/MOUTH	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TEETH DISORD	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HAIR	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ALOPECIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HEAD	TOTAL	38 (32.8%)	34 (26.2%)	30 (25.0%)	102 (27.9%)
	HEADACHE	38 (32.8%)	34 (26.2%)	30 (25.0%)	102 (27.9%)
HEART	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	CARDIAC MURMURS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
HEART	EXTRASYSTOLES	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
INNER EAR	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VESTIBULAR DISORD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
INTESTINES	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	INTEST OBSTRUCTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
JOINT	TOTAL	9 (7.8%)	7 (5.4%)	5 (4.2%)	21 (5.7%)
	ARTHRITIS, RHEUMATOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ARTHROPATHY	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	DEFORMITY, ACQUIRED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DENTOFACIAL ANOM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OPERATION, BONE/JOINT	5 (4.3%)	7 (5.4%)	2 (1.7%)	14 (3.8%)
	OSTEOARTHROSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PAIN, JOINT	3 (2.6%)	0 (0.0%)	2 (1.7%)	5 (1.4%)
KIDNEY	TOTAL	0 (0.0%)	3 (2.3%)	3 (2.5%)	6 (1.6%)
	KIDNEY DISORD	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	KIDNEY INFECT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	KIDNEY/URETER, CALCULUS	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
LARGE INTESTINE	TOTAL	5 (4.3%)	2 (1.5%)	0 (0.0%)	7 (1.9%)
	CONSTIPATION	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
	DIGESTIVE DISORD, OTHER	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
	ENTERITIS/COLITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LENS	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	VISUAL DISTURB	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LEUKOCYTES	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	LEUKOPENIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LIGAMENT	TOTAL	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	OPERATION, BONE/JOINT	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SOFT TISSUE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SPRAINS/STRAINS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LIP	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
LIP	OPERATION, NOSE/MOUTH	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ORAL SOFT TISSUE DIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LIVER	TOTAL	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
	HEPATITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HEPATITIS, VIRAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	INJURY, CHEST/ABD/PELV	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LOWER EXTREMITY	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CONG ANOM, MUSCULOSKEL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LOWER PHARYNX	TOTAL	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	PAIN, THROAT	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
LUNG	TOTAL	4 (3.4%)	0 (0.0%)	3 (2.5%)	7 (1.9%)
	PNEUMONIA, OTHER	4 (3.4%)	0 (0.0%)	3 (2.5%)	7 (1.9%)
LYMPH NODE	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	BLOOD DIS, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
MENINGES	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MENINGITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
METABOLIC/NUTRITIONA L/IMMUNE	TOTAL	0 (0.0%)	1 (0.8%)	3 (2.5%)	4 (1.1%)
	ANOREXIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OBESITY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	POLYDIPSIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	WEIGHT LOSS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MIDDLE EAR	TOTAL	1 (0.9%)	3 (2.3%)	2 (1.7%)	6 (1.6%)
	EAR/MASTOID DISORD	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	OPERATION, EAR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OTITIS MEDIA	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
MOUTH/OROPHARYNX	TOTAL	1 (0.9%)	0 (0.0%)	3 (2.5%)	4 (1.1%)
	OPERATION, NOSE/MOUTH	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TEETH DISORD	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
MULTISYSTEMIC	TOTAL	4 (3.4%)	9 (6.9%)	8 (6.7%)	21 (5.7%)
	ALLERGY, NEC	3 (2.6%)	5 (3.8%)	6 (5.0%)	14 (3.8%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
MULTISYSTEMIC	OPERATION, CNS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PREGNANCY, COMPLICATIONS	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
	TYPHOID INFECT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	VIRUS/CHLAMYD DIS, OTHER	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MUSCLE	TOTAL	3 (2.6%)	3 (2.3%)	3 (2.5%)	9 (2.5%)
	CERVICAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MYALGIA	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	SPASM, MUSCLE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
MUSCULAR/FASCIA	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	OPERATION, MUSCLE/TENDON	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	RHEUMATIC DISORD	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
MUSCULOSKELETAL	TOTAL	1 (0.9%)	3 (2.3%)	4 (3.3%)	8 (2.2%)
	DEFORMITY, ACQUIRED	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	JOINT DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPERATION, BONE/JOINT	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)
	SPRAINS/STRAINS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NASOPHARYNX	TOTAL	7 (6.0%)	9 (6.9%)	5 (4.2%)	21 (5.7%)
	NASOPHARYNGITIS, ACUTE	7 (6.0%)	9 (6.9%)	5 (4.2%)	21 (5.7%)
NECK	TOTAL	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	PAIN, NECK	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
NERVE	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	INJURY, NERV, SP CD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NEURALGIA, BACK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NERVOUS/SENSE ORGANS	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PARESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NON-ORGANIC	TOTAL	4 (3.4%)	7 (5.4%)	6 (5.0%)	17 (4.6%)
	ANXIETY	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	DEPRESSION	3 (2.6%)	6 (4.6%)	5 (4.2%)	14 (3.8%)
	NEUROSES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	STRESS REACTION	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
NOSE	TOTAL	11 (9.5%)	10 (7.7%)	9 (7.5%)	30 (8.2%)
	NASAL POLYPS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OPERATION, NOSE/MOUTH	2 (1.7%)	3 (2.3%)	2 (1.7%)	7 (1.9%)
	RHINITIS, ALLERGIC	9 (7.8%)	7 (5.4%)	7 (5.8%)	23 (6.3%)
	RHINITIS,NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
OVARY	TOTAL	4 (3.4%)	3 (2.3%)	4 (3.3%)	11 (3.0%)
	GENITAL FEMALE DISORD, OTHER	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)
	OPERATION, FEM GENITAL	3 (2.6%)	2 (1.5%)	2 (1.7%)	7 (1.9%)
PANCREAS/ENDOCRINE	TOTAL	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	DIABETES MELLITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
PSYCHOLOGICAL DISORDERS	TOTAL	5 (4.3%)	2 (1.5%)	2 (1.7%)	9 (2.5%)
	ANOREXIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NERVOUSNESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PREGNANCY, COMPLICATIONS	3 (2.6%)	1 (0.8%)	1 (0.8%)	5 (1.4%)
	TOBACCO USE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
REGION	TOTAL	0 (0.0%)	6 (4.6%)	0 (0.0%)	6 (1.6%)
	PAIN, LIMB	0 (0.0%)	5 (3.8%)	0 (0.0%)	5 (1.4%)
	TRAUMA/INJURIES, UNSPEC	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
RESPIRATORY	TOTAL	14 (12.1%)	7 (5.4%)	7 (5.8%)	28 (7.7%)
	COUGH	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	INFECTION, RESP	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	INFLUENZA	13 (11.2%)	5 (3.8%)	4 (3.3%)	22 (6.0%)
SEBACEOUS GLAND	TOTAL	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)
	SKIN/SUBCUT DISORD, OTHER	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)
SHOULDER	TOTAL	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	RHEUMATIC DISORD	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
SINUS	TOTAL	3 (2.6%)	3 (2.3%)	4 (3.3%)	10 (2.7%)
	OPERATION, NOSE/MOUTH	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SINUSITIS, CHRONIC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
SINUS	SINUSITIS,NOS	3 (2.6%)	3 (2.3%)	3 (2.5%)	9 (2.5%)
SKELETAL	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	BACK DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	BONE/CARTIL DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SKIN	TOTAL	7 (6.0%)	8 (6.2%)	10 (8.3%)	25 (6.8%)
	CARBUNCLE/FURUNCLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	INFLAM SKIN/SUBCUT	3 (2.6%)	5 (3.8%)	6 (5.0%)	14 (3.8%)
	NEOPLASM MALIG, SKIN	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	OPERATION, SKIN/SUBCUT	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	PRURITUS DISORD, UNSPEC	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	RASH/OTHER SKIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ERUPTION	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	SKIN/SUBCUT DISORD, OTHER	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	VIRUS/CHLAMYD DIS, OTHER	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SPINAL CORD	INJURY, NERV, SP CD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SPINAL NERVE	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	OPERATION, CNS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PERIPH NERV SYST DISORD	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
STOMACH	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	DYSPEPSIA	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	OPERATION/STOMACH	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SWEAT GLAND	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SKIN/SUBCUT DISORD, OTHER	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SYS UNSPEC	TOTAL	6 (5.2%)	5 (3.8%)	5 (4.2%)	16 (4.4%)
	ALLERGIC REACTION, FOOD	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
	COMPLIC OF MED CARE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	EDEMA	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	MYCOSES	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
SYS UNSPEC	OPERATION, HERNIA REPAIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PROCEDURE, SURGERY UNSP	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	VIRAL DIS/EXANTHEM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TEETH	TOTAL	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	OPERATION, NOSE/MOUTH	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
THORAX	TOTAL	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	PAIN UNSP, CHEST	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	PNEUMOTHORAX	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
THYROID GLAND	TOTAL	2 (1.7%)	3 (2.3%)	4 (3.3%)	9 (2.5%)
	GOITER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYPERTHYROIDISM	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	HYPOTHYROIDISM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	OPERATION, ENDOCR	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	THYROID DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	THYROIDITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TONSILS/ADENOIDS	TOTAL	8 (6.9%)	17 (13.1%)	12 (10.0%)	37 (10.1%)
	OPERATION, NOSE/MOUTH	7 (6.0%)	17 (13.1%)	12 (10.0%)	36 (9.8%)
	TONSILLITIS, ACUTE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
UPPER EXTREMITY	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CELLULITIS/ABSCCESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
UPPER RESPIRATORY TRACT	TOTAL	0 (0.0%)	5 (3.8%)	3 (2.5%)	8 (2.2%)
	PHARYNGITIS, ACUTE	0 (0.0%)	4 (3.1%)	0 (0.0%)	4 (1.1%)
	UPPER RESP DISORD, OTHER	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	UPPER RESP INFECT, ACUTE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
UPPER URINARY TRACT	OPERATION, KIDNEY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
URETHRA	OPERATION, OTHER URINARY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)

Table 12.20

Significant Medical / Surgical History and Physical Examination
Prior Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
URETHRA	URETHRAL DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
URINARY TRACT	TOTAL	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
	URINARY TRACT INFECTION	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
URINE	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HEMATURIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
UTERUS	TOTAL	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
	CONG ANOM, GU	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	NEOPLASMS BENIGN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OPERATION, FEM GENITAL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
VAGINA	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	OPERATION, FEM GENITAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VALVE	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MITRAL VALVE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VASCULAR	TOTAL	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	HEMORRHAGE, UNSPEC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	NEOPLASMS BENIGN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	OPERATION, OTHER VESSELS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PULM EMBOLISM AND INFARCT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VEIN	TOTAL	3 (2.6%)	1 (0.8%)	2 (1.7%)	6 (1.6%)
	HEMORRHOIDS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPERATION, ANUS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OPERATION, OTHER VESSELS	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
VITAMINS/MINERALS	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	VITAMIN DEFIC, OTHER	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
VULVA	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	INFLAM PELVIC DIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TOTAL	93 (80.2%)	103 (79.2%)	103 (85.8%)	299 (81.7%)
HEADACHE	38 (32.8%)	34 (26.2%)	30 (25.0%)	102 (27.9%)
GENITAL FEMALE DISORD, OTHER	31 (26.7%)	29 (22.3%)	23 (19.2%)	83 (22.7%)
OPERATION, FEM GENITAL	25 (21.6%)	23 (17.7%)	28 (23.3%)	76 (20.8%)
OPERATION, NOSE/MOUTH	9 (7.8%)	21 (16.2%)	17 (14.2%)	47 (12.8%)
MIGRAINE	10 (8.6%)	9 (6.9%)	11 (9.2%)	30 (8.2%)
OPERATION, APPENDIX	6 (5.2%)	12 (9.2%)	9 (7.5%)	27 (7.4%)
PREGNANCY, COMPLICATIONS	5 (4.3%)	10 (7.7%)	8 (6.7%)	23 (6.3%)
RHINITIS, ALLERGIC	9 (7.8%)	7 (5.4%)	7 (5.8%)	23 (6.3%)
INFLUENZA	13 (11.2%)	5 (3.8%)	4 (3.3%)	22 (6.0%)
PROCEDURE, OBSTETRICAL	5 (4.3%)	11 (8.5%)	6 (5.0%)	22 (6.0%)
NASOPHARYNGITIS, ACUTE	7 (6.0%)	9 (6.9%)	5 (4.2%)	21 (5.7%)
OPERATION, BONE/JOINT	6 (5.2%)	10 (7.7%)	5 (4.2%)	21 (5.7%)
BACK PAIN	7 (6.0%)	5 (3.8%)	5 (4.2%)	17 (4.6%)
PAIN, ABDOMINO-PELVIC	5 (4.3%)	7 (5.4%)	4 (3.3%)	16 (4.4%)
ALLERGY, NEC	3 (2.6%)	5 (3.8%)	6 (5.0%)	14 (3.8%)
ASTHMA	5 (4.3%)	4 (3.1%)	5 (4.2%)	14 (3.8%)
DEPRESSION	3 (2.6%)	6 (4.6%)	5 (4.2%)	14 (3.8%)
INFLAM SKIN/SUBCUT	3 (2.6%)	5 (3.8%)	6 (5.0%)	14 (3.8%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
MANAGEMENT, CONTRACEPTIVE	1 (0.9%)	5 (3.8%)	8 (6.7%)	14 (3.8%)
OPERATION, GB	3 (2.6%)	5 (3.8%)	5 (4.2%)	13 (3.6%)
OPERATION, OTHER ABDOM	3 (2.6%)	3 (2.3%)	6 (5.0%)	12 (3.3%)
OPERATION, BREAST	5 (4.3%)	2 (1.5%)	3 (2.5%)	10 (2.7%)
SINUSITIS, NOS	3 (2.6%)	3 (2.3%)	3 (2.5%)	9 (2.5%)
SKIN/SUBCUT DISORD, OTHER	3 (2.6%)	4 (3.1%)	1 (0.8%)	8 (2.2%)
ADVERSE EFF/ANTI-INFECT	2 (1.7%)	4 (3.1%)	1 (0.8%)	7 (1.9%)
ANEMIA, OTHER	1 (0.9%)	4 (3.1%)	2 (1.7%)	7 (1.9%)
PNEUMONIA, OTHER	4 (3.4%)	0 (0.0%)	3 (2.5%)	7 (1.9%)
PREGNANCY	3 (2.6%)	3 (2.3%)	1 (0.8%)	7 (1.9%)
CYSTITIS	2 (1.7%)	4 (3.1%)	0 (0.0%)	6 (1.6%)
DIARRHEA	1 (0.9%)	2 (1.5%)	3 (2.5%)	6 (1.6%)
OPERATION, HERNIA REPAIR	2 (1.7%)	2 (1.5%)	2 (1.7%)	6 (1.6%)
ADVERSE EFF/ANTIBIOTIC	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
INSOMNIA	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
INTERVERTEB DISC, ABN	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)
MALaise AND FATIGUE	3 (2.6%)	2 (1.5%)	0 (0.0%)	5 (1.4%)
OPERATION, EYE	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)
OPERATION, OTHER VESSELS	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
PAIN, JOINT	3 (2.6%)	0 (0.0%)	2 (1.7%)	5 (1.4%)
PAIN, LIMB	0 (0.0%)	5 (3.8%)	0 (0.0%)	5 (1.4%)
RHEUMATIC DISORD	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)
URINARY TRACT INFECTION	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
VIRUS/CHLAMYD DIS, OTHER	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)
ADVERSE EFF/ANALGESIC	0 (0.0%)	2 (1.5%)	2 (1.7%)	4 (1.1%)
ALLERGIC REACTION, FOOD	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
BRONCHITIS, OTHER	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
DEFORMITY, ACQUIRED	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
FRACTURE, UPPER LIMB	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
GASTRITIS/DUODENITIS	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
HYPERTENSION	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
MYALGIA	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
MYCOSES	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
NEOPLASMS BENIGN	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
OPERATION, SKIN/SUBCUT	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
PERIPH NERV SYST DISORD	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
PHARYNGITIS, ACUTE	0 (0.0%)	4 (3.1%)	0 (0.0%)	4 (1.1%)
SPASM, MUSCLE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
TEETH DISORD	1 (0.9%)	0 (0.0%)	3 (2.5%)	4 (1.1%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
VAGINITIS	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
BREAST DISORD	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
CHOLELITHIASIS	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
COMPLIC OF MED CARE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
CONSTIPATION	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
COUGH	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
DIABETES MELLITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
DIGESTIVE DISORD, OTHER	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
EDEMA	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
ENTERITIS/COLITIS	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
EYE DISORD, OTHER	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
HEARTBURN	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
INFECTION, RESP	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
KIDNEY/URETER, CALCULUS	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
OTITIS MEDIA	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
PAIN, GENERAL	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
PAIN, NECK	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
PAP SMEAR, ABN	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
VIRAL DIS/EXANTHEM	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
VIRAL INFECTION	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
ANEMIA, IRON DEFIC	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
ANOREXIA	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ANXIETY	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
BONE/CARTIL DISORD, OTHER	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
CARDIAC MURMURS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
DYSPEPSIA	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
EAR/MASTOID DISORD	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
EVALUATION, DX EXAM	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
HYPERTHYROIDISM	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
HYPOTENSION, OTHER	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
HYPOTHYROIDISM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
INFLAM PELVIC DIS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
INJURY, NERV, SP CD	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
JAW DIS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
KIDNEY DISORD	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
NAUSEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
NEOPLASM MALIG, SKIN	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
OPERATION, CNS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
OPERATION, EAR	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
OPERATION, ENDOCR	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
PAIN UNSP, CHEST	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
PAIN, THROAT	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
PROCEDURE, SURGERY UNSP	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
PRURITUS DISORD, UNSPEC	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
RADIOLOGY, DIAGNOSTIC	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
SPRAINS/STRAINS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
STRESS REACTION	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
SUICIDE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
TOBACCO USE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
TONSILLITIS, ACUTE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
UPPER RESP DISORD, OTHER	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
UPPER RESP INFECT, ACUTE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
VISUAL DISTURB	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
VITAMIN DEFIC, OTHER	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
ACCIDENT/MOTOR VEHICLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/HORMONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/OTHER DRUG	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/PSYCHOTROPICS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/SYST AGENT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ALOPECIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
AMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ANEMIA, PERNICIOUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
APPENDICITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ARTERIAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ARTHRITIS, RHEUMATOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ARTHROPATHY	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ARTHROPOD-BORNE DIS, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BACK DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BLOOD DIS, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BLOOD PRESSURE, DECREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BRONCHITIS, ACUTE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BRONCHITIS, CHRONIC	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CARBUNCLE/FURUNCLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CELLULITIS/ABSCESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CEREBRAL PALSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CERVICAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CONG ANOM, GU	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CONG ANOM, MUSCULOSKEL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CONJUNCTIVAL DISORD	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CONVULSIONS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DENTOFACIAL ANOM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
EPILEPSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ESOPHAGITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
EXTRASYSTOLES	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FLATULENCE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FRACTURE, LOWER LIMB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
GOITER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEARING LOSS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEMATURIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HEMORRHAGE, INTRACRANIAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEMORRHAGE, UNSPEC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEMORRHOIDS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEPATITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HEPATITIS, VIRAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HERNIA, ABDOMINAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
INJURY, CHEST/ABD/PELV	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
INTEST OBSTRUCTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
JOINT DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
KIDNEY INFECT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LEUKOPENIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MANAGEMENT, PROCREATIVE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MENINGITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MITRAL VALVE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NASAL POLYPS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
NEED/OTHER PROPHYLAXIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NEOPLASM MALIG, BONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NEOPLASM, UNSPEC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NERVOUSNESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NEURALGIA, BACK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NEUROSES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OBESITY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
OPERATION, ANUS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
OPERATION, KIDNEY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
OPERATION, MUSCLE/TENDON	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
OPERATION, OTHER URINARY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OPERATION/STOMACH	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ORAL SOFT TISSUE DIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OSTEOARTHROSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PARESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PNEUMOTHORAX	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
POLYDIPSIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PROCEDURES, REHAB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PULM EMBOLISM AND INFARCT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PYREXIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
RASH/OTHER SKIN ERUPTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

Table 12.21

Significant Medical / Surgical History and Physical Examination
Prior Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
RHINITIS, NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SINUSITIS, CHRONIC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SOFT TISSUE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
STOMACH/DUODENUM DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SUPERVISION/PREG	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SYNCOPE AND COLLAPSE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
THYROID DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
THYROIDITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TRANSAMINASE/LDH, ELEVATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TRAUMA/INJURIES, UNSPEC	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TYPHOID INFECT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
URETHRAL DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
VESTIBULAR DISORD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
WEIGHT LOSS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TOTAL	TOTAL	83 (71.6%)	87 (66.9%)	77 (64.2%)	247 (67.5%)
ABDOMEN	TOTAL	3 (2.6%)	7 (5.4%)	4 (3.3%)	14 (3.8%)
	HERNIA, ABDOMINAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPERATION, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ABDOM PAIN, ABDOMINO-PELVIC	3 (2.6%)	7 (5.4%)	3 (2.5%)	13 (3.6%)
ARTERY	TOTAL	12 (10.3%)	10 (7.7%)	10 (8.3%)	32 (8.7%)
	ARTERIAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MIGRAINE	12 (10.3%)	9 (6.9%)	10 (8.3%)	31 (8.5%)
ARTICULAR	TOTAL	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	INTERVERTEB DISC, ABN	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
BACK	TOTAL	6 (5.2%)	4 (3.1%)	5 (4.2%)	15 (4.1%)
	BACK PAIN	6 (5.2%)	4 (3.1%)	5 (4.2%)	15 (4.1%)
BLADDER	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CYSTITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
BONE	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	FRACTURE, LOWER LIMB	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FRACTURE, UPPER LIMB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BRAIN	TOTAL	3 (2.6%)	2 (1.5%)	2 (1.7%)	7 (1.9%)
	INSOMNIA	3 (2.6%)	2 (1.5%)	2 (1.7%)	7 (1.9%)
BREAST	TOTAL	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	BREAST DISORD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NEOPLASMS BENIGN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
BRONCHUS	TOTAL	7 (6.0%)	5 (3.8%)	5 (4.2%)	17 (4.6%)
	ASTHMA	5 (4.3%)	5 (3.8%)	5 (4.2%)	15 (4.1%)
	BRONCHITIS, CHRONIC	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
CAPILLARY	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CAPILLARY DIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CARDIOVASCULAR	TOTAL	6 (5.2%)	2 (1.5%)	3 (2.5%)	11 (3.0%)
	HYPERTENSION	4 (3.4%)	2 (1.5%)	2 (1.7%)	8 (2.2%)
	HYPOTENSION, OTHER	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CAUSES OF INJURY	TOTAL	4 (3.4%)	12 (9.2%)	5 (4.2%)	21 (5.7%)
	ACCIDENT/MOTOR VEHICLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/ANALGESIC	0 (0.0%)	2 (1.5%)	2 (1.7%)	4 (1.1%)
	ADVERSE EFF/ANTI-INFECTION	2 (1.7%)	4 (3.1%)	1 (0.8%)	7 (1.9%)
	ADVERSE EFF/ANTIBIOTIC	3 (2.6%)	6 (4.6%)	3 (2.5%)	12 (3.3%)
	ADVERSE EFF/OTHER DRUG	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/PSYCHOTROPICS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ADVERSE EFF/SYST AGENT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	POISONING	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CENTRAL NERVOUS	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CEREBRAL PALSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CEREBRAL CORTEX	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	EPILEPSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CERVIX	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PAP SMEAR, ABN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CONJUNCTIVA	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CONJUNCTIVAL DISORD	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DIAGNOSTIC/THERAPEUTIC PROCS	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	EVALUATION, DX EXAM	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
DIGESTIVE	TOTAL	3 (2.6%)	7 (5.4%)	6 (5.0%)	16 (4.4%)
	DIARRHEA	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)
	FLATULENCE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	GASTRITIS/DUODENITIS	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)
	HEARTBURN	0 (0.0%)	2 (1.5%)	3 (2.5%)	5 (1.4%)
EAR/AUDITION, NOS	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	HEARING LOSS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
ENDOCRINE	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ENDOCR DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ENZYME	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	TRANSAMINASE/LDH, ELEVATION	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ERYTHROCYTES	TOTAL	4 (3.4%)	2 (1.5%)	4 (3.3%)	10 (2.7%)
	ANEMIA, IRON DEFIC	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	ANEMIA, OTHER	3 (2.6%)	1 (0.8%)	3 (2.5%)	7 (1.9%)
ESOPHAGUS	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	ESOPHAGITIS	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
EYE/VISION, NOS	TOTAL	2 (1.7%)	2 (1.5%)	2 (1.7%)	6 (1.6%)
	EYE DISORD, OTHER	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	OPERATION, EYE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VISUAL DISTURB	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
FACTORS INFLUENCING HEALTH	TOTAL	2 (1.7%)	6 (4.6%)	7 (5.8%)	15 (4.1%)
	MANAGEMENT, CONTRACEPTIVE	2 (1.7%)	6 (4.6%)	5 (4.2%)	13 (3.6%)
	NEED/OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PROPHYLAXIS PROCEDURES, REHAB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FALLOPIAN TUBE	TOTAL	3 (2.6%)	2 (1.5%)	4 (3.3%)	9 (2.5%)
	OPERATION, FEM GENITAL	3 (2.6%)	2 (1.5%)	4 (3.3%)	9 (2.5%)
FEMALE REPRODUCTIVE	TOTAL	28 (24.1%)	34 (26.2%)	25 (20.8%)	87 (23.8%)
	GENITAL FEMALE DISORD, OTHER	28 (24.1%)	34 (26.2%)	25 (20.8%)	87 (23.8%)
	MYCOSES	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	VAGINITIS	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
FLUID BALANCE	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	FLUID OVERLOAD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GENERAL BODY OR SYS UNSPEC	TOTAL	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)
	MALAISE AND FATIGUE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	PAIN, GENERAL	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	VIRAL INFECTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GENITOURINARY	TOTAL	3 (2.6%)	2 (1.5%)	0 (0.0%)	5 (1.4%)
	VIRAL DIS/EXANTHEM	3 (2.6%)	2 (1.5%)	0 (0.0%)	5 (1.4%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
HAIR	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ALOPECIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HEAD	TOTAL	40 (34.5%)	39 (30.0%)	36 (30.0%)	115 (31.4%)
	HEADACHE	40 (34.5%)	39 (30.0%)	36 (30.0%)	115 (31.4%)
HEART	TOTAL	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CARDIAC MURMURS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	EXTRASYSTOLES	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TACHYCARDIA, UNSPEC	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
INNER EAR	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	VESTIBULAR DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
JOINT	TOTAL	7 (6.0%)	3 (2.3%)	3 (2.5%)	13 (3.6%)
	ARTHRITIS, RHEUMATOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ARTHROPATHY	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	DENTOFACIAL ANOM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OPERATION, BONE/JOINT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	OSTEOARTHROSIS	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	PAIN, JOINT	4 (3.4%)	1 (0.8%)	1 (0.8%)	6 (1.6%)
KIDNEY	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	KIDNEY DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LARGE INTESTINE	TOTAL	4 (3.4%)	3 (2.3%)	0 (0.0%)	7 (1.9%)
	CONSTIPATION	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
	DIGESTIVE DISORD, OTHER	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	ENTERITIS/COLITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LENS	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VISUAL DISTURB	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LIGAMENT	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SOFT TISSUE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LYMPHATIC	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NEOPLASM MALIG, LYMPH/HEMAT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
METABOLIC/NUTRITIONAL/IMMUNE	TOTAL	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	OBESITY	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	POLYDIPSIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
MIDDLE EAR	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OTITIS MEDIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MOUTH/OROPHARYNX	TOTAL	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	OPERATION, NOSE/MOUTH	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TEETH DISORD	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	VIRAL DIS/EXANTHEM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MULTISYSTEMIC	TOTAL	4 (3.4%)	6 (4.6%)	5 (4.2%)	15 (4.1%)
	ALLERGY, NEC	4 (3.4%)	6 (4.6%)	5 (4.2%)	15 (4.1%)
MUSCLE	TOTAL	1 (0.9%)	3 (2.3%)	4 (3.3%)	8 (2.2%)
	CERVICAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MYALGIA	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	SPASM, MUSCLE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
MUSCULAR/FASCIA	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	RHEUMATIC DISORD	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MUSCULOSKELETAL	TOTAL	1 (0.9%)	2 (1.5%)	3 (2.5%)	6 (1.6%)
	DEFORMITY, ACQUIRED	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)
	SPRAINS/STRAINS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NAIL	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MYCOSES	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NASOPHARYNX	TOTAL	2 (1.7%)	3 (2.3%)	1 (0.8%)	6 (1.6%)
	NASOPHARYNGITIS, ACUTE	2 (1.7%)	3 (2.3%)	1 (0.8%)	6 (1.6%)
NECK	TOTAL	1 (0.9%)	3 (2.3%)	2 (1.7%)	6 (1.6%)
	CERVICAL DISORD, OTHER	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PAIN, NECK	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
NERVE	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	CERVICOBRACHIAL SYNDROME	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
NERVE	INJURY, NERV, SP CD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NEURALGIA, BACK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NERVOUS/SENSE ORGANS	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	DIZZINESS AND GIDDINESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NON-ORGANIC	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	ANXIETY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	NEUROSES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NOSE	TOTAL	18 (15.5%)	7 (5.4%)	10 (8.3%)	35 (9.6%)
	RHINITIS, ALLERGIC	16 (13.8%)	7 (5.4%)	9 (7.5%)	32 (8.7%)
	RHINITIS,NOS	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
OVARY	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	GENITAL FEMALE DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PANCREAS/ENDOCRINE	TOTAL	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	DIABETES MELLITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
PSYCHOLOGICAL DISORDERS	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TOBACCO USE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
REGION	TOTAL	0 (0.0%)	7 (5.4%)	0 (0.0%)	7 (1.9%)
	LIMB, DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PAIN, LIMB	0 (0.0%)	5 (3.8%)	0 (0.0%)	5 (1.4%)
	TRAUMA/INJURIES, UNSPEC	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
RESPIRATORY	TOTAL	1 (0.9%)	3 (2.3%)	2 (1.7%)	6 (1.6%)
	COUGH	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DYSPNEA, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	INFLUENZA	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
SEBACEOUS GLAND	TOTAL	4 (3.4%)	3 (2.3%)	4 (3.3%)	11 (3.0%)
	SKIN/SUBCUT DISORD, OTHER	4 (3.4%)	3 (2.3%)	4 (3.3%)	11 (3.0%)
SHOULDER	TOTAL	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	RHEUMATIC DISORD	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
SINUS	TOTAL	6 (5.2%)	3 (2.3%)	6 (5.0%)	15 (4.1%)
	SINUSITIS,NOS	6 (5.2%)	3 (2.3%)	6 (5.0%)	15 (4.1%)
SKELETAL	TOTAL	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	BONE/CARTIL DISORD, OTHER	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
SKIN	TOTAL	5 (4.3%)	10 (7.7%)	10 (8.3%)	25 (6.8%)
	CARBUNCLE/FURUNCLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DYSCHROMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	INFLAM SKIN/SUBCUT	4 (3.4%)	6 (4.6%)	6 (5.0%)	16 (4.4%)
	MYCOSES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PRURITUS DISORD, UNSPEC	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	RASH/OTHER SKIN ERUPTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SKIN INFECT, LOCAL, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SKIN/SUBCUT DISORD, OTHER	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SPINAL NERVE	PERIPH NERV SYST DISORD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
STOMACH	DYSPEPSIA	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SWEAT GLAND	SKIN/SUBCUT DISORD, OTHER	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SYS UNSPEC	TOTAL	3 (2.6%)	3 (2.3%)	4 (3.3%)	10 (2.7%)
	ADVERSE EFF/OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ALLERGIC REACTION, FOOD	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
	EDEMA	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	PROCEDURE, SURGERY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	UNSP VIRAL DIS/EXANTHEM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
THORAX	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	PAIN UNSP, CHEST	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
THYROID GLAND	TOTAL	4 (3.4%)	5 (3.8%)	9 (7.5%)	18 (4.9%)
	GOITER	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)
	HYPERTHYROIDISM	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	HYPOTHYROIDISM	3 (2.6%)	4 (3.1%)	3 (2.5%)	10 (2.7%)
	THYROID DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	THYROID FUNCTION, ABN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
UPPER RESPIRATORY TRACT	TOTAL	1 (0.9%)	4 (3.1%)	1 (0.8%)	6 (1.6%)
	INFECTION, BACTERIAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PHARYNGITIS, ACUTE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	UPPER RESP DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	UPPER RESP INFECT, ACUTE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
URINARY TRACT	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	URINARY TRACT INFECTION	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
URINE	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HEMATURIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
UTERUS	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NEOPLASMS BENIGN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
VALVE	TOTAL	0 (0.0%)	4 (3.1%)	0 (0.0%)	4 (1.1%)
	MITRAL VALVE DISORD	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
	TRICUSPID VALVE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VASCULAR	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CIRCULATORY SYST DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VEIN	TOTAL	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	HEMORRHOIDS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	VARICES	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
VITAMINS/MINERALS	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	VITAMIN DEFIC, OTHER	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
VULVA	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

Table 12.22

Significant Medical / Surgical History and Physical Examination
Active Conditions Ordered by Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
VULVA	INFLAM PELVIC DIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TOTAL	83 (71.6%)	87 (66.9%)	77 (64.2%)	247 (67.5%)
HEADACHE	40 (34.5%)	39 (30.0%)	36 (30.0%)	115 (31.4%)
GENITAL FEMALE DISORD, OTHER	28 (24.1%)	34 (26.2%)	25 (20.8%)	87 (23.8%)
RHINITIS, ALLERGIC	16 (13.8%)	7 (5.4%)	9 (7.5%)	32 (8.7%)
MIGRAINE	12 (10.3%)	9 (6.9%)	10 (8.3%)	31 (8.5%)
INFLAM SKIN/SUBCUT	4 (3.4%)	6 (4.6%)	6 (5.0%)	16 (4.4%)
ALLERGY, NEC	4 (3.4%)	6 (4.6%)	5 (4.2%)	15 (4.1%)
ASTHMA	5 (4.3%)	5 (3.8%)	5 (4.2%)	15 (4.1%)
BACK PAIN	6 (5.2%)	4 (3.1%)	5 (4.2%)	15 (4.1%)
SINUSITIS, NOS	6 (5.2%)	3 (2.3%)	6 (5.0%)	15 (4.1%)
SKIN/SUBCUT DISORD, OTHER	5 (4.3%)	5 (3.8%)	5 (4.2%)	15 (4.1%)
MANAGEMENT, CONTRACEPTIVE	2 (1.7%)	6 (4.6%)	5 (4.2%)	13 (3.6%)
PAIN, ABDOMINO-PELVIC	3 (2.6%)	7 (5.4%)	3 (2.5%)	13 (3.6%)
ADVERSE EFF/ANTIBIOTIC	3 (2.6%)	6 (4.6%)	3 (2.5%)	12 (3.3%)
HYPOTHYROIDISM	3 (2.6%)	4 (3.1%)	3 (2.5%)	10 (2.7%)
OPERATION, FEM GENITAL	3 (2.6%)	2 (1.5%)	4 (3.3%)	9 (2.5%)
HYPERTENSION	4 (3.4%)	2 (1.5%)	2 (1.7%)	8 (2.2%)
ADVERSE EFF/ANTI-INFECTION	2 (1.7%)	4 (3.1%)	1 (0.8%)	7 (1.9%)
ANEMIA, OTHER	3 (2.6%)	1 (0.8%)	3 (2.5%)	7 (1.9%)
INSOMNIA	3 (2.6%)	2 (1.5%)	2 (1.7%)	7 (1.9%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
VIRAL DIS/EXANTHEM	4 (3.4%)	2 (1.5%)	1 (0.8%)	7 (1.9%)
NASOPHARYNGITIS, ACUTE	2 (1.7%)	3 (2.3%)	1 (0.8%)	6 (1.6%)
PAIN, JOINT	4 (3.4%)	1 (0.8%)	1 (0.8%)	6 (1.6%)
RHEUMATIC DISORD	3 (2.6%)	1 (0.8%)	2 (1.7%)	6 (1.6%)
DEFORMITY, ACQUIRED	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)
DIARRHEA	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)
GASTRITIS/DUODENITIS	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)
GOITER	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)
HEARTBURN	0 (0.0%)	2 (1.5%)	3 (2.5%)	5 (1.4%)
PAIN, LIMB	0 (0.0%)	5 (3.8%)	0 (0.0%)	5 (1.4%)
PAIN, NECK	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
ADVERSE EFF/ANALGESIC	0 (0.0%)	2 (1.5%)	2 (1.7%)	4 (1.1%)
ALLERGIC REACTION, FOOD	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
CONSTIPATION	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
INFLUENZA	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)
INTERVERTEB DISC, ABN	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
SPASM, MUSCLE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
VISUAL DISTURB	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
ANEMIA, IRON DEFIC	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
DIABETES MELLITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
EDEMA	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ESOPHAGITIS	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
HYPOTENSION, OTHER	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
MITRAL VALVE DISORD	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
MYALGIA	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
MYCOSES	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
PRURITUS DISORD, UNSPEC	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
RHINITIS,NOS	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
URINARY TRACT INFECTION	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
ARTHROPATHY	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
BONE/CARTIL DISORD, OTHER	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
BRONCHITIS, CHRONIC	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
CERVICAL DISORD, OTHER	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
DIGESTIVE DISORD, OTHER	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
DYSPEPSIA	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
EVALUATION, DX EXAM	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
EYE DISORD, OTHER	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
HEARING LOSS	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
HYPERTHYROIDISM	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MALAISE AND FATIGUE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
NEOPLASMS BENIGN	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
OBESITY	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
OSTEOARTHROSIS	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
PAIN UNSP, CHEST	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
PAIN, GENERAL	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
PHARYNGITIS, ACUTE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
TEETH DISORD	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
TOBACCO USE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
TRANSAMINASE/LDH, ELEVATION	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
UPPER RESP INFECT, ACUTE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
VAGINITIS	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
VITAMIN DEFIC, OTHER	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
ACCIDENT/MOTOR VEHICLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ADVERSE EFF/OTHER DRUG	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/PSYCHOTROPICS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ADVERSE EFF/SYST AGENT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ALOPECIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ANXIETY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ARTERIAL DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ARTHRITIS, RHEUMATOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BREAST DISORD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CAPILLARY DIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CARBUNCLE/FURUNCLE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CARDIAC MURMURS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CEREBRAL PALSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CERVICOBRACHIAL SYNDROME	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CIRCULATORY SYST DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CONJUNCTIVAL DISORD	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
COUGH	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CYSTITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DENTOFACIAL ANOM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DIZZINESS AND GIDDINESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DYSCHROMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DYSPNEA, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ENDOCR DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ENTERITIS/COLITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
EPILEPSY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
EXTRASYSTOLES	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FLATULENCE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FLUID OVERLOAD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
FRACTURE, LOWER LIMB	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FRACTURE, UPPER LIMB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEMATURIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HEMORRHOIDS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HERNIA, ABDOMINAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
INFECTION, BACTERIAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
INFLAM PELVIC DIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
INJURY, NERV, SP CD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
KIDNEY DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LIMB, DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NEED/OTHER PROPHYLAXIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NEOPLASM MALIG, LYMPH/HEMAT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NEURALGIA, BACK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NEUROSES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OPERATION, BONE/JOINT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OPERATION, EYE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
OPERATION, NOSE/MOUTH	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
OPERATION, OTHER ABDOM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PAP SMEAR, ABN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

Table 12.23

Significant Medical / Surgical History and Physical Examination
Active Conditions by Preferred Term Ordered in Decreasing Frequency
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
PERIPH NERV SYST DISORD	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
POISONING	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
POLYDIPSIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PROCEDURE, SURGERY UNSP	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PROCEDURES, REHAB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
RASH/OTHER SKIN ERUPTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SKIN INFECT, LOCAL, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SOFT TISSUE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SPRAINS/STRAINS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TACHYCARDIA, UNSPEC	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
THYROID DISORD, OTHER	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
THYROID FUNCTION, ABN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TRAUMA/INJURIES, UNSPEC	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TRICUSPID VALVE DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
UPPER RESP DISORD, OTHER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
VARICES	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
VESTIBULAR DISORD	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VIRAL INFECTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

Table 12.24

Number (%) of Subjects with other Psychiatric Disorders (from full psychiatric history and MINI interview)
Intention-to-Treat Population

Psychiatric Disorder Decoded	Status	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TOTAL	TOTAL	7 (6.0%)	9 (6.9%)	5 (4.2%)	21 (5.7%)
(Hypo)manic Episode	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	Past	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
Agoraphobia	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	Past	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
Bulimia Nervosa	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	Past	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
Major Depressive Episode	TOTAL	4 (3.4%)	5 (3.8%)	3 (2.5%)	12 (3.3%)
	Past	3 (2.6%)	5 (3.8%)	3 (2.5%)	11 (3.0%)
	Present	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
OTHER (DSM IV Code - 300.29)	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	Present	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	Unknown	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
Panic Disorder	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	Past	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
Suicidality	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	Past	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)

Table 12.25

Relationship to Onset of PMDD Symptoms by Category
Intention-to-Treat Population

Onset of PMDD Coincided with	Treatment Group			Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
TOTAL	115 (99.1%)	130 (100.0%)	120 (100.0%)	365 (99.7%)
Childbirth	40 (34.5%)	46 (35.4%)	35 (29.2%)	121 (33.1%)
Menarche	14 (12.1%)	19 (14.6%)	12 (10.0%)	45 (12.3%)
Sterilization	4 (3.4%)	1 (0.8%)	2 (1.7%)	7 (1.9%)
Stopping Oral Contraception	5 (4.3%)	9 (6.9%)	9 (7.5%)	23 (6.3%)
Starting Oral Contraception	1 (0.9%)	1 (0.8%)	5 (4.2%)	7 (1.9%)
Other	8 (6.9%)	11 (8.5%)	13 (10.8%)	32 (8.7%)
Nothing Specified	47 (40.5%)	50 (38.5%)	46 (38.3%)	143 (39.1%)

A Subject can be included in more than one category

Table 12.26

Summary Statistics for Persistency of PMDD, Age at Onset of PMDD Symptoms and Duration of PMDD Symptoms
Intention-to-Treat Population

PMDD History	Statistic	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Persisted Since Initial Onset?	No	7 (6.0%)	5 (3.8%)	9 (7.5%)	21 (5.7%)
	Yes	108 (93.1%)	125 (96.2%)	111 (92.5%)	344 (94.0%)
Age at Onset of PMDD	N	115	130	120	365
	MEAN	26.5	25.7	26.8	26.3
	STD	7.56	7.41	7.57	7.50
	MEDIAN	28.0	27.0	27.0	27.0
	MINIMUM	11.0	11.0	12.0	11.0
	MAXIMUM	42.0	39.0	42.0	42.0
Duration (yrs) if Persisted	N	108	125	111	344
	MEAN	10.5	10.5	10.4	10.5
	STD	7.02	7.41	7.35	7.25
	MEDIAN	9.3	9.0	8.5	9.0
	MINIMUM	1.0	0.9	1.0	0.9
	MAXIMUM	34.0	33.0	33.0	34.0
Duration (yrs) of Longest Episode	N	7	5	9	21
	MEAN	11.0	10.1	6.5	8.8
	STD	4.58	7.35	3.79	5.24
	MEDIAN	10.0	11.0	7.2	9.0
	MINIMUM	5.0	0.5	1.0	0.5
	MAXIMUM	19.0	18.0	12.0	19.0
Duration (yrs) of Current Episode	N	7	5	9	21
	MEAN	8.2	7.0	3.9	6.1
	STD	4.40	6.69	3.69	4.91
	MEDIAN	9.0	5.0	3.0	4.5
	MINIMUM	1.5	0.5	0.3	0.3
	MAXIMUM	15.0	18.0	12.0	18.0

Table 12.27

Obstetrics and Gynaecological History by Treatment Group
Intention-to-Treat Population

Obstetrics and Gynaecological History	Value	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
No. of Pregnancies	0	17 (14.7%)	25 (19.2%)	21 (17.5%)	63 (17.2%)
	1	16 (13.8%)	18 (13.8%)	19 (15.8%)	53 (14.5%)
	2	37 (31.9%)	34 (26.2%)	34 (28.3%)	105 (28.7%)
	3	21 (18.1%)	30 (23.1%)	25 (20.8%)	76 (20.8%)
	4	12 (10.3%)	12 (9.2%)	10 (8.3%)	34 (9.3%)
	>4	13 (11.2%)	11 (8.5%)	11 (9.2%)	35 (9.6%)
No. of Children	0	25 (21.6%)	30 (23.1%)	28 (23.3%)	83 (22.7%)
	1	22 (19.0%)	23 (17.7%)	25 (20.8%)	70 (19.1%)
	2	43 (37.1%)	49 (37.7%)	44 (36.7%)	136 (37.2%)
	3	18 (15.5%)	22 (16.9%)	11 (9.2%)	51 (13.9%)
	4	6 (5.2%)	5 (3.8%)	10 (8.3%)	21 (5.7%)
	>4	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)
No. of Miscarriages	0	84 (72.4%)	104 (80.0%)	95 (79.2%)	283 (77.3%)
	1	26 (22.4%)	20 (15.4%)	18 (15.0%)	64 (17.5%)
	2	4 (3.4%)	3 (2.3%)	3 (2.5%)	10 (2.7%)
	3	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	4	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	>4	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
No. of Terminations	0	90 (77.6%)	95 (73.1%)	95 (79.2%)	280 (76.5%)
	1	18 (15.5%)	30 (23.1%)	19 (15.8%)	67 (18.3%)
	2	5 (4.3%)	3 (2.3%)	2 (1.7%)	10 (2.7%)
	3	3 (2.6%)	1 (0.8%)	3 (2.5%)	7 (1.9%)
	4	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
No. of D&Cs	0	89 (76.7%)	95 (73.1%)	91 (75.8%)	275 (75.1%)
	1	16 (13.8%)	30 (23.1%)	19 (15.8%)	65 (17.8%)
	2	8 (6.9%)	3 (2.3%)	7 (5.8%)	18 (4.9%)
	3	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
	4	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	>4	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
Heavy Periods?	No	72 (62.1%)	64 (49.2%)	58 (48.3%)	194 (53.0%)
	Yes	44 (37.9%)	66 (50.8%)	62 (51.7%)	172 (47.0%)
Painful Periods?	No	53 (45.7%)	52 (40.0%)	59 (49.2%)	164 (44.8%)
	Yes	63 (54.3%)	78 (60.0%)	61 (50.8%)	202 (55.2%)

Table 12.28

Number (%) of Subjects by Previous Treatment for PMDD
Intention-to-Treat Population

Treatment	Response Rating	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
TOTAL	TOTAL	62 (53.4%)	61 (46.9%)	58 (48.3%)	181 (49.5%)
Antidepressants, anxiolytics, lithium or other psychotropic drugs	TOTAL	3 (2.6%)	5 (3.8%)	3 (2.5%)	11 (3.0%)
	None	1 (33.3%)	3 (60.0%)	2 (66.7%)	6 (54.5%)
	Mild	0 (0.0%)	2 (40.0%)	1 (33.3%)	3 (27.3%)
	Moderate	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (9.1%)
	Marked	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (9.1%)
Oral contraception or hormone preparation	TOTAL	16 (13.8%)	18 (13.8%)	19 (15.8%)	53 (14.5%)
	None	9 (56.3%)	7 (38.9%)	9 (47.4%)	25 (47.2%)
	Mild	6 (37.5%)	9 (50.0%)	6 (31.6%)	21 (39.6%)
	Moderate	1 (6.3%)	2 (11.1%)	2 (10.5%)	5 (9.4%)
	Marked	0 (0.0%)	0 (0.0%)	2 (10.5%)	2 (3.8%)
Pyridoxine (Vitamin B6)	TOTAL	25 (21.6%)	20 (15.4%)	21 (17.5%)	66 (18.0%)
	None	16 (64.0%)	16 (80.0%)	10 (47.6%)	42 (63.6%)
	Mild	8 (32.0%)	3 (15.0%)	9 (42.9%)	20 (30.3%)
	Moderate	1 (4.0%)	1 (5.0%)	2 (9.5%)	4 (6.1%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gamma-linolenic acid (Evening Primrose Oil)	TOTAL	21 (18.1%)	19 (14.6%)	18 (15.0%)	58 (15.8%)
	None	15 (71.4%)	10 (52.6%)	12 (66.7%)	37 (63.8%)
	Mild	4 (19.0%)	7 (36.8%)	6 (33.3%)	17 (29.3%)
	Moderate	2 (9.5%)	2 (10.5%)	0 (0.0%)	4 (6.9%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
d-Fenfluramine	TOTAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	None	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-steroidal anti-inflammatory drug	TOTAL	11 (9.5%)	14 (10.8%)	9 (7.5%)	34 (9.3%)
	None	3 (27.3%)	5 (35.7%)	5 (55.6%)	13 (38.2%)
	Mild	5 (45.5%)	5 (35.7%)	3 (33.3%)	13 (38.2%)
	Moderate	1 (9.1%)	3 (21.4%)	1 (11.1%)	5 (14.7%)
	Marked	2 (18.2%)	1 (7.1%)	0 (0.0%)	3 (8.8%)
Tryptophan	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	None	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Subjects can have more than one treatment in the 'other treatment' category

Table 12.28

Number (%) of Subjects by Previous Treatment for PMDD
Intention-to-Treat Population

Treatment	Response Rating	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Tryptophan	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
L-Dopa	TOTAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	None	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Bromocriptine	TOTAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	None	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mefenamic acid	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	None	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (50.0%)
	Mild	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diuretics	TOTAL	6 (5.2%)	6 (4.6%)	8 (6.7%)	20 (5.5%)
	None	2 (33.3%)	3 (50.0%)	4 (50.0%)	9 (45.0%)
	Mild	3 (50.0%)	2 (33.3%)	3 (37.5%)	8 (40.0%)
	Moderate	1 (16.7%)	1 (16.7%)	1 (12.5%)	3 (15.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clonidine	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	None	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Beta Blockers	TOTAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	None	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Verapamil	TOTAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	None	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Subjects can have more than one treatment in the 'other treatment' category

Table 12.28

Number (%) of Subjects by Previous Treatment for PMDD
Intention-to-Treat Population

Treatment	Response Rating	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Calcium	TOTAL	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
	None	1 (50.0%)	0 (0.0%)	2 (100.0%)	3 (75.0%)
	Mild	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Moderate	1 (50.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)
	Marked	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other treatment	TOTAL	16 (13.8%)	22 (16.9%)	16 (13.3%)	54 (14.8%)
	None	10 (62.5%)	13 (59.1%)	11 (68.8%)	34 (63.0%)
	Mild	5 (31.3%)	12 (54.5%)	8 (50.0%)	25 (46.3%)
	Moderate	0 (0.0%)	1 (4.5%)	1 (6.3%)	2 (3.7%)
	Marked	1 (6.3%)	1 (4.5%)	0 (0.0%)	2 (3.7%)

Subjects can have more than one treatment in the 'other treatment' category

Table 12.29

Summary Statistics for MADRS Total Score at Screening
Intention-to-Treat Population

Visit	Statistic	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Screening	N	116	130	120	366
	MEAN	1.2	1.1	1.4	1.2
	STD	1.66	1.80	1.89	1.79
	MEDIAN	1	0	1	0
	MINIMUM	0	0	0	0
	MAXIMUM	7	9	8	9

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
TOTAL	TOTAL	335	(27.0%)
ALIMENTARY TRACT/METAB	TOTAL	76	(6.1%)
	ACEROLA	1	(0.1%)
	ACETYLSALICYLATE	1	(0.1%)
	LYSINE		
	ACETYLSALICYLIC ACID	8	(0.6%)
	ALGELDRATE	1	(0.1%)
	ALUMINIUM HYDROXIDE GEL	1	(0.1%)
	ASCORBIC ACID	6	(0.5%)
	ATROPINE SULFATE	1	(0.1%)
	BIOTIN	2	(0.2%)
	CALCIUM	6	(0.5%)
	CALCIUM CARBONATE	1	(0.1%)
	CALCIUM CITRATE	1	(0.1%)
	CIMETIC ACID	1	(0.1%)
	CIMETIDINE	1	(0.1%)
	CISAPRIDE	1	(0.1%)
	COD-LIVER OIL	1	(0.1%)
	CYANOCOBALAMIN	1	(0.1%)
	CYANOCOBALAMIN-TANNI N COMPLEX	1	(0.1%)
	DICLOFENAC SODIUM	2	(0.2%)
	DIMETICONE	1	(0.1%)
	DOMPERIDONE	1	(0.1%)
	ERGOCALCIFEROL	3	(0.2%)
	FAMOTIDINE	2	(0.2%)
	FERROUS CARBONATE	1	(0.1%)
	FOLIC ACID	3	(0.2%)
	GINSENG	1	(0.1%)
	HERBS NOS	1	(0.1%)
	INSULIN INJECTION, ISOPHANE	1	(0.1%)
	INSULIN LISPRO	1	(0.1%)
	IRON	2	(0.2%)
	LACTOBACILLUS ACIDOPHILUS	1	(0.1%)
	LANSOPRAZOLE	3	(0.2%)
	LAXATIVES, NOS	1	(0.1%)
	LOPERAMIDE	2	(0.2%)
	HYDROCHLORIDE		
	MAGALDRATE	1	(0.1%)
	MAGNESIUM HYDROXIDE	2	(0.2%)
	MAGNESIUM NOS	5	(0.4%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
ALIMENTARY TRACT/METAB	MAGNESIUM PHOSPHATE MONOBASIC	1	(0.1%)
	MANGANESE SULFATE	1	(0.1%)
	MERCURIC CYANIDE	1	(0.1%)
	MESALAZINE	1	(0.1%)
	METFORMIN	1	(0.1%)
	METOCLOPRAMIDE	1	(0.1%)
	METOCLOPRAMIDE HYDROCHLORIDE	1	(0.1%)
	METRONIDAZOLE	3	(0.2%)
	MINERALS NOS	7	(0.6%)
	MISOPROSTOL	2	(0.2%)
	MOLYBDENUM	1	(0.1%)
	SESQUIOXIDE		
	NICOTINIC ACID	1	(0.1%)
	OMEPRazole	7	(0.6%)
	PINAVERIUM BROMIDE	2	(0.2%)
	POTASSIUM DICHROMATE	1	(0.1%)
	PYRIDOXINE	5	(0.4%)
	HYDROCHLORIDE		
	RANITIDINE	1	(0.1%)
	HYDROCHLORIDE		
	RIBOFLAVIN	1	(0.1%)
	SIBUTRAMINE	1	(0.1%)
	SODIUM BORATE	1	(0.1%)
	SODIUM CHLORIDE	1	(0.1%)
	SULFASALAZINE	1	(0.1%)
	THIAMINE	1	(0.1%)
	HYDROCHLORIDE		
	TOCOPHEROL	4	(0.3%)
	TRACE ELEMENTS, NOS	1	(0.1%)
	TRIAMCINOLONE	1	(0.1%)
	ACETONIDE		
	VITAMIN B SUBSTANCES	1	(0.1%)
	VITAMINS NOS	25	(2.0%)
	ZINC	1	(0.1%)
	ZINC SULFATE	1	(0.1%)
ANTIINFECTIVES, SYSTE MIC	TOTAL	48	(3.9%)
	ACICLOVIR	1	(0.1%)
	AMOXICILLIN	4	(0.3%)
	AMOXICILLIN TRIHYDRATE	3	(0.2%)
	ANTIBIOTIC NOS	3	(0.2%)
	AZITHROMYCIN	4	(0.3%)
	CEFADROXIL	1	(0.1%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
ANTIINFECTIVES, SYSTEMIC	CEFALEXIN	1	(0.1%)
	CEFALOTIN SODIUM	1	(0.1%)
	CEFUROXIME	1	(0.1%)
	CLARITHROMYCIN	5	(0.4%)
	CLAVULANIC ACID	1	(0.1%)
	CLINDAMYCIN	2	(0.2%)
	CLINDAMYCIN HYDROCHLORIDE	1	(0.1%)
	CLOXACILLIN	1	(0.1%)
	DOXYCYCLINE	3	(0.2%)
	DOXYCYCLINE HYCLATE	2	(0.2%)
	ERYTHROMYCIN	1	(0.1%)
	FLUCLOXACILLIN	2	(0.2%)
	FLUCONAZOLE	1	(0.1%)
	INFLUENZA VIRUS VACCINE POLYVALENT	1	(0.1%)
	ITRACONAZOLE	2	(0.2%)
	LORACARBEF	1	(0.1%)
	METRONIDAZOLE	3	(0.2%)
	MICONAZOLE NITRATE	1	(0.1%)
	OFLOXACIN	1	(0.1%)
	PENCICLOVIR	2	(0.2%)
	PENICILLIN NOS	1	(0.1%)
	PHENOXYMETHYLPENICILLIN	1	(0.1%)
	PHENOXYMETHYLPENICILLIN POTASSIUM	1	(0.1%)
	PIVMECILLINAM HYDROCHLORIDE	2	(0.2%)
	SULFAMETHOXAZOLE	2	(0.2%)
	TETRACYCLINE HYDROCHLORIDE	1	(0.1%)
	TRIMETHOPRIM	3	(0.2%)
BLOOD/BLOOD FORM ORGANS	TOTAL	32	(2.6%)
	ACETYLSALICYLIC ACID	8	(0.6%)
	ATORVASTATIN CALCIUM	2	(0.2%)
	BIOTIN	1	(0.1%)
	CHONDROITIN SULFATE	1	(0.1%)
	CIMETIC ACID	1	(0.1%)
	CYANOCOBALAMIN	1	(0.1%)
	EVENING PRIMROSE OIL	2	(0.2%)
	FERROUS FUMARATE	1	(0.1%)
	FERROUS GLUCONATE	1	(0.1%)
	FERROUS SULFATE	3	(0.2%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
BLOOD/BLOOD FORM ORGANS	FOLIC ACID	3	(0.2%)
	GLUCOSAMINE SULFATE	1	(0.1%)
	HERBS NOS	1	(0.1%)
	IRON	1	(0.1%)
	MINERALS NOS	1	(0.1%)
	NICOTINIC ACID	1	(0.1%)
	PYRIDOXINE	2	(0.2%)
	HYDROCHLORIDE		
	RIBOFLAVIN	1	(0.1%)
	SIMVASTATIN	1	(0.1%)
	SODIUM CHLORIDE	1	(0.1%)
	THIAMINE	1	(0.1%)
	HYDROCHLORIDE		
	TRANEXAMIC ACID	8	(0.6%)
CARDIOVASCULAR	TOTAL	20	(1.6%)
	AMLODIPINE	1	(0.1%)
	ATENOLOL	3	(0.2%)
	BETAXOLOL	1	(0.1%)
	CINCHOCAINE	1	(0.1%)
	HYDROCHLORIDE		
	ENALAPRIL MALEATE	1	(0.1%)
	FUROSEMIDE	3	(0.2%)
	HYDROCHLOROTHIAZIDE	2	(0.2%)
	HYPERICUM	1	(0.1%)
	HYPERICUM EXTRACT	4	(0.3%)
	METOPROLOL	1	(0.1%)
	METOPROLOL TARTRATE	1	(0.1%)
	PREDNISOLONE	1	(0.1%)
	CAPROATE		
	PROPRANOLOL	1	(0.1%)
	RAMIPRIL	1	(0.1%)
	THEOPHYLLINE	1	(0.1%)
	TRIAMTERENE	2	(0.2%)
CENTRAL NERVOUS SYSTEM	TOTAL	242	(19.5%)
	ACETYLSALICYLATE	1	(0.1%)
	CALCIUM		
	ACETYLSALICYLATE	1	(0.1%)
	LYSINE		
	ACETYLSALICYLIC ACID	24	(1.9%)
	ALUMINIUM GLYCINATE	2	(0.2%)
	AMITRIPTYLINE	1	(0.1%)
	APROBARBITAL	1	(0.1%)
	ASCORBIC ACID	1	(0.1%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
CENTRAL NERVOUS SYSTEM	ASPARTAN	1	(0.1%)
	BUTALBITAL	1	(0.1%)
	CAFFEINE	17	(1.4%)
	CHLORCYCLIZINE	1	(0.1%)
	HYDROCHLORIDE		
	CHLORPHENAMINE	1	(0.1%)
	MALEATE		
	CINNAMEDRINE	3	(0.2%)
	HYDROCHLORIDE		
	CITRIC ACID	1	(0.1%)
	CLONAZEPAM	2	(0.2%)
	CODEINE	1	(0.1%)
	CODEINE PHOSPHATE	11	(0.9%)
	DEXTROMETHORPHAN	3	(0.2%)
	HYDROBROMIDE		
	DIAZEPAM	3	(0.2%)
	DIPHENHYDRAMINE	3	(0.2%)
	HYDROCHLORIDE		
	DOXYLAMINE SUCCINATE	2	(0.2%)
	ELETRIPTAN	1	(0.1%)
	HYDROBROMIDE		
	ERGOTAMINE TARTRATE	1	(0.1%)
	HEXETYLAMINE CITRATE	1	(0.1%)
	HYDROXYZINE	1	(0.1%)
	HYDROCHLORIDE		
	HYPERICUM	1	(0.1%)
	HYPERICUM EXTRACT	4	(0.3%)
	IBUPROFEN	117	(9.4%)
	MAGNESIUM CARBONATE	2	(0.2%)
	MEPROBAMATE	1	(0.1%)
	MEPYRAMINE MALEATE	5	(0.4%)
	METAMIZOLE SODIUM	1	(0.1%)
	METHAPYRILENE	1	(0.1%)
	HYDROCHLORIDE		
	METOCLOPRAMIDE	1	(0.1%)
	MORPHINE	1	(0.1%)
	OXAZEPAM	1	(0.1%)
	PAMABROM	5	(0.4%)
	PARACETAMOL	143	(11.5%)
	PHENAZONE	1	(0.1%)
	PHENIRAMINE MALEATE	1	(0.1%)
	PHENYLEPHRINE	1	(0.1%)
	HYDROCHLORIDE		
	PROPYPHENAZONE	2	(0.2%)
	PSEUDOEPHEDRINE	6	(0.5%)
	HYDROCHLORIDE		

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
CENTRAL NERVOUS SYSTEM	SALICYLAMIDE	2	(0.2%)
	SIBUTRAMINE	1	(0.1%)
	SODIUM BICARBONATE	1	(0.1%)
	SODIUM CARBONATE	1	(0.1%)
	SORBITOL	1	(0.1%)
	SUMATRIPTAN	4	(0.3%)
	TEMAZEPAM	1	(0.1%)
	TRAZODONE	1	(0.1%)
	ZOPICLONE	1	(0.1%)
DERMATOLOGICALS	TOTAL	42	(3.4%)
	BETAMETHASONE	2	(0.2%)
	VALERATE		
	BUDESONIDE	8	(0.6%)
	CALCIPOTRIOL	1	(0.1%)
	CINCHOCAINE	1	(0.1%)
	HYDROCHLORIDE		
	CLOBETASOL	1	(0.1%)
	PROPIONATE		
	COD-LIVER OIL	1	(0.1%)
	DIPHENHYDRAMINE	1	(0.1%)
	HYDROCHLORIDE		
	ERYTHROMYCIN	1	(0.1%)
	FLUTICASONE	8	(0.6%)
	PROPIONATE		
	HYDROCORTISONE	3	(0.2%)
	HYDROXYQUINOLINE	1	(0.1%)
	SULFATE		
	METRONIDAZOLE	3	(0.2%)
	MICONAZOLE NITRATE	2	(0.2%)
	MOMETASONE FUROATE	4	(0.3%)
	PENCICLOVIR	2	(0.2%)
	PRAMOCAINE	1	(0.1%)
	HYDROCHLORIDE		
	PREDNISOLONE	1	(0.1%)
	CAPROATE		
	SALMETEROL XINAFOATE	1	(0.1%)
	TERBINAFINE	1	(0.1%)
	TETRACYCLINE	1	(0.1%)
	HYDROCHLORIDE		
	TOCOPHEROL	4	(0.3%)
	TRIAMCINOLONE	1	(0.1%)
	ACETONIDE		
	ZINC OXIDE	1	(0.1%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
GU SYSTEM/SEX HORMONES	TOTAL	22	(1.8%)
	ANTIBIOTIC NOS	3	(0.2%)
	CRANBERRY	1	(0.1%)
	CYPROTERONE ACETATE	1	(0.1%)
	DIMETHYL SULFONE	3	(0.2%)
	ETHINYLESTRADIOL	3	(0.2%)
	HYPERICUM	1	(0.1%)
	HYPERICUM EXTRACT	4	(0.3%)
	METRONIDAZOLE	3	(0.2%)
	MICONAZOLE NITRATE	1	(0.1%)
	NITROFURANTOIN	3	(0.2%)
	NORETHISTERONE ACETATE	2	(0.2%)
	NORFLOXACIN	2	(0.2%)
	OFLOXACIN	1	(0.1%)
MUSCULO-SKELETAL	TOTAL	165	(13.3%)
	ADRENAL CORTICAL EXTRACT	1	(0.1%)
	BETA-HEPARIN	1	(0.1%)
	CARISOPRODOL	1	(0.1%)
	CELECOXIB	5	(0.4%)
	CHONDROITIN SULFATE	1	(0.1%)
	CODEINE PHOSPHATE	1	(0.1%)
	DEXIBUPROFEN	1	(0.1%)
	DICLOFENAC	2	(0.2%)
	DICLOFENAC POTASSIUM	1	(0.1%)
	DICLOFENAC SODIUM	7	(0.6%)
	DIMETHYL SULFONE	3	(0.2%)
	FLURBIPROFEN	1	(0.1%)
	GLUCOSAMINE SULFATE	1	(0.1%)
	IBUPROFEN	118	(9.5%)
	KETOPROFEN	2	(0.2%)
	KETOROLAC	3	(0.2%)
	TROMETHAMINE		
	MEFENAMIC ACID	3	(0.2%)
	MELOXICAM	2	(0.2%)
	METHOCARBAMOL	1	(0.1%)
	MISOPROSTOL	2	(0.2%)
	NAPROXEN	15	(1.2%)
	NAPROXEN SODIUM	14	(1.1%)
	NIMESULIDE	2	(0.2%)
	PARACETAMOL	1	(0.1%)
	PSEUDOEPHEDRINE	2	(0.2%)
	HYDROCHLORIDE		
	ROFECOXIB	2	(0.2%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
MUSCULO-SKELETAL	SALICYLIC ACID	1	(0.1%)
	TIZANIDINE	2	(0.2%)
	HYDROCHLORIDE		
	TOLFENAMIC ACID	1	(0.1%)
PARASITOLOGY	TOTAL	4	(0.3%)
	MEBENDAZOLE	1	(0.1%)
	METRONIDAZOLE	3	(0.2%)
RESPIRATORY	TOTAL	80	(6.4%)
	ACETYLCYSTEINE	2	(0.2%)
	ACETYLSALICYLIC ACID	3	(0.2%)
	ACONITE	1	(0.1%)
	ACRIVASTINE	5	(0.4%)
	ADONIS VERNALIS	1	(0.1%)
	GLYCOSIDES		
	ALIMEMAZINE TARTRATE	1	(0.1%)
	ASCORBIC ACID	4	(0.3%)
	BECLOMETASONE	2	(0.2%)
	DIPROPIONATE		
	BELLADONNA ALKALOIDS	1	(0.1%)
	BUDESONIDE	8	(0.6%)
	CAFFEINE	3	(0.2%)
	CASCARA LIQUID	2	(0.2%)
	EXTRACT		
	CETIRIZINE	2	(0.2%)
	CETIRIZINE	5	(0.4%)
	HYDROCHLORIDE		
	CHLORPHENAMINE	3	(0.2%)
	MALEATE		
	CITRIC ACID	1	(0.1%)
	COCILLANA LIQUID	2	(0.2%)
	EXTRACT		
	CODEINE PHOSPHATE	2	(0.2%)
	DESLORATADINE	1	(0.1%)
	DEXTROMETHORPHAN	4	(0.3%)
	HYDROBROMIDE		
	DIMENHYDRINATE	1	(0.1%)
	DIPHENHYDRAMINE	4	(0.3%)
	HYDROCHLORIDE		
	DOXYLAMINE SUCCINATE	2	(0.2%)
	ECHINACEA EXTRACT	1	(0.1%)
	ETHYLMORPHINE	2	(0.2%)
	HYDROCHLORIDE		
	EUPATORIUM	1	(0.1%)
	PERFOLIATUM		

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)
RESPIRATORY	EUPHORBIA LIQUID EXTRACT	2 (0.2%)
	FEXOFENADINE HYDROCHLORIDE	4 (0.3%)
	FLUTICASONE PROPIONATE	8 (0.6%)
	FORMOTEROL	1 (0.1%)
	GENTIAN	1 (0.1%)
	GLYCEROL 85%	1 (0.1%)
	GUAIFENESIN	2 (0.2%)
	HEXETHYLAMINE CITRATE	1 (0.1%)
	IBUPROFEN	1 (0.1%)
	IPRATROPIUM BROMIDE	1 (0.1%)
	LACTUCA SYRUP	2 (0.2%)
	LORATADINE	7 (0.6%)
	MAGNESIUM OXIDE	1 (0.1%)
	MIZOLASTINE	1 (0.1%)
	MOMETASONE FUROATE	4 (0.3%)
	MONTELUKAST SODIUM	1 (0.1%)
	MYRISTICA	1 (0.1%)
	NAPROXEN SODIUM	1 (0.1%)
	NOSCAPINE	2 (0.2%)
	HYDROCHLORIDE	
	OXYMETAZOLINE	3 (0.2%)
	HYDROCHLORIDE	
	PARACETAMOL	9 (0.7%)
	PENTOXYVERINE	1 (0.1%)
	CITRATE	
	PHENIRAMINE MALEATE	2 (0.2%)
	PHENYLEPHRINE	1 (0.1%)
	PHENYLEPHRINE	3 (0.2%)
	HYDROCHLORIDE	
	PHENYLPROPANOLAMINE	1 (0.1%)
	HYDROCHLORIDE	
	POLYGALA SENEGA	2 (0.2%)
	POTASSIUM IODIDE	4 (0.3%)
	PREDNISONE	1 (0.1%)
	PRIMULA FLOWERS	1 (0.1%)
	PROPYPHENAZONE	1 (0.1%)
	PSEUDOEPHEDRINE	3 (0.2%)
	PSEUDOEPHEDRINE	13 (1.0%)
	HYDROCHLORIDE	
	PSEUDOEPHEDRINE	2 (0.2%)
	SULFATE	
	RUMICIS ASETOSA	1 (0.1%)
	SALBUTAMOL	5 (0.4%)
	SALBUTAMOL SULFATE	2 (0.2%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
RESPIRATORY	SALICYLAMIDE	1	(0.1%)
	SALMETEROL	1	(0.1%)
	HYDROXYNAPHTHOATE		
	SALMETEROL XINAFOATE	1	(0.1%)
	SAMBUCUS FLOWERS	1	(0.1%)
	SODIUM CHLORIDE	1	(0.1%)
	SODIUM CITRATE	1	(0.1%)
	SQUILL EXTRACT	2	(0.2%)
	TERBUTALINE	1	(0.1%)
	TERBUTALINE SULFATE	4	(0.3%)
	TETRYZOLINE	1	(0.1%)
	HYDROCHLORIDE		
	THEOPHYLLINE	1	(0.1%)
	TRIAMCINOLONE	1	(0.1%)
	ACETONIDE		
	VERBENA HERB	1	(0.1%)
	XYLOMETAZOLINE	4	(0.3%)
	HYDROCHLORIDE		
SENSORY ORGANS	TOTAL	26	(2.1%)
	BETAXOLOL	1	(0.1%)
	DICLOFENAC SODIUM	5	(0.4%)
	ERYTHROMYCIN	1	(0.1%)
	FLURBIPROFEN	1	(0.1%)
	HYDROCORTISONE	2	(0.2%)
	KETOROLAC	3	(0.2%)
	TROMETHAMINE		
	OFLOXACIN	1	(0.1%)
	OXYMETAZOLINE	3	(0.2%)
	HYDROCHLORIDE		
	POTASSIUM IODIDE	4	(0.3%)
	SODIUM CHLORIDE	1	(0.1%)
	TETRACYCLINE	1	(0.1%)
	HYDROCHLORIDE		
	TETRYZOLINE	1	(0.1%)
	HYDROCHLORIDE		
	TRIAMCINOLONE	1	(0.1%)
	ACETONIDE		
	XYLOMETAZOLINE	3	(0.2%)
	HYDROCHLORIDE		
SYSTEMIC HORMONAL	TOTAL	25	(2.0%)
	HYDROCORTISONE	2	(0.2%)
	LEVOTHYROXINE SODIUM	17	(1.4%)
	POTASSIUM IODIDE	5	(0.4%)
	PREDNISONE	1	(0.1%)

Table 12.30

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Screening Only Population

ATC Level 1	Generic Term	Treatment Group No Therapy Dispensed (N=1242)	
SYSTEMIC HORMONAL	TRIAMCINOLONE ACETONIDE	1	(0.1%)
VARIOUS	TOTAL	26	(2.1%)
	CAFFEINE	1	(0.1%)
	CAPSICUM	1	(0.1%)
	CHROMIUM	1	(0.1%)
	CRANBERRY	1	(0.1%)
	DIMETHYL SULFONE	3	(0.2%)
	ECHINACEA	1	(0.1%)
	AUGUSTIFOLIA		
	ECHINACEA EXTRACT	2	(0.2%)
	ECHINACEA PURPUREA	1	(0.1%)
	EPHEDRA	1	(0.1%)
	GINGER	1	(0.1%)
	GINSENG	2	(0.2%)
	HERBAL MEDICATION	2	(0.2%)
	HOMEOPATHIC PREPARATIONS	2	(0.2%)
	HYDROXYCITRIC ACID	1	(0.1%)
	HYPERICUM	1	(0.1%)
	HYPERICUM EXTRACT	4	(0.3%)
	MINERALS NOS	1	(0.1%)
	NICOTINE	2	(0.2%)
	NICOTINE RESIN	1	(0.1%)
	NUTRITIONAL	1	(0.1%)
	SUPPLEMENT NOS		
	POTASSIUM IODIDE	4	(0.3%)
	TRACE ELEMENTS, NOS	1	(0.1%)
	UMCKALOABO	1	(0.1%)
	VITAMINS NOS	1	(0.1%)
	WILLOW BARK	1	(0.1%)

Table 12.31

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Randomised (non-ITT) Population

ATC Level 1	Generic Term	Treatment Group			Total (N=7)
		Paroxetine CR 25 mg (N=3)	Paroxetine CR 12.5 mg (N=1)	Placebo (N=3)	
TOTAL	TOTAL	3 (100.0%)	1 (100.0%)	2 (66.7%)	6 (85.7%)
ALIMENTARY TRACT/METAB	TOTAL	2 (66.7%)	0 (0.0%)	0 (0.0%)	2 (28.6%)
	MINERALS NOS	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	NICOTINAMIDE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	PANTHENOL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	PYRIDOXINE HYDROCHLORIDE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	RIBOFLAVIN	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	THIAMINE HYDROCHLORIDE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	TRACE ELEMENTS, NOS	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	VITAMINS NOS	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
ANTIINFECTIVES, SYSTE MIC	TOTAL	1 (33.3%)	0 (0.0%)	1 (33.3%)	2 (28.6%)
	AMOXICILLIN	1 (33.3%)	0 (0.0%)	1 (33.3%)	2 (28.6%)
	TETRACYCLINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
BLOOD/BLOOD FORM ORGANS	TOTAL	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	IRON	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
CENTRAL NERVOUS SYSTEM	TOTAL	3 (100.0%)	1 (100.0%)	1 (33.3%)	5 (71.4%)
	IBUPROFEN	3 (100.0%)	1 (100.0%)	1 (33.3%)	5 (71.4%)
	PARACETAMOL	2 (66.7%)	1 (100.0%)	0 (0.0%)	3 (42.9%)
	TOLPERISONE HYDROCHLORIDE	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (14.3%)
DERMATOLOGICALS	TOTAL	1 (33.3%)	1 (100.0%)	1 (33.3%)	3 (42.9%)
	FLUTICASONE PROPIONATE	1 (33.3%)	1 (100.0%)	0 (0.0%)	2 (28.6%)
	TETRACYCLINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
MUSCULO-SKELETAL	TOTAL	3 (100.0%)	1 (100.0%)	1 (33.3%)	5 (71.4%)
	IBUPROFEN	3 (100.0%)	1 (100.0%)	1 (33.3%)	5 (71.4%)
	NAPROXEN	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	ROFECOXIB	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (14.3%)

'Prior' : start date prior to start of randomised study medication,
or all medication if no study medication taken

Table 12.31

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Randomised (non-ITT) Population

ATC Level 1	Generic Term	Treatment Group			Total (N=7)
		Paroxetine CR 25 mg (N=3)	Paroxetine CR 12.5 mg (N=1)	Placebo (N=3)	
RESPIRATORY	TOTAL	1 (33.3%)	1 (100.0%)	0 (0.0%)	2 (28.6%)
	CODEINE PHOSPHATE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	FLUTICASONE PROPIONATE	1 (33.3%)	1 (100.0%)	0 (0.0%)	2 (28.6%)
	ORCIPRENALINE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	PSEUDOEPHEDRINE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	PSEUDOEPHEDRINE HYDROCHLORIDE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
	TRIPROLIDINE HYDROCHLORIDE	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)
SENSORY ORGANS	TOTAL	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	TETRACYCLINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
VARIOUS	TOTAL	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	COLOCYNTH	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	CRAMP BARK	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	MAGNESIUM PHOSPHATE	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	SEPIA	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	SODIUM CHLORIDE	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)
	VERATRUM LUTEUM	0 (0.0%)	0 (0.0%)	1 (33.3%)	1 (14.3%)

'Prior' : start date prior to start of randomised study medication,
or all medication if no study medication taken

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	TOTAL	82 (70.7%)	89 (68.5%)	83 (69.2%)		254 (69.4%)
ALIMENTARY TRACT/METAB	TOTAL	17 (14.7%)	22 (16.9%)	24 (20.0%)		63 (17.2%)
	ACETYLSALICYLIC ACID	2 (1.7%)	3 (2.3%)	4 (3.3%)		9 (2.5%)
	ALGIN	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	ALGINIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	ALUMINIUM HYDROXIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	AMINO BENZOIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	AMOXICILLIN	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	ASCORBIC ACID	2 (1.7%)	2 (1.5%)	4 (3.3%)		8 (2.2%)
	BISMUTH	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	SUBSALICYLATE					
	CALCIUM	2 (1.7%)	1 (0.8%)	7 (5.8%)		10 (2.7%)
	CALCIUM CARBONATE	0 (0.0%)	1 (0.8%)	1 (0.8%)		2 (0.5%)
	CALCIUM PANTOTHENATE	0 (0.0%)	2 (1.5%)	1 (0.8%)		3 (0.8%)
	CHROMIUM PICOLINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	CISAPRIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	CYSTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	DIMETICONE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	EQUISETUM ARVENSE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	ESOMEPRAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	FERROUS CARBONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	FOLIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	GAMOLENIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	GINSENG	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	HYOSCYAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	INSULIN HUMAN	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	INSULIN INJECTION, ISOPHANE	0 (0.0%)	0 (0.0%)	2 (1.7%)		2 (0.5%)
	INSULIN LISPRO	0 (0.0%)	1 (0.8%)	1 (0.8%)		2 (0.5%)
	IRON	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	ISPAGHULA	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	KERATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	LACTOBACILLI NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	LACTOBACILLUS	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	ACIDOPHILUS					
	LANSOPRAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	LOPERAMIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)		3 (0.8%)
	HYDROCHLORIDE					
	MAGNESIUM CARBONATE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	MAGNESIUM HYDROXIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	MAGNESIUM NOS	1 (0.9%)	1 (0.8%)	2 (1.7%)		4 (1.1%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ALIMENTARY TRACT/METAB	MAGNESIUM PHOSPHATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MONOBASIC				
	MAGNESIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TRISILICATE				
	MANGANESE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	METRONIDAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MINERALS NOS	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
	MOLYBDENUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SESQUIOXIDE				
	NICOTINAMIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	OMEPRAZOLE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	PAPAVERINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	PSYLLIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HYDROPHILIC				
	MUCILLOID				
	PYRIDOXINE	2 (1.7%)	1 (0.8%)	3 (2.5%)	6 (1.6%)
	HYDROCHLORIDE				
	RANITIDINE	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	HYDROCHLORIDE				
	RIBOFLAVIN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	SODIUM BICARBONATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SODIUM BORATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SODIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TARAXACUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	THIAMINE	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	HYDROCHLORIDE				
	THIAMINE MONONITRATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	TRACE ELEMENTS, NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRIAMCINOLONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ACETONIDE				
	VITAMIN B	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	VITAMINS NOS	7 (6.0%)	7 (5.4%)	9 (7.5%)	23 (6.3%)
	YEAST DRIED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ZINC	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	ZINC SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ANTIINFECTIVES, SYSTE MIC	TOTAL	19 (16.4%)	18 (13.8%)	17 (14.2%)	54 (14.8%)
	ACICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	AMOXICILLIN	1 (0.9%)	4 (3.1%)	5 (4.2%)	10 (2.7%)
	AMOXICILLIN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	TRIHYDRATE				

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ANTIINFECTIVES, SYSTEMIC	AMPICILLIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	AZITHROMYCIN	0 (0.0%)	2 (1.5%)	5 (4.2%)	7 (1.9%)
	CEFALEXIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CEFALEXIN MONOHYDRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CIPROFLOXACIN HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	CLARITHROMYCIN	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
	CLAVULANATE POTASSIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CLAVULANIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	DOXYCYCLINE	4 (3.4%)	1 (0.8%)	1 (0.8%)	6 (1.6%)
	DOXYCYCLINE HYCLATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DOXYCYCLINE MONOHYDRATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ERYTHROMYCIN	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	FAMCICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FLUCONAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	FUSIDIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	LEVOFLOXACIN	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	LYMECYCLINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	METRONIDAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MICONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	MINOCYCLINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OMEPRazole	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PENICILLIN NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PHENOXYMETHYLPENICILLIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PHENOXYMETHYLPENICILLIN POTASSIUM	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
	SULFAMETHOXAZOLE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRIMETHOPRIM	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	VALACYCLOVIR	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	HYDROCHLORIDE				
ANTINEOPLASTIC & IMMUNOSUP	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
BLOOD/BLOOD FORM ORGANS	TOTAL	8 (6.9%)	6 (4.6%)	9 (7.5%)	23 (6.3%)
	ACETYLSALICYLIC ACID	2 (1.7%)	3 (2.3%)	4 (3.3%)	9 (2.5%)
	AMINOACETIC ACID	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	EVENING PRIMROSE OIL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FERROUS ASPARTATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FERROUS FUMARATE	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
	FERROUS SULFATE	3 (2.6%)	2 (1.5%)	1 (0.8%)	6 (1.6%)
	IRON	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	TRANEXAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CARDIOVASCULAR	TOTAL	8 (6.9%)	4 (3.1%)	6 (5.0%)	18 (4.9%)
	AMILORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	HYDROCHLORIDE				
	AMLODIPINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ATENOLOL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	BENDROFLUMETHIAZIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CELIPROLOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	CINCHOCAINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	ENALAPRIL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	EQUISETUM ARVENSE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ESCULIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FRAMYCETIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FUROSEMIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	HYDROCHLOROTHIAZIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	HYDROCORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ACETATE				
	HYPERICUM EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LOSARTAN POTASSIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	METOPROLOL TARTRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	PAMABROM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PAPAVERINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	PARACETAMOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TARAXACUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VALSARTAN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
CENTRAL NERVOUS SYSTEM	TOTAL	62 (53.4%)	74 (56.9%)	62 (51.7%)	198 (54.1%)
	ACETYLSALICYLIC ACID	5 (4.3%)	6 (4.6%)	7 (5.8%)	18 (4.9%)
	ASCORBIC ACID	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CENTRAL NERVOUS SYSTEM	ASPARTAN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	BUPRENORPHINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CAFFEINE	5 (4.3%)	5 (3.8%)	4 (3.3%)	14 (3.8%)
	CHLORCYCLIZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CINNAMEDRINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CITALOPRAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CITRIC ACID	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	CODEINE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	CODEINE PHOSPHATE	6 (5.2%)	4 (3.1%)	2 (1.7%)	12 (3.3%)
	DEXTROPROPOXYPHENE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	DIPHENHYDRAMINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ERGOTAMINE TARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	GABAPENTIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROXYZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYPERICUM EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	IBUPROFEN	35 (30.2%)	39 (30.0%)	27 (22.5%)	101 (27.6%)
	LORAZEPAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MEPROBAMATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MEPYRAMINE MALEATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	OXAZEPAM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PAMABROM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	PARACETAMOL	36 (31.0%)	47 (36.2%)	41 (34.2%)	124 (33.9%)
	PASSIFLORA EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PHENACETIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	PHENAZONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PHENYLPROPANOLAMINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PHENYLTOLOXAMINE CITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PROMETHAZINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PSEUDOEPHEDRINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	QUININE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SALICYLAMIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	SODIUM BICARBONATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SODIUM CARBONATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SORBITOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
CENTRAL NERVOUS SYSTEM	SUMATRIPTAN	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	TEMAZEPAM	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	TETRAZEPAM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TRAMADOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TRAMADOL HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	ZOLMITRIPTAN	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	ZOLPIDEM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HEMITARTRATE ZOPICLONE	3 (2.6%)	0 (0.0%)	1 (0.8%)	4 (1.1%)
DERMATOLOGICALS	TOTAL	15 (12.9%)	9 (6.9%)	12 (10.0%)	36 (9.8%)
	ADAPALENE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	BETAMETHASONE VALERATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	BUDESONIDE	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	CETYLPIRIDINIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CLOTRIMAZOLE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ECONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ERYTHROMYCIN	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	FLUTICASONE PROPIONATE	5 (4.3%)	2 (1.5%)	2 (1.7%)	9 (2.5%)
	FUSIDIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ISOTRETINOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	LIDOCAINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LINOLEIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	METRONIDAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MICONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	1 (0.8%)	4 (1.1%)
	SALMETEROL XINAFOATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TERBINAFINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GU SYSTEM/SEX HORMONES	TOTAL	6 (5.2%)	7 (5.4%)	5 (4.2%)	18 (4.9%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
GU SYSTEM/SEX HORMONES	CHLORMADINONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CIPROFLOXACIN HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	CLOTRIMAZOLE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	DANAZOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ECONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	EQUISETUM ARVENSE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ETHINYLESTRADIOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYPERICUM EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MESTRANOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	METRONIDAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MICONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	NITROFURANTOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NORGESTREL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PHENAZOPYRIDINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TARAXACUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MUSCULO-SKELETAL	TOTAL	42 (36.2%)	49 (37.7%)	41 (34.2%)	132 (36.1%)
	ACETYLSALICYLIC ACID	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	CELECOXIB	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	CHLORZOXAZONE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	CODEINE PHOSPHATE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	DEXIBUPROFEN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	DICLOFENAC	0 (0.0%)	2 (1.5%)	6 (5.0%)	8 (2.2%)
	DICLOFENAC SODIUM	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	GLUCOSAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	IBUPROFEN	35 (30.2%)	39 (30.0%)	27 (22.5%)	101 (27.6%)
	KETOPROFEN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MEFENAMIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MELOXICAM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	METHOCARBAMOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	NAPROXEN	6 (5.2%)	4 (3.1%)	5 (4.2%)	15 (4.1%)
	NAPROXEN SODIUM	1 (0.9%)	4 (3.1%)	1 (0.8%)	6 (1.6%)
	NIMESULIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PSEUDOEPHEDRINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	ROFECOXIB	1 (0.9%)	3 (2.3%)	0 (0.0%)	4 (1.1%)
	TIZANIDINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	HYDROCHLORIDE				
PARASITOLOGY	TOTAL	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
PARASITOLOGY	ATOVAQUONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	METRONIDAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	1 (0.3%)
	PROGUANIL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	PROGUANIL HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	1 (0.3%)
RESPIRATORY	TOTAL	21 (18.1%)	29 (22.3%)	23 (19.2%)	73 (19.9%)	73 (19.9%)
	ACETYLCYSTEINE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)	2 (0.5%)
	ACETYLSALICYLIC ACID	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)	4 (1.1%)
	ACRIVASTINE	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)	4 (1.1%)
	AMMONIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	AMYLMETACRESOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	ANTIHIISTAMINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	ASCORBIC ACID	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)	4 (1.1%)
	BROMHEXINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	BUDESONIDE	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)	4 (1.1%)
	CAFFEINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)	2 (0.5%)
	CASCARA LIQUID EXTRACT	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)	3 (0.8%)
	CETIRIZINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	CETIRIZINE HYDROCHLORIDE	0 (0.0%)	5 (3.8%)	1 (0.8%)	6 (1.6%)	6 (1.6%)
	CHLORPHENAMINE MALEATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	COCILLANA LIQUID EXTRACT	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)	4 (1.1%)
	CODEINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	1 (0.3%)
	DESLOFATADINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	DEXTROMETHORPHAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	DICHLOROBENZYL ALCOHOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	DIMENHYDRINATE	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)	3 (0.8%)
	DIPHENHYDRAMINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	1 (0.3%)
	EBASTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	EPHEDRINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.3%)
	ETHYLMORPHINE HYDROCHLORIDE	3 (2.6%)	2 (1.5%)	0 (0.0%)	5 (1.4%)	5 (1.4%)
	EUPHORBIA LIQUID EXTRACT	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)	4 (1.1%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
RESPIRATORY	FEXOFENADINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FLUTICASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FLUTICASONE PROPIONATE	5 (4.3%)	2 (1.5%)	2 (1.7%)	9 (2.5%)
	FORMOTEROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	FRANGULA EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	GENTIAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	GLYCYRRHIZA EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	GUAIFENESIN	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	IBUPROFEN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	IPRATROPIUM BROMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LACTUCA SYRUP	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
	LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	LORATADINE	4 (3.4%)	2 (1.5%)	1 (0.8%)	7 (1.9%)
	MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	1 (0.8%)	4 (1.1%)
	MONTELUKAST SODIUM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	MYRTOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OXYMETAZOLINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PAMABROM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PARACETAMOL	0 (0.0%)	1 (0.8%)	3 (2.5%)	4 (1.1%)
	PHENYLEPHRINE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	PHENYLPROPANOLAMINE HYDROCHLORIDE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	PHOLCODINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	POLYGALA SENEGA	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
	POLYSORBATE 20	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PRIMULA FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PSEUDOEPHEDRINE	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)
	PSEUDOEPHEDRINE HYDROCHLORIDE	1 (0.9%)	3 (2.3%)	6 (5.0%)	10 (2.7%)
	PSEUDOEPHEDRINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	RUMICIS ASETOSA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SALBUTAMOL	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)
	SALBUTAMOL SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SALMETEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROXYNAPHTHOATE				
	SALMETEROL XINAFOATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SAMBUCUS FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
RESPIRATORY	SQUILL EXTRACT	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
	TERBUTALINE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	VERBENA HERB	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	XYLOMETAZOLINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
	TOTAL	5 (4.3%)	12 (9.2%)	11 (9.2%)	28 (7.7%)
SENSORY ORGANS	CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CIPROFLOXACIN HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DEXAMETHASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DEXAMETHASONE ISONICOTINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DICLOFENAC SODIUM	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	ERYTHROMYCIN	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
	FUSIDIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	GENTAMICIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	LEVOCABASTINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE OXYMETAZOLINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	XYLOMETAZOLINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
	TOTAL	4 (3.4%)	7 (5.4%)	8 (6.7%)	19 (5.2%)
	CARBIMAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SYSTEMIC HORMONAL	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	DEXAMETHASONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ISONICOTINATE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	LEVOTHYROXINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LEVOTHYROXINE SODIUM	3 (2.6%)	4 (3.1%)	4 (3.3%)	11 (3.0%)
	LIOthyronine SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TOTAL	4 (3.4%)	7 (5.4%)	8 (6.7%)	19 (5.2%)

'Prior' : start date prior to start of randomised study medication

Table 12.32

Number (%) of Subjects with Prior Medication by ATC Classification and Generic Term
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
SYSTEMIC HORMONAL	POTASSIUM IODIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VARIOUS	TOTAL	4 (3.4%)	5 (3.8%)	5 (4.2%)	14 (3.8%)
	ALLERGENIC EXTRACT, NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ECHINACEA EXTRACT	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	ECHINACEA PURPUREA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	EQUISETUM ARVENSE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	GINSENG	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HERBAL MEDICATION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HOMEOPATHIC PREPARATIONS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HYDRASTIS CANADENSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYPERICUM EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MILK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MINERALS NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NATURAL INGREDIENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NICOTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NICOTINE RESIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TARAXACUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TRACE ELEMENTS, NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	VITAMINS NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TOTAL	82 (70.7%)	89 (68.5%)	83 (69.2%)	254 (69.4%)
PARACETAMOL	36 (31.0%)	47 (36.2%)	41 (34.2%)	124 (33.9%)
IBUPROFEN	35 (30.2%)	39 (30.0%)	27 (22.5%)	101 (27.6%)
ACETYLSALICYLIC ACID	7 (6.0%)	7 (5.4%)	11 (9.2%)	25 (6.8%)
VITAMINS NOS	7 (6.0%)	7 (5.4%)	9 (7.5%)	23 (6.3%)
CAFFEINE	6 (5.2%)	6 (4.6%)	4 (3.3%)	16 (4.4%)
CODEINE PHOSPHATE	7 (6.0%)	4 (3.1%)	4 (3.3%)	15 (4.1%)
NAPROXEN	6 (5.2%)	4 (3.1%)	5 (4.2%)	15 (4.1%)
ASCORBIC ACID	3 (2.6%)	3 (2.3%)	7 (5.8%)	13 (3.6%)
LEVOTHYROXINE SODIUM	3 (2.6%)	4 (3.1%)	4 (3.3%)	11 (3.0%)
AMOXICILLIN	1 (0.9%)	4 (3.1%)	5 (4.2%)	10 (2.7%)
CALCIUM	2 (1.7%)	1 (0.8%)	7 (5.8%)	10 (2.7%)
PSEUDOEPHEDRINE HYDROCHLORIDE	1 (0.9%)	3 (2.3%)	6 (5.0%)	10 (2.7%)
FLUTICASONE PROPIONATE	5 (4.3%)	2 (1.5%)	2 (1.7%)	9 (2.5%)
DICLOFENAC	0 (0.0%)	2 (1.5%)	6 (5.0%)	8 (2.2%)
AZITHROMYCIN	0 (0.0%)	2 (1.5%)	5 (4.2%)	7 (1.9%)
LORATADINE	4 (3.4%)	2 (1.5%)	1 (0.8%)	7 (1.9%)
CETIRIZINE HYDROCHLORIDE	0 (0.0%)	5 (3.8%)	1 (0.8%)	6 (1.6%)
DOXYCYCLINE	4 (3.4%)	1 (0.8%)	1 (0.8%)	6 (1.6%)
FERROUS SULFATE	3 (2.6%)	2 (1.5%)	1 (0.8%)	6 (1.6%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
NAPROXEN SODIUM	1 (0.9%)	4 (3.1%)	1 (0.8%)	6 (1.6%)
PYRIDOXINE HYDROCHLORIDE	2 (1.7%)	1 (0.8%)	3 (2.5%)	6 (1.6%)
ETHYLMORPHINE HYDROCHLORIDE	3 (2.6%)	2 (1.5%)	0 (0.0%)	5 (1.4%)
MINERALS NOS	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
SALBUTAMOL	2 (1.7%)	2 (1.5%)	1 (0.8%)	5 (1.4%)
ACRIVASTINE	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)
BUDESONIDE	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)
CLARITHROMYCIN	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
COCILLANA LIQUID EXTRACT	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
DICLOFENAC SODIUM	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
EUPHORBIA LIQUID EXTRACT	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
FERROUS FUMARATE	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
LACTUCA SYRUP	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
MAGNESIUM NOS	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	1 (0.8%)	4 (1.1%)
PHENOXYMETHYLPENICIL LIN POTASSIUM	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
PHENYLPROPANOLAMINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
POLYGALA SENEGA	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
PSEUDOEPHEDRINE	0 (0.0%)	3 (2.3%)	1 (0.8%)	4 (1.1%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ROFECOXIB	1 (0.9%)	3 (2.3%)	0 (0.0%)	4 (1.1%)
SQUILL EXTRACT	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
XYLOMETAZOLINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
ZOLMITRIPTAN	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
ZOPICLONE	3 (2.6%)	0 (0.0%)	1 (0.8%)	4 (1.1%)
CALCIUM PANTOTHENATE	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
CASCARA LIQUID EXTRACT	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
CHLORZOXAZONE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
CLOTRIMAZOLE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
DEXTROPROPOXYPHENE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
DIMENHYDRINATE	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
ECHINACEA EXTRACT	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
ERYTHROMYCIN	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
FUROSEMIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
GUAIFENESIN	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
IRON	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
LEVOFLOXACIN	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
LOPERAMIDE HYDROCHLORIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
OMEPRazole	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
RANITIDINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
SULFAMETHOXAZOLE	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
SUMATRIPTAN	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
TEMAZEPAM	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
THIAMINE HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
TRIMETHOPRIM	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
ZINC	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
ACETYLCYSTEINE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
AMILORIDE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
AMINOACETIC ACID	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
AMOXICILLIN TRIHYDRATE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ATENOLOL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
CALCIUM CARBONATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
CELECOXIB	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
CIPROFLOXACIN HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
CITRIC ACID	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
CODEINE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
DEXIBUPROFEN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
FLUCONAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
HYDROCHLOROTHIAZIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
INSULIN INJECTION, ISOPHANE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
INSULIN LISPRO	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
LYMECYCLINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MEPYRAMINE MALEATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
METOPROLOL TARTRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MICONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MONTELUKAST SODIUM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
NICOTINAMIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
PAMABROM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
PHENACETIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
PHENYLEPHRINE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
POTASSIUM IODIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
RIBOFLAVIN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
SALICYLAMIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
SODIUM BICARBONATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
TIZANIDINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
TRAMADOL HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
VALACYCLOVIR HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
VALSARTAN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
VITAMIN B	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
XYLOMETAZOLINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ACICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ADAPALENE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ALGIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ALGINIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ALLERGENIC EXTRACT, NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ALUMINIUM HYDROXIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
AMINOBENZOIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
AMLODIPINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
AMMONIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
AMPICILLIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
AMYLMETACRESOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ANTIHIISTAMINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ASPARTAN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ATOVAQUONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
BENDROFLUMETHIAZIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
BETAMETHASONE VALERATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BISMUTH SUBSALICYLATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BROMHEXINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BUPRENORPHINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CARBIMAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CEFALEXIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CEFALEXIN MONOHYDRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CELIPROLOL HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CETIRIZINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CETYLPYRIDINIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CHLORCYCLIZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CHLORMADINONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CHLORPHENAMINE MALEATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CHROMIUM PICOLINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CINCHOCAINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CINNAMEDRINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CISAPRIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CITALOPRAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CLAVULANATE POTASSIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CLAVULANIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CYSTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DANAZOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DESLOMATADINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DEXAMETHASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DEXAMETHASONE ISONICOTINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DEXTROMETHORPHAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DICHLOROBENZYL ALCOHOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DIMETICONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DIPHENHYDRAMINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DOXYCYCLINE HYCLATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DOXYCYCLINE MONOHYDRATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EBASTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ECHINACEA PURPUREA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ECONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ENALAPRIL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EPHEDRINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
EQUISETUM ARVENSE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ERGOTAMINE TARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ESCULIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ESOMEPRAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ETHINYLESTRADIOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EVENING PRIMROSE OIL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FAMCICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FERROUS ASPARTATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FERROUS CARBONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FEXOFENADINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FLUTICASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FOLIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FORMOTEROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FRAMYCETIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FRANGULA EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FUSIDIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
GABAPENTIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
GAMOLENIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
GENTAMICIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
GENTIAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GINSENG	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GLUCOSAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GLYCYRRHIZA EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HERBAL MEDICATION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HOMEOPATHIC PREPARATIONS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HYDRASTIS CANADENSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HYDROCORTISONE ACETATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HYDROXYZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
HYOSCYAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HYPERICUM EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
INSULIN HUMAN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
IPRATROPIUM BROMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ISOTRETINOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ISPAGHULA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
KERATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
KETOPROFEN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
LACTOBACILLI NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LACTOBACILLUS ACIDOPHILUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LANSOPRAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LEVOTHYROXINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LIDOCAINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LINOLEIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LIOTHYRONINE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LORAZEPAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LOSARTAN POTASSIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MAGNESIUM CARBONATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MAGNESIUM HYDROXIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MAGNESIUM PHOSPHATE MONOBASIC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MAGNESIUM TRISILICATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MANGANESE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MEFENAMIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MELOXICAM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MEPROBAMATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MESTRANOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
METHOCARBAMOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METRONIDAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MILK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MINOCYCLINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MOLYBDENUM SESQUIOXIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MYRTOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NATURAL INGREDIENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NICOTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NICOTINE RESIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NIMESULIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NITROFURANTOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NORGESTREL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
OXAZEPAM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
OXYMETAZOLINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PAPAVERINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PASSIFLORA EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PENICILLIN NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PHENAZONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PHENAZOPYRIDINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
PHENOXYMETHYLPENICIL LIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PHENYLTOLOXAMINE CITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PHOLCODINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
POLYSORBATE 20	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PRIMULA FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PROGUANIL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PROGUANIL HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PROMETHAZINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PSEUDOEPHEDRINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PSYLLIUM HYDROPHILIC MUCILLOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
QUININE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
RUMICIS ASETOSA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SALBUTAMOL SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SALMETEROL HYDROXYNAPHTHOATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SALMETEROL XINAFOATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SAMBUCUS FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SODIUM BORATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SODIUM CARBONATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.33

Number (%) of Subjects with Prior Medication by Preferred Term
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
SODIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SORBITOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TARAXACUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TERBINAFINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TERBUTALINE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TETRAZEPAM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
THIAMINE MONONITRATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TRACE ELEMENTS, NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TRAMADOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TRANEXAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VERBENA HERB	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
YEAST DRIED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ZINC SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ZOLPIDEM HEMITARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

'Prior' : start date prior to start of randomised study medication

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	TOTAL	78 (67.2%)	75 (57.7%)	81 (67.5%)		234 (63.9%)
ALIMENTARY TRACT/METAB	TOTAL	20 (17.2%)	18 (13.8%)	19 (15.8%)		57 (15.6%)
	ACETYLSALICYLIC ACID	3 (2.6%)	5 (3.8%)	2 (1.7%)		10 (2.7%)
	ALUMINIUM HYDROXIDE	2 (1.7%)	0 (0.0%)	0 (0.0%)		2 (0.5%)
	AMINOBENZOIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	AMOXICILLIN	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	ASCORBIC ACID	1 (0.9%)	2 (1.5%)	5 (4.2%)		8 (2.2%)
	BENZYLAMINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	BISMUTH	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	BISMUTH SUBSALICYLATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	CALCIUM	2 (1.7%)	1 (0.8%)	6 (5.0%)		9 (2.5%)
	CALCIUM CARBONATE	1 (0.9%)	2 (1.5%)	1 (0.8%)		4 (1.1%)
	CALCIUM PANTOTHENATE	0 (0.0%)	2 (1.5%)	0 (0.0%)		2 (0.5%)
	CHROMIUM PICOLINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	CYNARA SCOLYMUS	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	CYSTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	DIMETICONE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	DIMETICONE, ACTIVATED	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	ERGOCALCIFEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	ESOMEPRAZOLE	1 (0.9%)	1 (0.8%)	1 (0.8%)		3 (0.8%)
	ETHYLPARABEN	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	GINSENG	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	GLYCEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	HYOSCYAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	INSULIN HUMAN	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	INSULIN INJECTION, ISOPHANE	0 (0.0%)	0 (0.0%)	2 (1.7%)		2 (0.5%)
	INSULIN LISPRO	0 (0.0%)	1 (0.8%)	1 (0.8%)		2 (0.5%)
	IRON	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)
	ISPAGHULA	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	KERATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)
	LACTOBACILLUS ACIDOPHILUS	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)
	MAGNESIUM CARBONATE	1 (0.9%)	1 (0.8%)	0 (0.0%)		2 (0.5%)
	MAGNESIUM HYDROXIDE	2 (1.7%)	0 (0.0%)	0 (0.0%)		2 (0.5%)
	MAGNESIUM NOS	1 (0.9%)	1 (0.8%)	1 (0.8%)		3 (0.8%)
	METOCLOPRAMIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ALIMENTARY TRACT/METAB	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	MINERALS NOS	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	MOUTHWASH, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NICOTINAMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	OMEPRazole	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	PANTOPRAZOL SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PAPAVERINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	PROPYL PARABEN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PSYLLIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HYDROPHILIC				
	MUCILLOID				
	PYRIDOXINE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	HYDROCHLORIDE				
	RANITIDINE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	HYDROCHLORIDE				
	RIBOFLAVIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SACCHARIN SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SODIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	STERCULIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	THIAMINE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	HYDROCHLORIDE				
	THIAMINE MONONITRATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TILACTASE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	TRACE ELEMENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VITAMIN B	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	VITAMINS NOS	7 (6.0%)	4 (3.1%)	8 (6.7%)	19 (5.2%)
	YEAST DRIED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ZINC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ANTIINFECTIVES, SYSTE MIC	TOTAL	20 (17.2%)	12 (9.2%)	12 (10.0%)	44 (12.0%)
	ACICLOVIR	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	AMOXICILLIN	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	AMOXICILLIN TRIHYDRATE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	AZITHROMYCIN	1 (0.9%)	2 (1.5%)	3 (2.5%)	6 (1.6%)
	CEFACLO	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ANTIINFECTIVES, SYSTEMIC	CEFALEXIN MONOHYDRATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	CEFUROXIME AXETIL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CIPROFLOXACIN HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CLARITHROMYCIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CLAVULANATE POTASSIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CLAVULANIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CLINDAMYCIN HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CLOXACILLIN SODIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	DOXYCYCLINE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	ERYTHROMYCIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FLUCLOXACILLIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	FUSIDATE SODIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HEPATITIS VACCINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LYMECYCLINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	MINOCYCLINE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	OMEPRazole	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PHENOXYMETHYLPENICILLIN POTASSIUM	1 (0.9%)	3 (2.3%)	0 (0.0%)	4 (1.1%)
	PIVMECILLINAM HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	POLIOMYELITIS VACCINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ROXITHROMYCIN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	SULFAMETHOXAZOLE	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	TETANUS TOXOID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRIMETHOPRIM	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	VALACYCLOVIR HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ANTINEOPLASTIC & IMMUNOSUP	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
BLOOD/BLOOD FORM ORGANS	TOTAL	7 (6.0%)	7 (5.4%)	4 (3.3%)	18 (4.9%)	
	ACETYLSALICYLIC ACID	3 (2.6%)	5 (3.8%)	2 (1.7%)	10 (2.7%)	
	AMINOACETIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	FERROUS FUMARATE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)	
	FERROUS SULFATE	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)	
	IRON	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	TRANEXAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
CARDIOVASCULAR	TOTAL	8 (6.9%)	4 (3.1%)	5 (4.2%)	17 (4.6%)	
	AMILORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)	
	HYDROCHLORIDE					
	AMLODIPINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	ATENOLOL	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)	
	BENDROFLUMETHIAZIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	CELIPROLOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	HYDROCHLORIDE					
	CINCHOCAINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	HYDROCHLORIDE					
	ESCULIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	FRAMYCETIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	FUROSEMIDE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)	
	HYDROCHLOROTHIAZIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)	
	HYDROCORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	ACETATE					
	LOSARTAN POTASSIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	METOPROLOL TARTRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	PAMABROM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	PAPAVERINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	HYDROCHLORIDE					
	PARACETAMOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	PREDNISOLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	VALSARTAN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)	
CENTRAL NERVOUS SYSTEM	TOTAL	50 (43.1%)	58 (44.6%)	61 (50.8%)	169 (46.2%)	
	ACETYLSALICYLIC ACID	3 (2.6%)	9 (6.9%)	6 (5.0%)	18 (4.9%)	
	ALUMINIUM GLYCINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	ASCORBIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	BUPRENORPHINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	CAFFEINE	2 (1.7%)	5 (3.8%)	3 (2.5%)	10 (2.7%)	

'Concomitant' : start date on or after start of randomised study medication and on or before last date of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CENTRAL NERVOUS SYSTEM	CHLORCYCLIZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CHLORPHENAMINE MALEATE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	CITRIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CODEINE PHOSPHATE	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	DEXTROMETHORPHAN HYDROBROMIDE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	DEXTROPROPOXYPHENE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	DOXYLAMINE SUCCINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	ERGOTAMINE TARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCODONE BITARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROXYZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	IBUPROFEN	26 (22.4%)	33 (25.4%)	24 (20.0%)	83 (22.7%)
	LOCAL ANESTHESIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LORAZEPAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MAGNESIUM CARBONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MEPROBAMATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	METAMIZOLE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OXAZEPAM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PAMABROM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PARACETAMOL	30 (25.9%)	26 (20.0%)	40 (33.3%)	96 (26.2%)
	PHENAZONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PHENIRAMINE MALEATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PHENYLEPHRINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PROMETHAZINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PSEUDOEPHEDRINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	SALICYLAMIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SUMATRIPTAN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TEMAZEPAM	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	TRAMADOL HYDROCHLORIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	ZOLMITRIPTAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ZOLPIDEM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HEMITARTRATE				
	ZOPICLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

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Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
DERMATOLOGICALS	TOTAL	17 (14.7%)	10 (7.7%)	13 (10.8%)	40 (10.9%)	
	ADAPALENE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	BETAMETHASONE VALERATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	BORIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	BUDESONIDE	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)	
	CLOTRIMAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	DIPHENHYDRAMINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)	
	ECONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	ENTEROCOCCI	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	ERYTHROMYCIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	ESCHERICHIA COLI	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	FLUTICASONE PROPIONATE	5 (4.3%)	1 (0.8%)	0 (0.0%)	6 (1.6%)	
	FUSIDATE SODIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	ISOTRETINOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	LEMON BALM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	LOCAL ANESTHESIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)	
	NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	PHENOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	PODOPHYLLOTOXIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	PREDNISOLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	PSEUDOMONAS AURUGINOSA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	SALICYLIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	SALMETEROL XINAFOATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	
	STAPHYLOCOCCUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	STREPTOCOCCUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)	
	TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	ZINC OXIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
GU SYSTEM/SEX HORMONES	TOTAL	6 (5.2%)	4 (3.1%)	3 (2.5%)	13 (3.6%)	
	CIMICIFUGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	

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Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
GU SYSTEM/SEX HORMONES	CIPROFLOXACIN HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	CLOTRIMAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	DANAZOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	DROSPIRENONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	DYDROGESTERONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	ETHINYLESTRADIOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	LEVONORGESTREL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)	
	METHENAMINE HIPURATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	NITROFURANTOIN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)	
	NORFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
MUSCULO-SKELETAL	TOTAL	34 (29.3%)	40 (30.8%)	38 (31.7%)	112 (30.6%)	
	ACETYLSALICYLIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	ASCORBIC ACID	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)	
	CARISOPRODOL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)	
	CELECOXIB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	DEXIBUPROFEN	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)	
	DICLOFENAC	0 (0.0%)	0 (0.0%)	4 (3.3%)	4 (1.1%)	
	DICLOFENAC SODIUM	0 (0.0%)	3 (2.3%)	3 (2.5%)	6 (1.6%)	
	FLURBIPROFEN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	GLUCOSAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	IBUPROFEN	26 (22.4%)	33 (25.4%)	24 (20.0%)	83 (22.7%)	
	KETOPROFEN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	KETOROLAC	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	TROMETHAMINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	MEFENAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	METAXALONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	METHOCARBAMOL	4 (3.4%)	2 (1.5%)	4 (3.3%)	10 (2.7%)	
	NAPROXEN	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)	
	PSEUDOEPHEDRINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	ROFECOXIB	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)	
	TIZANIDINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	

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of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
PARASITOLOGY	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
RESPIRATORY	TOTAL	20 (17.2%)	24 (18.5%)	22 (18.3%)	66 (18.0%)
	ACETYLSALICYLIC ACID	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	ACRIVASTINE	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
	ANTIHISTAMINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	ASCORBIC ACID	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
	BECLOMETASONE DIPROPIONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	BUDESONIDE	0 (0.0%)	4 (3.1%)	2 (1.7%)	6 (1.6%)
	CAFFEINE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	CAMPHOR	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CASCARA LIQUID EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CETIRIZINE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	CETIRIZINE HYDROCHLORIDE	0 (0.0%)	5 (3.8%)	3 (2.5%)	8 (2.2%)
	CHLORPHENAMINE MALEATE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	CIMICIFUGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	COCILLANA LIQUID EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	DESLOMATADINE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	DEXTROMETHORPHAN HYDROBROMIDE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
	DIMENHYDRINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DIPHENHYDRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DIPHENHYDRAMINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	DOXYLAMINE SUCCINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	EBASTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ETHYLMORPHINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	EUCALYPTUS OIL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	EUPHORBIA LIQUID EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	FEXOFENADINE HYDROCHLORIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	FLUTICASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
RESPIRATORY	FLUTICASONE	5 (4.3%)	1 (0.8%)	0 (0.0%)	6 (1.6%)
	PROPIONATE				
	FORMOTEROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	GENTIAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HYDROCODONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	BITARTRATE				
	IBUPROFEN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	IPRATROPIUM BROMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LACTUCA SYRUP	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LEVOCABASTINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	LORATADINE	6 (5.2%)	3 (2.3%)	1 (0.8%)	10 (2.7%)
	MAGNESIUM OXIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MENTHOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	MONTELUKAST SODIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	MYRTOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	NOSCAPINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	PAMABROM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PARACETAMOL	2 (1.7%)	0 (0.0%)	4 (3.3%)	6 (1.6%)
	PHENIRAMINE MALEATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PHENYLEPHRINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PHENYLEPHRINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	PHENYLPROPANOLAMINE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	HYDROCHLORIDE				
	POLYGALA SENEGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PREDNISOLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PRIMULA FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PSEUDOEPHEDRINE	0 (0.0%)	2 (1.5%)	2 (1.7%)	4 (1.1%)
	PSEUDOEPHEDRINE	1 (0.9%)	2 (1.5%)	4 (3.3%)	7 (1.9%)
	HYDROCHLORIDE				
	PSEUDOEPHEDRINE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	SULFATE				
	RUMICIS ASETOSA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SALBUTAMOL	2 (1.7%)	2 (1.5%)	2 (1.7%)	6 (1.6%)
	SALBUTAMOL SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SALMETEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROXYNAPHTHOATE				

'Concomitant' : start date on or after start of randomised study medication and on or before last date of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
RESPIRATORY	SALMETEROL XINAFOATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	SAMBUCUS FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SQUILL EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TERBUTALINE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TURPENTINE OIL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	VERBENA HERB	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	XYLOMETAZOLINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
SENSORY ORGANS	TOTAL	6 (5.2%)	9 (6.9%)	10 (8.3%)	25 (6.8%)
	BORIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CIPROFLOXACIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	DEXAMETHASONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ISONICOTINATE				
	DICLOFENAC SODIUM	0 (0.0%)	3 (2.3%)	3 (2.5%)	6 (1.6%)
	ERYTHROMYCIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FLURBIPROFEN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	KETOROLAC	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TROMETHAMINE				
	LEVOCABASTINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PREDNISOLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	XYLOMETAZOLINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
SYSTEMIC HORMONAL	TOTAL	5 (4.3%)	6 (4.6%)	7 (5.8%)	18 (4.9%)
	CARBIMAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DEXAMETHASONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ISONICOTINATE				
	LEVOTHYROXINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LEVOTHYROXINE SODIUM	3 (2.6%)	4 (3.1%)	4 (3.3%)	11 (3.0%)
	LIOTHYRONINE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date of study medication or ongoing from pre-treatment

Table 12.34

Number (%) of Subjects with Concomitant Medication by ATC Classification and Generic Term
Treatment Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
SYSTEMIC HORMONAL	POTASSIUM IODIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	PREDNISOLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
VARIOUS	TOTAL	5 (4.3%)	4 (3.1%)	5 (4.2%)	14 (3.8%)
	ALLERGENIC EXTRACT, NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CARDIOSPERMUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HALICACABUM				
	ECHINACEA EXTRACT	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	ESCULIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	GINSENG	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	HERBAL MEDICATION	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	HOMEOPATHIC PREPARATIONS	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
	HYDRASTIS CANADENSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	MILK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MINERALS NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NATURAL INGREDIENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NICOTINE RESIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TRACE ELEMENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VITAMINS NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VITIS VINIFERA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group				Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	78 (67.2%)	75 (57.7%)	81 (67.5%)	234 (63.9%)	
PARACETAMOL	30 (25.9%)	26 (20.0%)	40 (33.3%)	96 (26.2%)	
IBUPROFEN	26 (22.4%)	33 (25.4%)	24 (20.0%)	83 (22.7%)	
ACETYLSALICYLIC ACID	3 (2.6%)	10 (7.7%)	9 (7.5%)	22 (6.0%)	
VITAMINS NOS	7 (6.0%)	4 (3.1%)	8 (6.7%)	19 (5.2%)	
ASCORBIC ACID	1 (0.9%)	3 (2.3%)	9 (7.5%)	13 (3.6%)	
CAFFEINE	2 (1.7%)	5 (3.8%)	5 (4.2%)	12 (3.3%)	
LEVOTHYROXINE SODIUM	3 (2.6%)	4 (3.1%)	4 (3.3%)	11 (3.0%)	
LORATADINE	6 (5.2%)	3 (2.3%)	1 (0.8%)	10 (2.7%)	
NAPROXEN	4 (3.4%)	2 (1.5%)	4 (3.3%)	10 (2.7%)	
CALCIUM	2 (1.7%)	1 (0.8%)	6 (5.0%)	9 (2.5%)	
CETIRIZINE HYDROCHLORIDE	0 (0.0%)	5 (3.8%)	3 (2.5%)	8 (2.2%)	
PSEUDOEPHEDRINE HYDROCHLORIDE	1 (0.9%)	2 (1.5%)	4 (3.3%)	7 (1.9%)	
AZITHROMYCIN	1 (0.9%)	2 (1.5%)	3 (2.5%)	6 (1.6%)	
BUDESONIDE	0 (0.0%)	4 (3.1%)	2 (1.7%)	6 (1.6%)	
DICLOFENAC SODIUM	0 (0.0%)	3 (2.3%)	3 (2.5%)	6 (1.6%)	
FLUTICASONE PROPIONATE	5 (4.3%)	1 (0.8%)	0 (0.0%)	6 (1.6%)	
SALBUTAMOL	2 (1.7%)	2 (1.5%)	2 (1.7%)	6 (1.6%)	
CALCIUM CARBONATE	1 (0.9%)	2 (1.5%)	1 (0.8%)	4 (1.1%)	

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CETIRIZINE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
CHLORPHENAMINE MALEATE	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
CODEINE PHOSPHATE	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
DICLOFENAC	0 (0.0%)	0 (0.0%)	4 (3.3%)	4 (1.1%)
MINERALS NOS	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
NAPROXEN SODIUM	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
PHENOXYMETHYLPENICIL LIN POTASSIUM	1 (0.9%)	3 (2.3%)	0 (0.0%)	4 (1.1%)
PSEUDOEPHEDRINE	0 (0.0%)	2 (1.5%)	2 (1.7%)	4 (1.1%)
XYLOMETAZOLINE HYDROCHLORIDE	2 (1.7%)	2 (1.5%)	0 (0.0%)	4 (1.1%)
ACRIVASTINE	0 (0.0%)	2 (1.5%)	1 (0.8%)	3 (0.8%)
AMOXICILLIN	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
ATENOLOL	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
DESLORATADINE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
DEXIBUPROFEN	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
DEXTROMETHORPHAN HYDROBROMIDE	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
DIPHENHYDRAMINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
DOXYCYCLINE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
ESOMEPRAZOLE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
 Ordered by Decreasing Frequency
 Treatment Phase
 Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
FERROUS FUMARATE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
FERROUS SULFATE	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
FEXOFENADINE HYDROCHLORIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
HYDROCHLOROTHIAZIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
MAGNESIUM CARBONATE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
MAGNESIUM NOS	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
MINOCYCLINE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
RANITIDINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
SULFAMETHOXAZOLE	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
TEMAZEPAM	1 (0.9%)	0 (0.0%)	2 (1.7%)	3 (0.8%)
TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
TRAMADOL HYDROCHLORIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
TRIMETHOPRIM	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (0.8%)
ACICLOVIR	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
ALUMINIUM HYDROXIDE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
AMILORIDE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
AMOXICILLIN TRIHYDRATE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)

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Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
CALCIUM PANTOTHENATE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
CARISOPRODOL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
CEFALEXIN MONOHYDRATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
DEXTROPROPOXYPHENE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
ECHINACEA EXTRACT	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
ESCULIN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
FUROSEMIDE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
GINSENG	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
HERBAL MEDICATION	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
HOMEOPATHIC PREPARATIONS	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
INSULIN INJECTION, ISOPHANE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
INSULIN LISPRO	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
IRON	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
KETOPROFEN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
LEVONORGESTREL	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
LYMECYCLINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MAGNESIUM HYDROXIDE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
METOPROLOL TARTRATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
METRONIDAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
NITROFURANTOIN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
OMEPRAZOLE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
PHENYLPROPANOLAMINE HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
PIVMECILLINAM HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
POTASSIUM IODIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
PSEUDOEPHEDRINE SULFATE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
PYRIDOXINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
ROFECOXIB	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ROXITHROMYCIN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
SALMETEROL XINAFOATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
SUMATRIPTAN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
THIAMINE HYDROCHLORIDE	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (0.5%)
TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
VALSARTAN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
VITAMIN B	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
XYLOMETAZOLINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ADAPALENE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ALLERGENIC EXTRACT, NOS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ALUMINIUM GLYCINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
AMINOACETIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
AMINO BENZOIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
AMLODIPINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ANTI HISTAMINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
BECLOMETASONE DIPROPIONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BENDROFLUMETHIAZIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BENZYLAMINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BETAMETHASONE VALERATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BISMUTH	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
BISMUTH SUBSALICYLATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BORIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BUPRENORPHINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CAMPHOR	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CARBIMAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CARDIOSPERMUM HALICACABUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group				Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
CASCARA LIQUID EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CEFACLO	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CEFUROXIME AXETIL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CELECOXIB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
CELIPROLOL HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
CHLORCYCLIZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
CHROMIUM PICOLINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CIMICIFUGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CINCHOCAINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
CIPROFLOXACIN HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
CITRIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CLARITHROMYCIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CLAVULANATE POTASSIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
CLAVULANIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
CLINDAMYCIN HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
CLOTRIMAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
CLOXACILLIN SODIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	

'Concomitant' : start date on or after start of randomised study medication and on or before last date of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
COCILLANA LIQUID EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CYNARA SCOLYMUS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CYSTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DANAZOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DEXAMETHASONE ISONICOTINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DIMENHYDRINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DIMETICONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DIMETICONE, ACTIVATED	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DIPHENHYDRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DOXYLAMINE SUCCINATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DROSPIRENONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
DYDROGESTERONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EBASTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ECONAZOLE NITRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ENTEROCOCCI	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ERGOCALCIFEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ERGOTAMINE TARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
ERYTHROMYCIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ESCHERICHIA COLI	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ETHINYLESTRADIOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ETHYLMORPHINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ETHYLPARABEN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EUCALYPTUS OIL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
EUPHORBIA LIQUID EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FLUCLOXACILLIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FLURBIPROFEN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FLUTICASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FORMOTEROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FRAMYCETIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FUSIDATE SODIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
GENTIAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GLUCOSAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GLYCEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HEPATITIS VACCINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
HYDRASTIS CANADENSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
HYDROCODONE BITARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
HYDROCORTISONE ACETATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HYDROXYZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
HYOSCYAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
INSULIN HUMAN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
IPRATROPIUM BROMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ISOTRETINOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ISPAGHULA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
KERATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
KETOROLAC TROMETHAMINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LACTOBACILLUS ACIDOPHILUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LACTUCA SYRUP	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LEMON BALM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LEVOTHYROXINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LIOTHYRONINE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LOCAL ANESTHESIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LORAZEPAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

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Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
Ordered by Decreasing Frequency
Treatment Phase
Intention-to-Treat Population

Generic Term	Treatment Group			Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
LOSARTAN POTASSIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MAGNESIUM OXIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MEFENAMIC ACID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MENTHOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
MEPROBAMATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MEPYRAMINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METAMIZOLE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METAXALONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METHENAMINE HIPURATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
METHOCARBAMOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
METOCLOPRAMIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MILK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MONTELUKAST SODIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
MOUTHWASH, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MYRTOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NATURAL INGREDIENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NICOTINAMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NICOTINE RESIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NORFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

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of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
 Ordered by Decreasing Frequency
 Treatment Phase
 Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
NOSCAPINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
OXAZEPAM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PAMABROM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PANTOPRAZOL SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PAPAVERINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PHENAZONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PHENIRAMINE MALEATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PHENOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PHENYLEPHRINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PHENYLEPHRINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PODOPHYLLOTOXIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
POLIOMYELITIS VACCINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
POLYGALA SENEGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PREDNISOLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PRIMULA FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PROMETHAZINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PROPYL PARABEN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
 of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
 Ordered by Decreasing Frequency
 Treatment Phase
 Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
PSEUDOMONAS AURUGINOSA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PSYLLIUM HYDROPHILIC MUCILLOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
RIBOFLAVIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
RUMICIS ASETOSA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SACCHARIN SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SALBUTAMOL SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SALICYLAMIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SALICYLIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SALMETEROL HYDROXYNAPHTHOATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SAMBUCUS FLOWERS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SODIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SQUILL EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
STAPHYLOCOCCUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
STERCULIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
STREPTOCOCCUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TERBUTALINE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TETANUS TOXOID	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
THIAMINE MONONITRATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
 of study medication or ongoing from pre-treatment

Table 12.35

Number (%) of Subjects with Concomitant Medication by Preferred Term
 Ordered by Decreasing Frequency
 Treatment Phase
 Intention-to-Treat Population

Generic Term	Treatment Group			Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
TILACTASE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TIZANIDINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TRACE ELEMENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TRANEXAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TURPENTINE OIL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
VALACYCLOVIR HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
VERBENA HERB	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VITIS VINIFERA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
YEAST DRIED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ZINC	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ZINC OXIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ZOLMITRIPTAN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ZOLPIDEM HEMITARTRATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ZOPICLONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

'Concomitant' : start date on or after start of randomised study medication and on or before last date
 of study medication or ongoing from pre-treatment

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=365)	
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)			
TOTAL	TOTAL	63 (54.3%)	61 (47.3%)	52 (43.3%)		176 (48.2%)	
ALIMENTARY TRACT/METAB	TOTAL	15 (12.9%)	16 (12.4%)	18 (15.0%)		49 (13.4%)	
	ACETYLSALICYLIC ACID	1 (0.9%)	3 (2.3%)	1 (0.8%)		5 (1.4%)	
	AMINO BENZOIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	ASCORBIC ACID	0 (0.0%)	2 (1.6%)	5 (4.2%)		7 (1.9%)	
	CALCIUM	2 (1.7%)	2 (1.6%)	6 (5.0%)		10 (2.7%)	
	CALCIUM CARBONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)	
	CALCIUM PANTOTHENATE	0 (0.0%)	3 (2.3%)	0 (0.0%)		3 (0.8%)	
	CHROMIUM PICOLINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	CYSTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	DIMETICONE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	
	DOMPERIDONE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	
	ERGOCALCIFEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)	
	ESOMEPRAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)		2 (0.5%)	
	GINSENG	2 (1.7%)	0 (0.0%)	0 (0.0%)		2 (0.5%)	
	HYOSCYAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	INSULIN HUMAN	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)	
	INSULIN INJECTION, ISOPHANE	0 (0.0%)	0 (0.0%)	2 (1.7%)		2 (0.5%)	
	INSULIN LISPRO	0 (0.0%)	1 (0.8%)	1 (0.8%)		2 (0.5%)	
	IRON	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	
	ISPAGHULA	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	KERATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	LACTOBACILLUS	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)	
	ACIDOPHILUS						
	LOPERAMIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)		2 (0.5%)	
	HYDROCHLORIDE						
	MAGNESIUM NOS	1 (0.9%)	2 (1.6%)	1 (0.8%)		4 (1.1%)	
	METOCLOPRAMIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)	
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	
	MINERALS NOS	3 (2.6%)	1 (0.8%)	1 (0.8%)		5 (1.4%)	
	NICOTINAMIDE	0 (0.0%)	2 (1.6%)	0 (0.0%)		2 (0.5%)	
	NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	OMEPRAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	
	PANTOPRAZOL SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.3%)	
	PAPAVERINE	1 (0.9%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	
	HYDROCHLORIDE						
	PSYLLIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.3%)	
	HYDROPHILIC						
	MUCILLOID						
	PYRIDOXINE	0 (0.0%)	2 (1.6%)	1 (0.8%)		3 (0.8%)	
	HYDROCHLORIDE						

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
ALIMENTARY TRACT/METAB	RANITIDINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	RIBOFLAVIN	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)
	SODIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	THIAMINE HYDROCHLORIDE	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
	THIAMINE MONONITRATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	TRACE ELEMENTS, NOS	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	VITAMIN B	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	VITAMINS NOS	8 (6.9%)	3 (2.3%)	8 (6.7%)	19 (5.2%)
	YEAST DRIED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ZINC	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
ANTIINFECTIVES, SYSTE MIC	TOTAL	9 (7.8%)	5 (3.9%)	3 (2.5%)	17 (4.7%)
	ACICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	AZITHROMYCIN	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CLARITHROMYCIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DOXYCYCLINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FAMCICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FLUCONAZOLE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	LYMECYCLINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MINOCYCLINE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	PENICILLIN NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PIVMECILLINAM HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ROXITHROMYCIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SULFAMETHOXAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRIMETHOPRIM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	VALACYCLOVIR HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ANTINEOPLASTIC & IMMUNOSUP	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
BLOOD/BLOOD FORM ORGANS	TOTAL	7 (6.0%)	5 (3.9%)	4 (3.3%)	16 (4.4%)
	ACENOCOUMAROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ACETYLSALICYLIC ACID	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
	FERROUS FUMARATE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	FERROUS GLYCINE SULFATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FERROUS SULFATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	HEPARIN-FRACTION, SODIUM SALT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	IRON	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	TRANEXAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CARDIOVASCULAR	TOTAL	7 (6.0%)	6 (4.7%)	5 (4.2%)	18 (4.9%)
	AMILORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	HYDROCHLORIDE				
	AMLODIPINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	ATENOLOL	1 (0.9%)	2 (1.6%)	0 (0.0%)	3 (0.8%)
	BENDROFLUMETHIAZIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	BETAHISTINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	CELIPROLOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	CINCHOCAINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	ESCULIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FRAMYCETIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FUROSEMIDE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	HYDROCHLOROTHIAZIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	HYDROCORTISONE ACETATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYPERICUM EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LISINOPRIL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LOSARTAN POTASSIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	METOPROLOL TARTRATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PAPAVERINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	VALSARTAN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
CENTRAL NERVOUS SYSTEM	TOTAL	27 (23.3%)	35 (27.1%)	29 (24.2%)	91 (24.9%)
	ACETYLSALICYLIC ACID	1 (0.9%)	4 (3.1%)	2 (1.7%)	7 (1.9%)
	ASCORBIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	BUPRENORPHINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
CENTRAL NERVOUS SYSTEM	CAFFEINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CHLORPROTHIXENE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CITALOPRAM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	CLONAZEPAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CODEINE PHOSPHATE	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
	DEXTROPROPOXYPHENE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	FLUOXETINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	HYDROXYZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYPERICUM EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	IBUPROFEN	9 (7.8%)	17 (13.2%)	9 (7.5%)	35 (9.6%)
	LORAZEPAM	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)
	METAMIZOLE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	OPIUM TINCTURE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PARACETAMOL	12 (10.3%)	10 (7.8%)	14 (11.7%)	36 (9.9%)
	PAROXETINE	5 (4.3%)	4 (3.1%)	1 (0.8%)	10 (2.7%)
	PAROXETINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SUMATRIPTAN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TRAMADOL HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	VENLAFAXINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ZOLMITRIPTAN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	ZOPICLONE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
DERMATOLOGICALS	TOTAL	14 (12.1%)	9 (7.0%)	8 (6.7%)	31 (8.5%)
	ADAPALENE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	BETAMETHASONE VALERATE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	BUDESONIDE	0 (0.0%)	2 (1.6%)	2 (1.7%)	4 (1.1%)
	CLOTRIMAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DEQUALONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DESONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DIPHENHYDRAMINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FLUTICASONE PROPIONATE	5 (4.3%)	1 (0.8%)	0 (0.0%)	6 (1.6%)
	ISOTRETINOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LEMON BALM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
DERMATOLOGICALS	LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PODOPHYLLOTOXIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SALMETEROL XINAFOATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
GU SYSTEM/SEX HORMONES	TOTAL	5 (4.3%)	6 (4.7%)	3 (2.5%)	14 (3.8%)
	CIMICIFUGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CLOTRIMAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	DANAZOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	DESOGESTREL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DROSPIRENONE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ETHINYLESTRADIOL	0 (0.0%)	2 (1.6%)	1 (0.8%)	3 (0.8%)
	ETONOGESTREL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYPERICUM EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	METHENAMINE HIPPURATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NITROFURANTOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	NORETHISTERONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
MUSCULO-SKELETAL	TOTAL	16 (13.8%)	22 (17.1%)	18 (15.0%)	56 (15.3%)
	CARISOPRODOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CELECOXIB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DEXIBUPROFEN	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	DICLOFENAC	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	DICLOFENAC SODIUM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	GLUCOSAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	IBUPROFEN	9 (7.8%)	17 (13.2%)	9 (7.5%)	35 (9.6%)
	KETOPROFEN	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	NAPROXEN	3 (2.6%)	2 (1.6%)	3 (2.5%)	8 (2.2%)
	NAPROXEN SODIUM	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
MUSCULO-SKELETAL	ROFECOXIB	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
PARASITOLOGY	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	METRONIDAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
RESPIRATORY	TOTAL	17 (14.7%)	13 (10.1%)	10 (8.3%)	40 (11.0%)
	ACETYLCYSTEINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ACRIVASTINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	ANTIHISTAMINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	BECLOMETASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	DIPROPIONATE				
	BUDESONIDE	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
	CETIRIZINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	CETIRIZINE	0 (0.0%)	5 (3.9%)	2 (1.7%)	7 (1.9%)
	HYDROCHLORIDE				
	CHLORPHENAMINE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	MALEATE				
	CIMICIFUGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CROMOGLICATE SODIUM	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
	DESLOMATADINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
	DIMETHYLDINATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
	DIMETHYLDENE MALEATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	DIPHENHYDRAMINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYDROCHLORIDE				
	EBASTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	FEXOFENADINE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
	HYDROCHLORIDE				
	FLUTICASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	FLUTICASONE	5 (4.3%)	1 (0.8%)	0 (0.0%)	6 (1.6%)
	PROPRIONATE				
	FORMOTEROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	IPRATROPIUM BROMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	LEVOCABASTINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	LORATADINE	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
	MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
	MONTelukast SODIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	PARACETAMOL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PHENYLEPHRINE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROCHLORIDE				
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	PREDNISONE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	PSEUDOEPHEDRINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group			
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
RESPIRATORY	PSEUDOEPHEDRINE SULFATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SALBUTAMOL	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
	SALBUTAMOL SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	SALMETEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	HYDROXYNAPHTHOATE				
	SALMETEROL XINAFOATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
	TERBUTALINE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	TRIAMCINOLONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ACETONIDE				
	XYLOMETAZOLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SENSORY ORGANS	TOTAL	1 (0.9%)	6 (4.7%)	7 (5.8%)	14 (3.8%)
	ATERILE AQUA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	BENZALKONIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	CROMOGLICATE SODIUM	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
	DEXAMETHASONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ISONICOTINATE				
	DICLOFENAC SODIUM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
	LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	SODIUM EDETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	XYLOMETAZOLINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SYSTEMIC HORMONAL	TOTAL	6 (5.2%)	7 (5.4%)	7 (5.8%)	20 (5.5%)
	CARBIMAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
	CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DEXAMETHASONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	ISONICOTINATE				
	LEVOTHYROXINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LEVOTHYROXINE SODIUM	3 (2.6%)	4 (3.1%)	4 (3.3%)	11 (3.0%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.36

Number (%) of Subjects with Medication by ATC Classification and Generic Term during the Follow-up Phase
Intention-to-Treat Population

ATC Level 1	Generic Term	Treatment Group				Total (N=365)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)		
SYSTEMIC HORMONAL	LIOTHYRONINE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	POTASSIUM IODIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	PREDNISONE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	
	TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
VARIOUS	TOTAL	4 (3.4%)	5 (3.9%)	3 (2.5%)	12 (3.3%)	
	CRAMPBARK	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	ECHINACEA EXTRACT	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)	
	GINSENG	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	
	HOMEOPATHIC PREPARATIONS	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)	
	HYDRASTIS CANADENSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	HYPERICUM EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	IODINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	JUNIPER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	MILK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	MINERALS NOS	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)	
	NATURAL INGREDIENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	NICOTINE RESIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	PARSLEY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	PLASTER CAST	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	POTASSIUM IODIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)	
	THUYA EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	TRACE ELEMENTS, NOS	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	
	UVA URSI LEAVES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)	
	VITAMINS NOS	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)	

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
TOTAL	63 (54.3%)	61 (47.3%)	52 (43.3%)	176 (48.2%)
PARACETAMOL	12 (10.3%)	10 (7.8%)	15 (12.5%)	37 (10.1%)
IBUPROFEN	9 (7.8%)	17 (13.2%)	9 (7.5%)	35 (9.6%)
VITAMINS NOS	8 (6.9%)	3 (2.3%)	8 (6.7%)	19 (5.2%)
LEVOTHYROXINE SODIUM	3 (2.6%)	4 (3.1%)	4 (3.3%)	11 (3.0%)
CALCIUM	2 (1.7%)	2 (1.6%)	6 (5.0%)	10 (2.7%)
PAROXETINE	5 (4.3%)	4 (3.1%)	1 (0.8%)	10 (2.7%)
ASCORBIC ACID	0 (0.0%)	2 (1.6%)	6 (5.0%)	8 (2.2%)
NAPROXEN	3 (2.6%)	2 (1.6%)	3 (2.5%)	8 (2.2%)
ACETYLSALICYLIC ACID	1 (0.9%)	4 (3.1%)	2 (1.7%)	7 (1.9%)
CETIRIZINE HYDROCHLORIDE	0 (0.0%)	5 (3.9%)	2 (1.7%)	7 (1.9%)
FLUTICASONE PROPIONATE	5 (4.3%)	1 (0.8%)	0 (0.0%)	6 (1.6%)
BUDESONIDE	0 (0.0%)	3 (2.3%)	2 (1.7%)	5 (1.4%)
MINERALS NOS	3 (2.6%)	1 (0.8%)	1 (0.8%)	5 (1.4%)
LORATADINE	3 (2.6%)	1 (0.8%)	0 (0.0%)	4 (1.1%)
MAGNESIUM NOS	1 (0.9%)	2 (1.6%)	1 (0.8%)	4 (1.1%)
SALBUTAMOL	1 (0.9%)	1 (0.8%)	2 (1.7%)	4 (1.1%)
ATENOLOL	1 (0.9%)	2 (1.6%)	0 (0.0%)	3 (0.8%)
AZITHROMYCIN	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
CALCIUM PANTOTHENATE	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
CODEINE PHOSPHATE	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
CROMOGLICATE SODIUM	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
DEXIBUPROFEN	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)
ETHINYLESTRADIOL	0 (0.0%)	2 (1.6%)	1 (0.8%)	3 (0.8%)
FERROUS FUMARATE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
FERROUS SULFATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
FEXOFENADINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
HYDROCHLOROTHIAZIDE	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
IRON	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
KETOPROFEN	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
MOMETASONE FUROATE	3 (2.6%)	0 (0.0%)	0 (0.0%)	3 (0.8%)
NAPROXEN SODIUM	2 (1.7%)	1 (0.8%)	0 (0.0%)	3 (0.8%)
PYRIDOXINE HYDROCHLORIDE	0 (0.0%)	2 (1.6%)	1 (0.8%)	3 (0.8%)
RANITIDINE HYDROCHLORIDE	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
THIAMINE HYDROCHLORIDE	0 (0.0%)	3 (2.3%)	0 (0.0%)	3 (0.8%)
TOCOPHEROL	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)
ACRIVASTINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
AMILORIDE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
AMLODIPINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
BETAMETHASONE VALERATE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
CETIRIZINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
CHLORPHENAMINE MALEATE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
CITALOPRAM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
DESLORATADINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
DEXTROPROPOXYPHENE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
DICLOFENAC	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
DICLOFENAC SODIUM	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
DIMENHYDRINATE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
DROSPIRENONE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
ECHINACEA EXTRACT	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ESOMEPRAZOLE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
FLUCONAZOLE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
FUROSEMIDE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
GINSENG	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
HOMEOPATHIC PREPARATIONS	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)
INSULIN INJECTION, ISOPHANE	0 (0.0%)	0 (0.0%)	2 (1.7%)	2 (0.5%)
INSULIN LISPRO	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
LOPERAMIDE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
LORAZEPAM	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
LYMECYCLINE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
MINOCYCLINE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
NICOTINAMIDE	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)
NITROFURANTOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
POTASSIUM IODIDE	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
PREDNISONE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
PSEUDOPHEDRINE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
RIBOFLAVIN	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (0.5%)
ROFECOXIB	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
SALMETEROL XINAFOATE	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
SUMATRIPTAN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
TRACE ELEMENTS, NOS	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)
TRETINOIN	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
VALSARTAN	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
VITAMIN B	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
ZINC	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (0.5%)
ZOLMITRIPTAN	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ZOPICLONE	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
ACENOCOUMAROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ACETYLCYSTEINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ACICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ADAPALENE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
AMINOBENZOIC ACID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ANTI HISTAMINE, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
ATERILE AQUA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BECLOMETASONE DIPROPIONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BENDROFLUMETHIAZIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BENZALKONIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
BETAHISTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
BUPRENORPHINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CAFFEINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CALCIUM CARBONATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CARBIMAZOLE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CARISOPRODOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CELECOXIB	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CELIPROLOL HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CHLORPROTHIXENE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CHROMIUM PICOLINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CIMICIFUGA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CINCHOCAINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CIPROFLOXACIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
CLARITHROMYCIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CLONAZEPAM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CLOTRIMAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
CORTISONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
CORTISONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CRAMPBARK	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
CYSTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DANAZOL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DEQUALONE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DESGESTREL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DESONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DEXAMETHASONE ISONICOTINATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
DIMETICONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DIMETINDENE MALEATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DOMPERIDONE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
DOXYCYCLINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
EBASTINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ERGOCALCIFEROL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ESCULIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
ESTRADIOL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
ETONOGESTREL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FAMCICLOVIR	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FERROUS GLYCINE SULFATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
FLUOXETINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FLUTICASONE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
FORMOTEROL	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
FRAMYCETIN SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
GLUCOSAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HEPARIN-FRACTION, SODIUM SALT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HYDRASTIS CANADENSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HYDROCORTISONE ACETATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
HYDROXYZINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
HYOSCYAMINE SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
HYPERICUM EXTRACT	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
INSULIN HUMAN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
IODINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
IPRATROPIUM BROMIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ISOTRETINOIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ISPAGHULA	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
JUNIPER	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
KERATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LACTOBACILLUS ACIDOPHILUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LEMON BALM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
LEVOCABASTINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LEVOTHYROXINE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LIOTHYRONINE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
LISINOPRIL	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
LOSARTAN POTASSIUM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
METAMIZOLE SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METHENAMINE HIPPURATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
METOCLOPRAMIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METOPROLOL TARTRATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
METRONIDAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MILK	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
MONTELUKAST SODIUM	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NATURAL INGREDIENTS, NOS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
NICOTINE RESIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
NORETHISTERONE ACETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
NYSTATIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
OMEPRAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
OPIUM TINCTURE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PANTOPRAZOL SODIUM	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PAPAVERINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PAROXETINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PARSLEY	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PENICILLIN NOS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PHENYLEPHRINE HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
PIVMECILLINAM HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PLASTER CAST	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PODOPHYLLOTOXIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
PSEUDOEPHEDRINE SULFATE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
PSYLLIUM HYDROPHILIC MUCILLOID	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
ROXITHROMYCIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
SALBUTAMOL SULFATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SALMETEROL HYDROXYNAPHTHOATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
SODIUM CHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
SODIUM EDETATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.37

Number (%) of Subjects with Medication by Preferred Term during the Follow-up Phase
Ordered by Decreasing Frequency
Intention-to-Treat Population

Generic Term	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)	Total (N=365)
SULFAMETHOXAZOLE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TERBUTALINE SULFATE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TETRACYCLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
THIAMINE MONONITRATE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
THUYA EXTRACT	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
TRAMADOL HYDROCHLORIDE	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TRANEXAMIC ACID	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.3%)
TRIAMCINOLONE ACETONIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
TRIMETHOPRIM	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
UVA URSI LEAVES	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
VALACYCLOVIR HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
VENLAFAXINE HYDROCHLORIDE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
XYLOMETAZOLINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
XYLOMETAZOLINE HYDROCHLORIDE	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
YEAST DRIED	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)

'Follow-up' : start date after last date of randomised study medication or ongoing from the treatment phase

Table 12.38

Number (%) of Subjects by Study Medication Capsule Compliance by Menstrual Cycle
Intention-to-Treat Population

Cycle	Paroxetine CR 25 mg (N=116) Non-			Treatment Group Paroxetine CR 12.5 mg (N=130) Non-			Placebo (N=120) Non-		
	Compliant	Compliant	Unknown	Compliant	Compliant	Unknown	Compliant	Compliant	Unknown
RC2	112 (96.6%)	4 (3.4%)		120 (92.3%)	10 (7.7%)		114 (95.0%)	6 (5.0%)	
TC1	106 (91.4%)	10 (8.6%)		127 (97.7%)	3 (2.3%)		116 (96.7%)	4 (3.3%)	
TC2	96 (96.0%)	4 (4.0%)		109 (92.4%)	8 (6.8%)	1 (0.8%)	110 (95.7%)	4 (3.5%)	1 (0.9%)
TC3	89 (94.7%)	4 (4.3%)	1 (1.1%)	107 (97.3%)	2 (1.8%)	1 (0.9%)	102 (95.3%)	5 (4.7%)	

NOTE: Compliance = ((Capsules dispensed - Capsules returned) * 100) / (stop-start date of medication+1)
Compliant: >=80% and <=120%, Non-compliant: <80% or >120%, Unknown=unconfirmed status due to missing data item
RC=Reference Cycle TC=Treatment Cycle

Table 12.39

Number (%) of Subjects by Study Medication Compliance for Interruption in Study drug and Adherence to taking medication during the luteal phase, and Overall Compliance by Menstrual Cycle
Intention-to-Treat Population

Treatment Group=Paroxetine CR 25 mg (N=116)

Cycle	Interruption of > 3 Days*			Adherence during Luteal phase**			Overall Compliance***		
	Yes	No	Unknown	Yes	No	Unknown	Yes	No	Unknown
RC2		116 (100%)		113(97.4%)	3 (2.6%)		109(94.0%)	7 (6.0%)	
TC1	6 (5.2%)	110(94.8%)		96(82.8%)	17(14.7%)	3 (2.6%)	89(76.7%)	27(23.3%)	
TC2	2 (2.0%)	98(98.0%)		91(91.0%)	9 (9.0%)		87(87.0%)	13(13.0%)	
TC3	2 (2.1%)	92(97.9%)		84(89.4%)	8 (8.5%)	2 (2.1%)	82(87.2%)	11(11.7%)	1 (1.1%)

* Based on tick-box response on Study Medication panel

** Study drug taken ≥ 7 days prior to Day 1 and discontinued on Day 1 or Day 2 of the next cycle and subject had a break of at least 7 days between discontinuation of medication on the previous cycle and the start of medication in this cycle
Unknown=unconfirmed status due to missing data item

*** The subject must be between 80% and 120% compliant and have no interruption of study medication of >3 consecutive days and be adherent to study medication during the luteal phase, otherwise if confirmed as non-compliant for ≥ 1 of the 3 definitions assigned as overall non-compliant, with the remaining subjects of 'unknown' status

RC=Reference Cycle TC=Treatment Cycle

Table 12.39

Number (%) of Subjects by Study Medication Compliance for Interruption in Study drug and Adherence to taking medication during the luteal phase, and Overall Compliance by Menstrual Cycle
Intention-to-Treat Population

Treatment Group=Paroxetine CR 12.5 mg (N=130)

Cycle	Interruption of > 3 Days*			Adherence during Luteal phase**			Overall Compliance***		
	Yes	No	Unknown	Yes	No	Unknown	Yes	No	Unknown
RC2	1 (0.8%)	129(99.2%)		120(92.3%)	10 (7.7%)		110(84.6%)	20(15.4%)	
TC1	8 (6.2%)	122(93.8%)		110(84.6%)	13(10.0%)	7 (5.4%)	107(82.3%)	17(13.1%)	6 (4.6%)
TC2	2 (1.7%)	114(96.6%)	2 (1.7%)	105(89.0%)	10 (8.5%)	3 (2.5%)	98(83.1%)	17(14.4%)	3 (2.5%)
TC3	1 (0.9%)	108(98.2%)	1 (0.9%)	98(89.1%)	8 (7.3%)	4 (3.6%)	96(87.3%)	11(10.0%)	3 (2.7%)

* Based on tick-box response on Study Medication panel

** Study drug taken ≥ 7 days prior to Day 1 and discontinued on Day 1 or Day 2 of the next cycle and subject had a break of at least 7 days between discontinuation of medication on the previous cycle and the start of medication in this cycle
Unknown=unconfirmed status due to missing data item

*** The subject must be between 80% and 120% compliant and have no interruption of study medication of >3 consecutive days and be adherent to study medication during the luteal phase, otherwise if confirmed as non-compliant for ≥ 1 of the 3 definitions assigned as overall non-compliant, with the remaining subjects of 'unknown' status

RC=Reference Cycle TC=Treatment Cycle

Table 12.39

Number (%) of Subjects by Study Medication Compliance for Interruption in Study drug and Adherence to taking medication during the luteal phase, and Overall Compliance by Menstrual Cycle
Intention-to-Treat Population

Treatment Group=Placebo (N=120)

Cycle	Interruption of > 3 Days*			Adherence during Luteal phase**			Overall Compliance***		
	Yes	No	Unknown	Yes	No	Unknown	Yes	No	Unknown
RC2		120 (100%)		115(95.8%)	5 (4.2%)		109(90.8%)	11 (9.2%)	
TC1	1 (0.8%)	119(99.2%)		111(92.5%)	9 (7.5%)		107(89.2%)	13(10.8%)	
TC2	4 (3.5%)	110(95.7%)	1 (0.9%)	108(93.9%)	5 (4.3%)	2 (1.7%)	104(90.4%)	9 (7.8%)	2 (1.7%)
TC3	1 (0.9%)	106(99.1%)		96(89.7%)	9 (8.4%)	2 (1.9%)	91(85.0%)	14(13.1%)	2 (1.9%)

* Based on tick-box response on Study Medication panel

** Study drug taken ≥ 7 days prior to Day 1 and discontinued on Day 1 or Day 2 of the next cycle and subject had a break of at least 7 days between discontinuation of medication on the previous cycle and the start of medication in this cycle
Unknown=unconfirmed status due to missing data item

*** The subject must be between 80% and 120% compliant and have no interruption of study medication of >3 consecutive days and be adherent to study medication during the luteal phase, otherwise if confirmed as non-compliant for ≥ 1 of the 3 definitions assigned as overall non-compliant, with the remaining subjects of 'unknown' status

RC=Reference Cycle TC=Treatment Cycle

13. DATA SOURCE TABLES: EFFICACY

	Page
Table 13.1 Summary of Adjusted Change from Baseline in Mean Luteal Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	336
Table 13.2 Summary of Adjusted Change from Baseline in Mean Luteal Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Per Protocol Population	337
Table 13.3 Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	338
Table 13.4 Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Per Protocol Population	339
Table 13.5 Summary Statistics for Mean Luteal Phase VAS-Mood Scores Intention-to-Treat Population.	340
Table 13.6 Summary Statistics for Mean Luteal Phase VAS-Mood Scores Per Protocol Population	341
Table 13.7 Summary Statistics for Mean Luteal Phase VAS-Mood Scores By Centre Group Intention-to-Treat Population	342
Table 13.8 Summary Statistics for Mean Luteal Phase VAS-Mood Scores By Centre Group Per Protocol Population	365
Table 13.9 Summary of Adjusted Change from Baseline in Luteal Phase VAS Physical Symptoms Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	388
Table 13.10 Summary of Analysis for Change from Baseline in Luteal Phase VAS Physical Symptoms Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	389
Table 13.11 Summary Statistics for Luteal Phase VAS Physical Symptoms Score Intention-to-Treat Population	390
Table 13.12 Summary of the Percentage of Subjects Responding (50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score) Intention-to-Treat Population.	391
Table 13.13.1 Summary of Logistic Regression for Subjects with a 50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	392
Table 13.13.2 Summary Statistics for Percentage Change from Baseline in Mean Luteal Phase VAS-Mood Score Intention-to-Treat Population	393
Table 13.14.1 Summary of the Percentage of Subjects Responding (Return to a score of Less Than or Equal to Baseline Mean Follicular Phase VAS-Mood Score) Intention-to-Treat Population.	394

Table 13.14.2 Summary of Logistic Regression for Subjects with a Return to a Score of Less Than or Equal to Baseline Mean Follicular Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	395
Table 13.15.1 Summary of Adjusted Change from Baseline in Mean Luteal Phase VAS Total Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	396
Table 13.15.2 Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS Total Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	397
Table 13.15.3 Summary Statistics for Mean Luteal Phase VAS Total Scores Intention-to-Treat Population	398
Table 13.15.4 Summary Statistics for Percentage Change from Baseline in Mean Luteal Phase VAS Total Scores Intention-to-Treat Population	399
Table 13.16 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Irritability VAS Item Score Intention-to-Treat Population . .	400
Table 13.17 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Tension VAS Item Score Intention-to-Treat Population . . .	401
Table 13.18 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Depressed Mood VAS Item Score Intention-to-Treat Population	402
Table 13.19 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Affective Lability VAS Item Score Intention-to-Treat Population	403
Table 13.20 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Decreased Interest VAS Item Score Intention-to-Treat Population	404
Table 13.21 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Difficulty Concentrating VAS Item Score Intention-to-Treat Population	405
Table 13.22 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Lack of Energy VAS Item Score Intention-to-Treat Population	406
Table 13.23 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Change in Appetite VAS Item Score Intention-to-Treat Population	407
Table 13.24 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Change in Sleep Pattern VAS Item Score Intention-to-Treat Population	408
Table 13.25 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Feeling Out of Control VAS Item Score Intention-to-Treat Population	409

Table 13.26 Summary Statistics for Baseline and Change from Baseline in Luteal Phase Physical Symptoms VAS Item Score Intention-to-Treat Population	410
Table 13.27 Summary of Adjusted Change from Baseline in Sheehan Disability Scale (Individual and Total Scores) Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	411
Table 13.28 Summary of Analysis for Change from Baseline in Sheehan Disability Scale (Individual and Total Scores) Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	415
Table 13.29 Summary Statistics for Sheehan Disability Scale (Individual and Total Scores) Intention-to-Treat Population	419
Table 13.30 Summary of Adjusted Change from Baseline in PMTS Total Scores Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	423
Table 13.31 Summary of Analysis for Change from Baseline in PMTS Total Scores Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	424
Table 13.32 Summary Statistics for PMTS Total Score Intention-to-Treat Population	425
Table 13.33 Summary Statistics for Baseline and Change from Baseline in CGI Severity of Illness Score Intention-to-Treat Population	426
Table 13.34.1 Summary of Adjusted Change from Baseline in CGI Severity of Illness Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	427
Table 13.34.2 Summary of Analysis for Change from Baseline in CGI Severity of Illness Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	428
Table 13.35 Number (%) of Subjects in Each Category of CGI Severity of Illness Score Intention-to-Treat Population	429
Table 13.36 Number (%) of Subjects by Change in the CGI Severity of Illness Score from Baseline Intention-to-Treat Population	430
Table 13.37 Summary of the Percentage of Subjects Responding on the CGI Global Improvement Item (score of 1 or 2) Intention-to-Treat Population	433
Table 13.38 Summary of Logistic Regression for Subjects Responding on the CGI Global Improvement Item Adjusted for Centre Group and Age Intention-to-Treat Population	434
Table 13.39 Number (%) of Subjects in Each Category of CGI Global Improvement Item Intention-to-Treat Population	435
Table 13.40 Summary of the Percentage of Subjects Responding on the Patient Global Evaluation (score of 1 or 2) Intention-to-Treat Population	436

Table 13.41 Summary of Logistic Regression for Subjects Responding on Patient Global Evaluation Adjusted for Centre Group and Age Intention-to-Treat Population.	437
Table 13.42 Number (%) of Subjects in Each Category of Patient Global Evaluation Intention-to-Treat Population.	438
Table 13.43 Summary of Adjusted Change from Baseline of AUC Daily Luteal Phase VAS-Mood Score Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	439
Table 13.44 Summary of Analysis for Change from Baseline for AUC Daily Luteal Phase VAS-Mood Scores Adjusted for Centre Group, Baseline Score and Age Intention-to-Treat Population	440
Table 13.45 Summary Statistics for AUC Daily Luteal Phase VAS-Mood Scores Intention-to-Treat Population	441
Table 13.46 Number (%) of Subjects in Each Category of Patient Evaluation of Study Medication Intention-to-Treat Population	442
Table 13.47 Number (%) of Subjects with a Missing Luteal VAS-Mood Score Intention-to-Treat Population.	443
Table 13.48 Number (%) of Subjects with Missing Mean Luteal Phase VAS Scores for the Core PMDD Symptoms Intention-to-Treat Population. . . .	444
Table 13.49 Number (%) of Subjects with Missing Daily Luteal Phase VAS Scores for the Core PMDD Symptoms Intention-to-Treat Population. . . .	447

Table 13.1

Summary of Adjusted Change from Baseline in Mean Luteal Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	302	-38.06	2.23	-25.04	2.09
	Paroxetine CR 12.5 mg vs Placebo	302	-32.83	2.08	-25.04	2.09
	Paroxetine CR 25 mg vs Paroxetine CR 12.5 mg	302	-38.06	2.23	-32.83	2.08
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	353	-34.73	2.09	-23.94	2.03
	Paroxetine CR 12.5 mg vs Placebo	353	-31.61	2.00	-23.94	2.03
	Paroxetine CR 25 mg vs Paroxetine CR 12.5 mg	353	-34.73	2.09	-31.61	2.00

Phase: Luteal Phase (days = -1 - -5)

Table 13.2

Summary of Adjusted Change from Baseline in Mean Luteal Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Per Protocol Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	242	-35.67	2.61	-23.00	2.30
	Paroxetine CR 12.5 mg vs Placebo	242	-32.50	2.26	-23.00	2.30
	Paroxetine CR 25 mg vs Paroxetine CR 12.5 mg	242	-35.67	2.61	-32.50	2.26
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	269	-36.03	2.51	-22.12	2.21
	Paroxetine CR 12.5 mg vs Placebo	269	-31.48	2.19	-22.12	2.21
	Paroxetine CR 25 mg vs Paroxetine CR 12.5 mg	269	-36.03	2.51	-31.48	2.19

Phase: Luteal Phase (days = -1 - -5)

Table 13.3

Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-13.02	[-18.98, -7.06]	<0.001
	Parox CR 12.5 mg vs Placebo	-7.78	[-13.56, -2.01]	0.008
	Parox CR 25.0 mg vs Parox CR 12.5 mg	-5.23	[-11.21, 0.74]	0.086
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-10.79	[-16.46, -5.12]	<0.001
	Parox CR 12.5 mg vs Placebo	-7.66	[-13.25, -2.08]	0.007
	Parox CR 25.0 mg vs Parox CR 12.5 mg	-3.13	[-8.81, 2.56]	0.280

* Difference in adjusted least square means are shown
Phase: Luteal Phase (days = -1 - -5)

Table 13.4

Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Per Protocol Population

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-12.67	[-19.46, -5.88]	<0.001
	Parox CR 12.5 mg vs Placebo	-9.50	[-15.79, -3.21]	0.003
	Parox CR 25.0 mg vs Parox CR 12.5 mg	-3.17	[-9.92, 3.58]	0.356
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-13.91	[-20.43, -7.38]	<0.001
	Parox CR 12.5 mg vs Placebo	-9.35	[-15.42, -3.29]	0.003
	Parox CR 25.0 mg vs Parox CR 12.5 mg	-4.55	[-11.03, 1.93]	0.168

* Difference in adjusted least square means are shown
Phase: Luteal Phase (days = -1 - -5)

Table 13.5

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	54.4	52.2	55.7
	STD	24.46	21.35	21.52
	MEDIAN	48.9	47.0	55.4
	MINIMUM	13.6	14.7	13.1
	MAXIMUM	99.4	100.0	96.3
Treatment Cycle 1	N	109	120	118
	MEAN	22.0	23.2	33.6
	STD	22.91	22.57	27.39
	MEDIAN	12.6	15.6	27.5
	MINIMUM	0.3	1.0	1.0
	MAXIMUM	93.9	100.0	100.0
Treatment Cycle 2	N	98	113	109
	MEAN	20.3	21.7	30.8
	STD	25.50	21.16	25.59
	MEDIAN	8.3	15.2	21.7
	MINIMUM	0.8	1.0	0.1
	MAXIMUM	95.1	82.4	98.9
Treatment Cycle 3	N	93	105	105
	MEAN	16.2	21.4	29.6
	STD	19.72	21.39	24.34
	MEDIAN	8.2	11.0	24.7
	MINIMUM	0.0	1.0	0.0
	MAXIMUM	90.4	87.9	94.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.6

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
Per Protocol Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	74	99	96
	MEAN	53.3	52.4	56.0
	STD	23.82	21.49	21.74
	MEDIAN	48.5	47.1	53.4
	MINIMUM	14.3	14.7	13.1
	MAXIMUM	99.4	100.0	96.3
Treatment Cycle 1	N	73	98	96
	MEAN	19.2	22.5	35.3
	STD	21.17	23.84	27.87
	MEDIAN	11.6	12.5	27.6
	MINIMUM	1.0	1.0	1.0
	MAXIMUM	93.8	100.0	100.0
Treatment Cycle 2	N	70	93	90
	MEAN	19.3	20.8	31.6
	STD	23.76	21.36	25.79
	MEDIAN	8.7	13.5	23.2
	MINIMUM	0.9	1.0	0.1
	MAXIMUM	95.1	82.4	98.9
Treatment Cycle 3	N	67	89	86
	MEAN	16.4	20.1	30.4
	STD	19.41	21.87	25.16
	MEDIAN	9.5	9.6	25.4
	MINIMUM	0.0	1.0	0.0
	MAXIMUM	77.1	87.9	94.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	4
	MEAN	57.6	44.9	55.1
	STD	35.58	26.31	9.71
	MEDIAN	61.5	33.0	55.0
	MINIMUM	17.1	32.3	43.8
	MAXIMUM	90.3	92.0	66.6
Treatment Cycle 1	N	3	5	4
	MEAN	15.6	8.1	8.9
	STD	22.98	10.65	7.01
	MEDIAN	3.5	2.1	7.0
	MINIMUM	1.1	1.0	2.8
	MAXIMUM	42.1	25.9	18.8
Treatment Cycle 2	N	3	5	4
	MEAN	32.5	13.3	24.8
	STD	54.14	12.89	17.99
	MEDIAN	1.6	8.2	21.6
	MINIMUM	1.0	1.4	6.6
	MAXIMUM	95.1	33.3	49.4
Treatment Cycle 3	N	3	5	3
	MEAN	26.6	9.9	12.7
	STD	43.71	5.05	9.63
	MEDIAN	1.8	11.4	7.4
	MINIMUM	1.0	1.6	6.9
	MAXIMUM	77.1	14.0	23.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■■■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	7	6	6
	MEAN	47.1	46.1	57.4
	STD	16.10	18.32	19.20
	MEDIAN	42.2	46.7	59.0
	MINIMUM	32.8	22.2	28.6
	MAXIMUM	77.4	67.9	80.3
Treatment Cycle 1	N	7	6	6
	MEAN	44.5	19.7	35.6
	STD	20.44	15.85	22.28
	MEDIAN	44.3	17.8	29.7
	MINIMUM	16.9	2.4	7.9
	MAXIMUM	79.1	43.2	71.8
Treatment Cycle 2	N	5	6	6
	MEAN	40.6	16.5	40.7
	STD	26.70	12.65	19.76
	MEDIAN	24.7	12.6	46.9
	MINIMUM	23.0	1.5	8.9
	MAXIMUM	85.3	37.0	59.1
Treatment Cycle 3	N	5	5	4
	MEAN	41.0	26.9	52.4
	STD	31.87	29.24	20.43
	MEDIAN	29.8	22.8	51.2
	MINIMUM	8.2	3.9	29.4
	MAXIMUM	90.4	75.7	77.7

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	5
	MEAN	49.3	42.5	60.2
	STD	29.05	16.04	23.83
	MEDIAN	45.7	42.7	66.0
	MINIMUM	18.3	24.6	19.0
	MAXIMUM	87.5	67.7	79.4
Treatment Cycle 1	N	4	5	5
	MEAN	3.8	20.9	28.2
	STD	2.54	12.74	27.13
	MEDIAN	3.4	22.7	16.4
	MINIMUM	1.3	2.5	1.3
	MAXIMUM	7.1	33.6	62.1
Treatment Cycle 2	N	3	5	3
	MEAN	5.3	39.4	12.2
	STD	5.64	14.29	3.22
	MEDIAN	3.3	39.8	14.0
	MINIMUM	1.0	21.2	8.5
	MAXIMUM	11.7	55.8	14.1
Treatment Cycle 3	N	3	4	4
	MEAN	1.9	30.7	22.1
	STD	1.10	26.39	23.56
	MEDIAN	1.3	30.1	21.1
	MINIMUM	1.2	6.7	1.2
	MAXIMUM	3.1	56.1	45.0

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■■■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	6	5	4
	MEAN	59.7	43.1	73.7
	STD	28.40	9.30	12.67
	MEDIAN	51.0	45.8	71.6
	MINIMUM	23.2	30.1	62.2
	MAXIMUM	94.1	54.5	89.6
Treatment Cycle 1	N	6	5	4
	MEAN	15.6	5.9	32.7
	STD	21.34	4.50	24.24
	MEDIAN	8.6	4.4	32.2
	MINIMUM	0.3	1.1	10.2
	MAXIMUM	57.4	11.5	56.2
Treatment Cycle 2	N	6	5	4
	MEAN	16.4	4.9	37.8
	STD	21.77	4.89	26.79
	MEDIAN	6.6	2.3	37.4
	MINIMUM	0.9	1.3	10.2
	MAXIMUM	58.3	13.0	66.0
Treatment Cycle 3	N	6	5	4
	MEAN	15.0	6.4	29.0
	STD	24.17	3.20	22.82
	MEDIAN	5.5	6.9	22.5
	MINIMUM	1.0	1.2	9.1
	MAXIMUM	63.4	9.6	61.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	5	3	6
	MEAN	56.5	54.7	38.7
	STD	21.66	31.57	17.77
	MEDIAN	59.2	49.5	37.1
	MINIMUM	31.0	26.0	20.7
	MAXIMUM	86.3	88.5	70.8
Treatment Cycle 1	N	5	3	6
	MEAN	38.8	16.9	27.1
	STD	24.31	19.93	15.72
	MEDIAN	27.5	10.4	22.2
	MINIMUM	23.4	1.0	12.9
	MAXIMUM	81.4	39.3	53.8
Treatment Cycle 2	N	3	3	5
	MEAN	34.3	29.0	41.2
	STD	26.12	43.54	20.29
	MEDIAN	38.4	5.9	44.5
	MINIMUM	6.4	1.9	18.7
	MAXIMUM	58.2	79.2	62.8
Treatment Cycle 3	N	3	3	5
	MEAN	29.2	6.8	23.0
	STD	22.59	3.46	10.37
	MEDIAN	26.6	5.5	24.7
	MINIMUM	8.1	4.3	8.1
	MAXIMUM	53.0	10.8	35.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	5
	MEAN	37.9	57.7	66.6
	STD	6.15	20.17	37.52
	MEDIAN	37.5	52.1	92.6
	MINIMUM	31.1	39.7	13.1
	MAXIMUM	45.6	88.5	93.6
Treatment Cycle 1	N	4	5	5
	MEAN	6.2	9.9	56.5
	STD	3.71	8.15	33.02
	MEDIAN	6.3	6.4	50.3
	MINIMUM	2.1	2.0	15.0
	MAXIMUM	9.9	19.6	92.6
Treatment Cycle 2	N	4	5	5
	MEAN	5.5	9.9	53.4
	STD	3.68	12.61	32.52
	MEDIAN	5.0	5.0	49.9
	MINIMUM	1.9	1.0	12.0
	MAXIMUM	10.3	31.6	91.5
Treatment Cycle 3	N	4	5	5
	MEAN	19.8	24.9	39.8
	STD	17.99	18.48	33.57
	MEDIAN	15.9	31.0	33.6
	MINIMUM	5.0	1.0	4.3
	MAXIMUM	42.4	46.2	94.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■■■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	7	8	6
	MEAN	37.6	50.9	42.6
	STD	18.03	26.66	22.06
	MEDIAN	34.2	41.0	46.7
	MINIMUM	19.4	24.3	13.9
	MAXIMUM	63.9	92.1	76.5
Treatment Cycle 1	N	7	7	6
	MEAN	14.3	7.9	18.0
	STD	16.72	7.36	9.45
	MEDIAN	8.3	4.5	19.6
	MINIMUM	1.1	1.1	1.2
	MAXIMUM	48.2	20.9	28.3
Treatment Cycle 2	N	7	7	7
	MEAN	3.9	11.9	13.4
	STD	2.90	9.73	9.18
	MEDIAN	4.5	6.3	16.0
	MINIMUM	1.0	2.1	1.0
	MAXIMUM	8.4	26.1	21.8
Treatment Cycle 3	N	7	7	7
	MEAN	5.9	12.7	26.9
	STD	6.25	12.81	29.40
	MEDIAN	2.9	7.1	14.0
	MINIMUM	1.0	2.6	1.1
	MAXIMUM	17.6	39.8	78.9

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	5	4	5
	MEAN	48.3	54.7	57.2
	STD	20.89	22.23	19.10
	MEDIAN	39.7	56.1	56.1
	MINIMUM	33.6	27.9	34.3
	MAXIMUM	84.0	79.0	84.0
Treatment Cycle 1	N	5	4	5
	MEAN	13.7	26.0	9.8
	STD	7.11	20.88	10.39
	MEDIAN	11.6	23.5	5.6
	MINIMUM	6.0	3.3	2.0
	MAXIMUM	23.5	53.6	27.7
Treatment Cycle 2	N	4	4	5
	MEAN	20.2	15.8	8.7
	STD	36.41	13.36	13.28
	MEDIAN	2.1	15.6	3.0
	MINIMUM	1.9	3.1	1.2
	MAXIMUM	74.9	29.2	32.3
Treatment Cycle 3	N	3	3	4
	MEAN	6.5	14.6	12.7
	STD	9.05	10.28	20.73
	MEDIAN	1.5	16.1	2.5
	MINIMUM	1.0	3.6	2.1
	MAXIMUM	16.9	24.0	43.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	4	4
	MEAN	32.4	62.4	58.0
	STD	8.97	27.09	23.65
	MEDIAN	31.7	58.4	54.4
	MINIMUM	22.1	34.0	36.6
	MAXIMUM	44.0	98.8	86.8
Treatment Cycle 1	N	4	3	4
	MEAN	9.6	4.6	30.4
	STD	9.06	3.35	43.87
	MEDIAN	7.5	4.5	12.9
	MINIMUM	1.0	1.4	1.5
	MAXIMUM	22.3	8.1	94.5
Treatment Cycle 2	N	3	3	3
	MEAN	10.5	1.8	22.8
	STD	3.56	0.59	18.52
	MEDIAN	8.7	1.6	12.4
	MINIMUM	8.2	1.3	11.9
	MAXIMUM	14.6	2.4	44.2
Treatment Cycle 3	N	3	3	4
	MEAN	11.3	4.5	7.1
	STD	1.00	4.71	3.73
	MEDIAN	11.8	2.7	8.3
	MINIMUM	10.2	1.0	1.8
	MAXIMUM	12.0	9.9	10.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	4
	MEAN	59.5	45.5	68.1
	STD	24.41	17.03	15.09
	MEDIAN	54.6	42.5	62.3
	MINIMUM	37.3	29.4	57.4
	MAXIMUM	91.5	73.5	90.4
Treatment Cycle 1	N	4	5	4
	MEAN	9.1	21.0	32.5
	STD	4.00	16.05	27.14
	MEDIAN	9.1	30.2	30.9
	MINIMUM	4.7	1.3	1.0
	MAXIMUM	13.3	34.8	67.0
Treatment Cycle 2	N	4	5	4
	MEAN	9.5	18.3	27.2
	STD	6.75	22.20	25.04
	MEDIAN	9.3	7.9	24.1
	MINIMUM	3.4	5.0	0.1
	MAXIMUM	15.9	57.2	60.4
Treatment Cycle 3	N	4	5	4
	MEAN	8.0	19.0	32.6
	STD	6.51	14.23	29.32
	MEDIAN	7.7	17.9	35.6
	MINIMUM	0.5	4.2	0.0
	MAXIMUM	16.1	42.3	59.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	6	6	6
	MEAN	53.0	45.4	42.4
	STD	25.20	11.48	13.30
	MEDIAN	59.3	43.4	41.5
	MINIMUM	21.5	30.2	25.2
	MAXIMUM	85.4	62.5	59.6
Treatment Cycle 1	N	6	5	6
	MEAN	25.7	12.6	24.7
	STD	21.88	15.88	34.42
	MEDIAN	21.5	6.7	10.5
	MINIMUM	2.4	3.0	3.8
	MAXIMUM	62.4	40.7	92.7
Treatment Cycle 2	N	5	4	6
	MEAN	48.3	10.2	25.2
	STD	33.97	4.46	24.73
	MEDIAN	50.9	10.3	16.2
	MINIMUM	1.9	4.8	7.7
	MAXIMUM	83.6	15.4	73.2
Treatment Cycle 3	N	3	4	6
	MEAN	7.5	25.3	20.3
	STD	7.63	22.70	17.30
	MEDIAN	3.9	17.8	17.1
	MINIMUM	2.3	8.1	3.1
	MAXIMUM	16.3	57.4	46.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	3
	MEAN	64.9	65.2	77.3
	STD	25.49	35.46	18.01
	MEDIAN	66.6	87.4	82.6
	MINIMUM	33.1	23.0	57.3
	MAXIMUM	93.4	92.9	92.1
Treatment Cycle 1	N	3	5	3
	MEAN	35.5	16.5	49.1
	STD	31.66	30.25	37.24
	MEDIAN	22.9	4.3	64.8
	MINIMUM	12.2	1.0	6.6
	MAXIMUM	71.6	70.5	75.9
Treatment Cycle 2	N	2	5	3
	MEAN	8.3	21.8	33.2
	STD	0.99	28.58	23.80
	MEDIAN	8.3	4.4	26.5
	MINIMUM	7.6	1.0	13.5
	MAXIMUM	9.0	65.4	59.7
Treatment Cycle 3	N	2	5	3
	MEAN	25.6	20.4	21.6
	STD	16.33	22.06	17.39
	MEDIAN	25.6	9.0	27.5
	MINIMUM	14.1	1.1	2.1
	MAXIMUM	37.2	45.8	35.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	4
	MEAN	31.9	39.6	42.6
	STD	12.03	7.73	12.73
	MEDIAN	35.9	36.5	43.4
	MINIMUM	14.3	32.3	27.0
	MAXIMUM	41.4	52.1	56.5
Treatment Cycle 1	N	4	4	4
	MEAN	19.8	35.1	13.0
	STD	21.50	19.41	12.02
	MEDIAN	13.0	40.5	10.4
	MINIMUM	2.1	9.4	1.7
	MAXIMUM	51.1	50.3	29.7
Treatment Cycle 2	N	4	3	3
	MEAN	22.6	26.3	41.3
	STD	28.03	39.69	22.58
	MEDIAN	11.6	5.7	49.4
	MINIMUM	3.2	1.1	15.8
	MAXIMUM	64.3	72.0	58.8
Treatment Cycle 3	N	4	2	3
	MEAN	11.8	5.8	21.3
	STD	14.46	2.30	15.18
	MEDIAN	5.2	5.8	13.9
	MINIMUM	3.5	4.2	11.3
	MAXIMUM	33.5	7.5	38.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	6	7	6
	MEAN	47.3	59.3	67.5
	STD	23.90	21.46	28.07
	MEDIAN	47.9	65.4	67.4
	MINIMUM	13.6	31.1	21.5
	MAXIMUM	81.9	84.0	96.3
Treatment Cycle 1	N	6	6	6
	MEAN	12.3	33.4	54.6
	STD	10.85	27.34	35.39
	MEDIAN	9.0	23.1	66.5
	MINIMUM	2.3	9.6	7.4
	MAXIMUM	31.8	76.4	96.2
Treatment Cycle 2	N	6	6	6
	MEAN	11.2	33.8	50.0
	STD	7.58	20.79	39.29
	MEDIAN	12.0	25.1	50.5
	MINIMUM	1.1	16.2	2.9
	MAXIMUM	20.3	71.8	96.4
Treatment Cycle 3	N	6	5	5
	MEAN	10.0	30.0	45.8
	STD	4.92	25.73	33.49
	MEDIAN	8.9	33.9	50.1
	MINIMUM	4.9	2.8	1.9
	MAXIMUM	17.5	67.7	88.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	5	4
	MEAN	68.7	47.4	44.7
	STD	10.94	22.31	27.79
	MEDIAN	67.1	33.7	33.0
	MINIMUM	58.7	30.1	26.9
	MAXIMUM	82.1	81.5	86.0
Treatment Cycle 1	N	4	5	4
	MEAN	30.3	27.2	23.6
	STD	32.85	28.95	20.64
	MEDIAN	14.9	13.9	21.6
	MINIMUM	12.1	2.4	5.5
	MAXIMUM	79.6	66.7	45.7
Treatment Cycle 2	N	3	4	3
	MEAN	61.1	15.5	39.5
	STD	32.47	8.75	24.84
	MEDIAN	65.7	14.2	49.2
	MINIMUM	26.6	6.3	11.3
	MAXIMUM	91.0	27.3	58.1
Treatment Cycle 3	N	3	4	3
	MEAN	35.2	26.7	23.1
	STD	24.68	31.04	11.49
	MEDIAN	21.1	17.7	16.8
	MINIMUM	20.9	1.8	16.3
	MAXIMUM	63.7	69.8	36.4

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	5	6	6
	MEAN	40.9	49.2	48.8
	STD	13.62	24.33	15.36
	MEDIAN	48.4	48.1	45.4
	MINIMUM	20.5	14.7	32.3
	MAXIMUM	53.5	84.5	76.1
Treatment Cycle 1	N	5	5	6
	MEAN	10.5	38.4	23.1
	STD	6.54	18.57	13.92
	MEDIAN	7.2	35.6	22.8
	MINIMUM	4.2	15.5	9.6
	MAXIMUM	18.7	67.3	39.0
Treatment Cycle 2	N	5	5	6
	MEAN	12.2	33.2	26.7
	STD	19.51	28.78	14.50
	MEDIAN	3.1	23.3	24.9
	MINIMUM	1.1	9.8	11.2
	MAXIMUM	46.8	81.4	43.0
Treatment Cycle 3	N	4	5	6
	MEAN	11.8	38.4	24.1
	STD	17.07	34.44	23.35
	MEDIAN	4.1	24.1	13.1
	MINIMUM	1.9	1.3	6.5
	MAXIMUM	37.3	79.3	61.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■■■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	4	4	4
	MEAN	78.5	57.1	52.7
	STD	32.13	22.08	27.37
	MEDIAN	92.1	55.0	57.8
	MINIMUM	30.7	37.5	19.0
	MAXIMUM	99.1	80.7	76.2
Treatment Cycle 1	N	4	4	4
	MEAN	49.3	35.4	34.6
	STD	39.96	40.58	17.95
	MEDIAN	46.6	21.9	34.7
	MINIMUM	9.9	3.9	13.1
	MAXIMUM	93.9	93.8	55.9
Treatment Cycle 2	N	4	3	4
	MEAN	21.7	24.5	21.0
	STD	25.37	21.58	27.13
	MEDIAN	13.2	15.7	11.0
	MINIMUM	2.3	8.8	1.1
	MAXIMUM	58.1	49.1	60.9
Treatment Cycle 3	N	4	3	4
	MEAN	11.9	10.1	28.3
	STD	7.73	11.87	26.22
	MEDIAN	12.1	5.7	22.7
	MINIMUM	3.6	1.1	3.3
	MAXIMUM	19.7	23.6	64.4

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	3	6	3
	MEAN	61.5	65.2	51.5
	STD	5.70	25.68	18.30
	MEDIAN	64.4	66.5	49.9
	MINIMUM	54.9	29.7	34.1
	MAXIMUM	65.1	91.1	70.6
Treatment Cycle 1	N	2	6	3
	MEAN	29.4	53.0	45.3
	STD	32.63	35.42	19.41
	MEDIAN	29.4	49.1	49.8
	MINIMUM	6.3	4.6	24.1
	MAXIMUM	52.5	100.0	62.1
Treatment Cycle 2	N	1	5	3
	MEAN	7.7	34.9	50.0
	STD		27.26	14.40
	MEDIAN	7.7	24.7	44.8
	MINIMUM	7.7	13.5	39.0
	MAXIMUM	7.7	82.4	66.3
Treatment Cycle 3	N	1	4	3
	MEAN	5.7	43.2	32.6
	STD		37.46	16.75
	MEDIAN	5.7	40.3	36.0
	MINIMUM	5.7	4.5	14.4
	MAXIMUM	5.7	87.9	47.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	7	7	7
	MEAN	77.4	61.5	62.6
	STD	19.82	14.46	21.04
	MEDIAN	79.8	53.6	62.4
	MINIMUM	36.9	48.5	35.7
	MAXIMUM	98.2	87.1	91.0
Treatment Cycle 1	N	5	6	7
	MEAN	42.8	36.0	52.4
	STD	38.31	30.76	31.52
	MEDIAN	27.3	25.4	47.7
	MINIMUM	6.5	4.7	5.4
	MAXIMUM	93.8	85.7	90.0
Treatment Cycle 2	N	6	6	7
	MEAN	35.1	35.1	35.5
	STD	38.79	29.85	35.88
	MEDIAN	19.2	32.4	30.8
	MINIMUM	2.4	2.8	0.3
	MAXIMUM	91.6	74.8	90.9
Treatment Cycle 3	N	6	6	7
	MEAN	31.7	24.9	43.9
	STD	30.32	32.65	28.48
	MEDIAN	25.8	6.3	59.0
	MINIMUM	2.0	1.4	1.1
	MAXIMUM	71.0	70.4	79.6

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	5	5	5
	MEAN	71.1	69.9	69.0
	STD	6.61	10.90	13.22
	MEDIAN	73.3	72.5	65.6
	MINIMUM	62.4	55.8	51.7
	MAXIMUM	79.5	84.2	86.5
Treatment Cycle 1	N	5	5	5
	MEAN	43.4	38.3	46.1
	STD	17.01	8.56	8.41
	MEDIAN	53.4	34.9	48.7
	MINIMUM	18.0	33.1	32.7
	MAXIMUM	56.6	53.5	55.1
Treatment Cycle 2	N	5	5	5
	MEAN	33.6	35.7	30.8
	STD	19.23	5.22	10.72
	MEDIAN	43.3	35.3	30.4
	MINIMUM	12.5	30.8	16.9
	MAXIMUM	54.0	44.4	44.3
Treatment Cycle 3	N	4	5	5
	MEAN	27.5	36.9	28.0
	STD	14.66	8.88	10.22
	MEDIAN	27.3	37.3	28.6
	MINIMUM	12.9	23.9	13.1
	MAXIMUM	42.7	45.9	38.2

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	5	10	7
	MEAN	62.4	51.2	61.1
	STD	33.40	24.68	20.96
	MEDIAN	44.3	43.4	52.6
	MINIMUM	31.5	27.0	38.1
	MAXIMUM	99.4	100.0	87.5
Treatment Cycle 1	N	5	9	7
	MEAN	2.2	16.8	51.0
	STD	2.35	11.52	38.62
	MEDIAN	1.2	15.8	44.1
	MINIMUM	1.0	3.2	9.8
	MAXIMUM	6.4	36.1	100.0
Treatment Cycle 2	N	5	7	7
	MEAN	2.2	17.9	27.9
	STD	2.36	27.11	35.88
	MEDIAN	1.2	7.4	12.9
	MINIMUM	0.8	1.8	1.5
	MAXIMUM	6.4	77.6	86.4
Treatment Cycle 3	N	5	6	6
	MEAN	1.8	16.8	61.3
	STD	2.22	16.52	26.30
	MEDIAN	1.0	8.6	67.0
	MINIMUM	0.1	5.1	16.7
	MAXIMUM	5.7	45.6	91.7

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	8	7	7
	MEAN	62.7	43.9	49.9
	STD	29.02	25.11	28.04
	MEDIAN	63.2	35.9	42.2
	MINIMUM	23.6	24.0	19.6
	MAXIMUM	96.8	82.4	84.2
Treatment Cycle 1	N	6	6	7
	MEAN	12.7	21.4	32.3
	STD	10.76	13.75	22.55
	MEDIAN	11.0	19.6	31.9
	MINIMUM	1.2	4.8	6.1
	MAXIMUM	33.0	39.4	67.7
Treatment Cycle 2	N	7	6	4
	MEAN	9.9	19.8	17.2
	STD	10.35	17.54	7.75
	MEDIAN	4.8	13.5	16.6
	MINIMUM	1.4	2.0	8.3
	MAXIMUM	29.6	49.7	27.2
Treatment Cycle 3	N	7	5	3
	MEAN	15.9	19.1	18.6
	STD	19.51	9.94	15.64
	MEDIAN	9.5	15.4	23.7
	MINIMUM	0.0	8.7	1.1
	MAXIMUM	53.3	34.5	31.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.7

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Intention-to-Treat Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	5	7	8
	MEAN	42.8	48.3	50.4
	STD	31.36	16.40	12.49
	MEDIAN	35.8	36.3	48.9
	MINIMUM	17.6	34.5	32.8
	MAXIMUM	96.6	73.0	70.3
Treatment Cycle 1	N	5	6	7
	MEAN	20.7	25.4	32.5
	STD	16.68	27.43	32.03
	MEDIAN	13.5	15.0	22.3
	MINIMUM	1.1	2.6	4.4
	MAXIMUM	39.9	66.8	96.7
Treatment Cycle 2	N	3	6	6
	MEAN	19.9	24.1	31.0
	STD	28.45	19.24	36.43
	MEDIAN	5.8	25.4	15.5
	MINIMUM	1.2	1.0	0.8
	MAXIMUM	52.6	44.7	98.9
Treatment Cycle 3	N	3	6	7
	MEAN	7.5	20.9	24.0
	STD	12.11	20.53	23.34
	MEDIAN	1.1	16.9	11.1
	MINIMUM	0.0	1.2	4.8
	MAXIMUM	21.5	47.6	65.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	2	5	2
	MEAN	87.4	44.9	47.7
	STD	4.07	26.31	5.52
	MEDIAN	87.4	33.0	47.7
	MINIMUM	84.5	32.3	43.8
	MAXIMUM	90.3	92.0	51.6
Treatment Cycle 1	N	1	5	2
	MEAN	1.1	8.1	5.7
	STD		10.65	4.14
	MEDIAN	1.1	2.1	5.7
	MINIMUM	1.1	1.0	2.8
	MAXIMUM	1.1	25.9	8.7
Treatment Cycle 2	N	2	5	2
	MEAN	48.0	13.3	21.6
	STD	66.50	12.89	4.14
	MEDIAN	48.0	8.2	21.6
	MINIMUM	1.0	1.4	18.7
	MAXIMUM	95.1	33.3	24.6
Treatment Cycle 3	N	2	5	2
	MEAN	39.1	9.9	7.1
	STD	53.81	5.05	0.35
	MEDIAN	39.1	11.4	7.1
	MINIMUM	1.0	1.6	6.9
	MAXIMUM	77.1	14.0	7.4

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	2	2	6
	MEAN	40.6	46.7	57.4
	STD	2.30	11.03	19.20
	MEDIAN	40.6	46.7	59.0
	MINIMUM	39.0	38.9	28.6
	MAXIMUM	42.2	54.5	80.3
Treatment Cycle 1	N	2	2	6
	MEAN	48.9	17.3	35.6
	STD	6.54	21.00	22.28
	MEDIAN	48.9	17.3	29.7
	MINIMUM	44.3	2.4	7.9
	MAXIMUM	53.5	32.1	71.8
Treatment Cycle 2	N	2	2	6
	MEAN	35.0	18.6	40.7
	STD	14.96	9.72	19.76
	MEDIAN	35.0	18.6	46.9
	MINIMUM	24.4	11.8	8.9
	MAXIMUM	45.6	25.5	59.1
Treatment Cycle 3	N	1	2	4
	MEAN	52.6	39.8	52.4
	STD		50.75	20.43
	MEDIAN	52.6	39.8	51.2
	MINIMUM	52.6	3.9	29.4
	MAXIMUM	52.6	75.7	77.7

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	4	2	2
	MEAN	49.3	29.3	68.3
	STD	29.05	6.56	6.58
	MEDIAN	45.7	29.3	68.3
	MINIMUM	18.3	24.6	63.7
	MAXIMUM	87.5	33.9	73.0
Treatment Cycle 1	N	4	2	2
	MEAN	3.8	12.6	8.8
	STD	2.54	14.25	10.68
	MEDIAN	3.4	12.6	8.8
	MINIMUM	1.3	2.5	1.3
	MAXIMUM	7.1	22.7	16.4
Treatment Cycle 2	N	3	2	2
	MEAN	5.3	38.5	11.2
	STD	5.64	24.51	3.92
	MEDIAN	3.3	38.5	11.2
	MINIMUM	1.0	21.2	8.5
	MAXIMUM	11.7	55.8	14.0
Treatment Cycle 3	N	3	1	2
	MEAN	1.9	9.3	1.8
	STD	1.10		0.81
	MEDIAN	1.3	9.3	1.8
	MINIMUM	1.2	9.3	1.2
	MAXIMUM	3.1	9.3	2.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	5	5	4
	MEAN	52.9	43.1	73.7
	STD	25.71	9.30	12.67
	MEDIAN	49.2	45.8	71.6
	MINIMUM	23.2	30.1	62.2
	MAXIMUM	94.1	54.5	89.6
Treatment Cycle 1	N	5	5	4
	MEAN	18.6	5.9	32.7
	STD	22.34	4.50	24.24
	MEDIAN	12.1	4.4	32.2
	MINIMUM	2.5	1.1	10.2
	MAXIMUM	57.4	11.5	56.2
Treatment Cycle 2	N	5	5	4
	MEAN	18.7	4.9	37.8
	STD	23.47	4.89	26.79
	MEDIAN	8.7	2.3	37.4
	MINIMUM	0.9	1.3	10.2
	MAXIMUM	58.3	13.0	66.0
Treatment Cycle 3	N	5	5	4
	MEAN	17.7	6.4	29.0
	STD	25.92	3.20	22.82
	MEDIAN	7.9	6.9	22.5
	MINIMUM	1.3	1.2	9.1
	MAXIMUM	63.4	9.6	61.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	3	2	4
	MEAN	51.8	37.7	35.1
	STD	18.30	16.58	7.52
	MEDIAN	59.2	37.7	37.1
	MINIMUM	31.0	26.0	24.7
	MAXIMUM	65.3	49.5	41.5
Treatment Cycle 1	N	3	2	4
	MEAN	25.4	5.7	17.8
	STD	2.03	6.65	5.01
	MEDIAN	25.3	5.7	18.1
	MINIMUM	23.4	1.0	12.9
	MAXIMUM	27.5	10.4	22.4
Treatment Cycle 2	N	3	2	4
	MEAN	34.3	3.9	35.8
	STD	26.12	2.86	18.82
	MEDIAN	38.4	3.9	33.2
	MINIMUM	6.4	1.9	18.7
	MAXIMUM	58.2	5.9	58.2
Treatment Cycle 3	N	3	2	4
	MEAN	29.2	4.9	20.0
	STD	22.59	0.85	8.98
	MEDIAN	26.6	4.9	21.6
	MINIMUM	8.1	4.3	8.1
	MAXIMUM	53.0	5.5	28.7

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■■■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	3	2	5
	MEAN	38.7	64.1	66.6
	STD	7.28	34.47	37.52
	MEDIAN	39.5	64.1	92.6
	MINIMUM	31.1	39.7	13.1
	MAXIMUM	45.6	88.5	93.6
Treatment Cycle 1	N	3	2	5
	MEAN	4.9	11.8	56.5
	STD	3.37	11.10	33.02
	MEDIAN	4.0	11.8	50.3
	MINIMUM	2.1	3.9	15.0
	MAXIMUM	8.7	19.6	92.6
Treatment Cycle 2	N	3	2	5
	MEAN	4.0	3.0	53.4
	STD	2.35	2.79	32.52
	MEDIAN	3.6	3.0	49.9
	MINIMUM	1.9	1.0	12.0
	MAXIMUM	6.5	5.0	91.5
Treatment Cycle 3	N	3	2	5
	MEAN	12.2	18.3	39.8
	STD	12.06	24.40	33.57
	MEDIAN	5.6	18.3	33.6
	MINIMUM	5.0	1.0	4.3
	MAXIMUM	26.2	35.5	94.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	6	7	6
	MEAN	40.5	54.7	42.6
	STD	17.94	26.34	22.06
	MEDIAN	37.6	41.7	46.7
	MINIMUM	19.4	25.1	13.9
	MAXIMUM	63.9	92.1	76.5
Treatment Cycle 1	N	6	6	6
	MEAN	8.7	7.7	18.0
	STD	8.19	8.02	9.45
	MEDIAN	8.0	3.8	19.6
	MINIMUM	1.1	1.1	1.2
	MAXIMUM	23.8	20.9	28.3
Treatment Cycle 2	N	6	6	6
	MEAN	3.7	10.6	12.1
	STD	3.15	10.01	9.37
	MEDIAN	2.8	5.7	13.4
	MINIMUM	1.0	2.1	1.0
	MAXIMUM	8.4	26.1	21.8
Treatment Cycle 3	N	6	7	6
	MEAN	5.7	12.7	22.3
	STD	6.79	12.81	29.34
	MEDIAN	2.1	7.1	12.5
	MINIMUM	1.0	2.6	1.1
	MAXIMUM	17.6	39.8	78.9

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	5	4	5
	MEAN	48.3	54.7	57.2
	STD	20.89	22.23	19.10
	MEDIAN	39.7	56.1	56.1
	MINIMUM	33.6	27.9	34.3
	MAXIMUM	84.0	79.0	84.0
Treatment Cycle 1	N	5	4	5
	MEAN	13.7	26.0	9.8
	STD	7.11	20.88	10.39
	MEDIAN	11.6	23.5	5.6
	MINIMUM	6.0	3.3	2.0
	MAXIMUM	23.5	53.6	27.7
Treatment Cycle 2	N	4	4	5
	MEAN	20.2	15.8	8.7
	STD	36.41	13.36	13.28
	MEDIAN	2.1	15.6	3.0
	MINIMUM	1.9	3.1	1.2
	MAXIMUM	74.9	29.2	32.3
Treatment Cycle 3	N	3	3	4
	MEAN	6.5	14.6	12.7
	STD	9.05	10.28	20.73
	MEDIAN	1.5	16.1	2.5
	MINIMUM	1.0	3.6	2.1
	MAXIMUM	16.9	24.0	43.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	3	3	4
	MEAN	32.6	71.9	58.0
	STD	10.97	23.73	23.65
	MEDIAN	31.9	63.0	54.4
	MINIMUM	22.1	53.9	36.6
	MAXIMUM	44.0	98.8	86.8
Treatment Cycle 1	N	3	3	4
	MEAN	9.9	4.6	30.4
	STD	11.06	3.35	43.87
	MEDIAN	6.5	4.5	12.9
	MINIMUM	1.0	1.4	1.5
	MAXIMUM	22.3	8.1	94.5
Treatment Cycle 2	N	2	3	3
	MEAN	11.6	1.8	22.8
	STD	4.17	0.59	18.52
	MEDIAN	11.6	1.6	12.4
	MINIMUM	8.7	1.3	11.9
	MAXIMUM	14.6	2.4	44.2
Treatment Cycle 3	N	2	3	4
	MEAN	11.9	4.5	7.1
	STD	0.18	4.71	3.73
	MEDIAN	11.9	2.7	8.3
	MINIMUM	11.8	1.0	1.8
	MAXIMUM	12.0	9.9	10.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	2	4	4
	MEAN	78.3	49.6	68.1
	STD	18.56	16.66	15.09
	MEDIAN	78.3	44.8	62.3
	MINIMUM	65.2	35.3	57.4
	MAXIMUM	91.5	73.5	90.4
Treatment Cycle 1	N	2	4	4
	MEAN	10.0	18.0	32.5
	STD	4.63	16.87	27.14
	MEDIAN	10.0	18.1	30.9
	MINIMUM	6.8	1.3	1.0
	MAXIMUM	13.3	34.8	67.0
Treatment Cycle 2	N	2	4	4
	MEAN	15.3	20.9	27.2
	STD	0.88	24.72	25.04
	MEDIAN	15.3	10.8	24.1
	MINIMUM	14.7	5.0	0.1
	MAXIMUM	15.9	57.2	60.4
Treatment Cycle 3	N	2	4	4
	MEAN	7.7	13.1	32.6
	STD	2.05	6.53	29.32
	MEDIAN	7.7	15.1	35.6
	MINIMUM	6.3	4.2	0.0
	MAXIMUM	9.2	18.2	59.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	1	5	5
	MEAN	68.4	45.4	39.0
	STD		12.84	11.52
	MEDIAN	68.4	41.5	41.0
	MINIMUM	68.4	30.2	25.2
	MAXIMUM	68.4	62.5	55.4
Treatment Cycle 1	N	1	5	5
	MEAN	35.2	12.6	28.9
	STD		15.88	36.72
	MEDIAN	35.2	6.7	14.4
	MINIMUM	35.2	3.0	4.2
	MAXIMUM	35.2	40.7	92.7
Treatment Cycle 2	N	1	4	5
	MEAN	28.5	10.2	26.0
	STD		4.46	27.56
	MEDIAN	28.5	10.3	11.3
	MINIMUM	28.5	4.8	7.7
	MAXIMUM	28.5	15.4	73.2
Treatment Cycle 3	N	1	4	5
	MEAN	16.3	25.3	23.7
	STD		22.70	16.89
	MEDIAN	16.3	17.8	26.4
	MINIMUM	16.3	8.1	6.1
	MAXIMUM	16.3	57.4	46.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	2	5	3
	MEAN	63.2	65.2	77.3
	STD	42.67	35.46	18.01
	MEDIAN	63.2	87.4	82.6
	MINIMUM	33.1	23.0	57.3
	MAXIMUM	93.4	92.9	92.1
Treatment Cycle 1	N	2	5	3
	MEAN	17.5	16.5	49.1
	STD	7.57	30.25	37.24
	MEDIAN	17.5	4.3	64.8
	MINIMUM	12.2	1.0	6.6
	MAXIMUM	22.9	70.5	75.9
Treatment Cycle 2	N	2	5	3
	MEAN	8.3	21.8	33.2
	STD	0.99	28.58	23.80
	MEDIAN	8.3	4.4	26.5
	MINIMUM	7.6	1.0	13.5
	MAXIMUM	9.0	65.4	59.7
Treatment Cycle 3	N	2	5	3
	MEAN	25.6	20.4	21.6
	STD	16.33	22.06	17.39
	MEDIAN	25.6	9.0	27.5
	MINIMUM	14.1	1.1	2.1
	MAXIMUM	37.2	45.8	35.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	3	4	2
	MEAN	30.9	41.4	43.4
	STD	14.53	7.60	6.97
	MEDIAN	37.0	39.0	43.4
	MINIMUM	14.3	35.5	38.5
	MAXIMUM	41.4	52.1	48.3
Treatment Cycle 1	N	3	4	2
	MEAN	22.2	35.1	21.3
	STD	25.69	19.41	11.88
	MEDIAN	13.3	40.5	21.3
	MINIMUM	2.1	9.4	12.9
	MAXIMUM	51.1	50.3	29.7
Treatment Cycle 2	N	3	3	2
	MEAN	29.1	26.3	32.6
	STD	30.44	39.69	23.72
	MEDIAN	12.5	5.7	32.6
	MINIMUM	10.6	1.1	15.8
	MAXIMUM	64.3	72.0	49.4
Treatment Cycle 3	N	3	2	2
	MEAN	14.6	5.8	25.1
	STD	16.36	2.30	19.45
	MEDIAN	5.5	5.8	25.1
	MINIMUM	4.9	4.2	11.3
	MAXIMUM	33.5	7.5	38.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	5	6	5
	MEAN	54.0	55.2	65.9
	STD	19.32	20.26	31.07
	MEDIAN	53.8	53.8	59.3
	MINIMUM	31.2	31.1	21.5
	MAXIMUM	81.9	78.1	96.3
Treatment Cycle 1	N	5	6	5
	MEAN	12.3	33.4	64.1
	STD	12.13	27.34	29.92
	MEDIAN	5.7	23.1	71.6
	MINIMUM	2.3	9.6	15.6
	MAXIMUM	31.8	76.4	96.2
Treatment Cycle 2	N	5	6	5
	MEAN	11.5	33.8	59.5
	STD	8.43	20.79	35.52
	MEDIAN	14.3	25.1	67.5
	MINIMUM	1.1	16.2	12.8
	MAXIMUM	20.3	71.8	96.4
Treatment Cycle 3	N	5	5	4
	MEAN	10.4	30.0	56.8
	STD	5.42	25.73	26.30
	MEDIAN	9.5	33.9	56.4
	MINIMUM	4.9	2.8	25.6
	MAXIMUM	17.5	67.7	88.8

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	2	4	3
	MEAN	59.8	51.0	50.7
	STD	1.56	24.01	30.75
	MEDIAN	59.8	46.2	36.1
	MINIMUM	58.7	30.1	30.0
	MAXIMUM	60.9	81.5	86.0
Treatment Cycle 1	N	2	4	3
	MEAN	45.8	17.4	19.2
	STD	47.69	21.68	22.90
	MEDIAN	45.8	9.1	6.6
	MINIMUM	12.1	2.4	5.5
	MAXIMUM	79.6	49.0	45.7
Treatment Cycle 2	N	2	4	2
	MEAN	46.1	15.5	34.7
	STD	27.68	8.75	33.07
	MEDIAN	46.1	14.2	34.7
	MINIMUM	26.6	6.3	11.3
	MAXIMUM	65.7	27.3	58.1
Treatment Cycle 3	N	2	4	2
	MEAN	42.4	26.7	26.3
	STD	30.16	31.04	14.25
	MEDIAN	42.4	17.7	26.3
	MINIMUM	21.1	1.8	16.3
	MAXIMUM	63.7	69.8	36.4

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	5	5	4
	MEAN	40.9	52.3	53.0
	STD	13.62	25.89	18.00
	MEDIAN	48.4	49.5	51.8
	MINIMUM	20.5	14.7	32.3
	MAXIMUM	53.5	84.5	76.1
Treatment Cycle 1	N	5	5	4
	MEAN	10.5	38.4	29.2
	STD	6.54	18.57	13.22
	MEDIAN	7.2	35.6	34.0
	MINIMUM	4.2	15.5	9.7
	MAXIMUM	18.7	67.3	39.0
Treatment Cycle 2	N	5	5	4
	MEAN	12.2	33.2	33.7
	STD	19.51	28.78	12.42
	MEDIAN	3.1	23.3	37.8
	MINIMUM	1.1	9.8	16.1
	MAXIMUM	46.8	81.4	43.0
Treatment Cycle 3	N	4	5	4
	MEAN	11.8	38.4	32.8
	STD	17.07	34.44	24.62
	MEDIAN	4.1	24.1	31.6
	MINIMUM	1.9	1.3	6.5
	MAXIMUM	37.3	79.3	61.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	1	4	4
	MEAN	89.5	57.1	52.7
	STD		22.08	27.37
	MEDIAN	89.5	55.0	57.8
	MINIMUM	89.5	37.5	19.0
	MAXIMUM	89.5	80.7	76.2
Treatment Cycle 1	N	1	4	4
	MEAN	71.5	35.4	34.6
	STD		40.58	17.95
	MEDIAN	71.5	21.9	34.7
	MINIMUM	71.5	3.9	13.1
	MAXIMUM	71.5	93.8	55.9
Treatment Cycle 2	N	1	3	4
	MEAN	19.6	24.5	21.0
	STD		21.58	27.13
	MEDIAN	19.6	15.7	11.0
	MINIMUM	19.6	8.8	1.1
	MAXIMUM	19.6	49.1	60.9
Treatment Cycle 3	N	1	3	4
	MEAN	17.1	10.1	28.3
	STD		11.87	26.22
	MEDIAN	17.1	5.7	22.7
	MINIMUM	17.1	1.1	3.3
	MAXIMUM	17.1	23.6	64.4

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	1	6	3
	MEAN	65.1	65.2	51.5
	STD		25.68	18.30
	MEDIAN	65.1	66.5	49.9
	MINIMUM	65.1	29.7	34.1
	MAXIMUM	65.1	91.1	70.6
Treatment Cycle 1	N	1	6	3
	MEAN	52.5	53.0	45.3
	STD		35.42	19.41
	MEDIAN	52.5	49.1	49.8
	MINIMUM	52.5	4.6	24.1
	MAXIMUM	52.5	100.0	62.1
Treatment Cycle 2	N		5	3
	MEAN		34.9	50.0
	STD		27.26	14.40
	MEDIAN		24.7	44.8
	MINIMUM		13.5	39.0
	MAXIMUM		82.4	66.3
Treatment Cycle 3	N		4	3
	MEAN		43.2	32.6
	STD		37.46	16.75
	MEDIAN		40.3	36.0
	MINIMUM		4.5	14.4
	MAXIMUM		87.9	47.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	3	5	6
	MEAN	81.9	62.9	67.1
	STD	7.98	16.59	19.03
	MEDIAN	79.8	53.6	65.4
	MINIMUM	75.2	48.5	41.5
	MAXIMUM	90.7	87.1	91.0
Treatment Cycle 1	N	3	5	6
	MEAN	60.1	39.4	60.3
	STD	41.32	33.12	26.01
	MEDIAN	72.5	31.7	58.5
	MINIMUM	14.0	4.7	27.6
	MAXIMUM	93.8	85.7	90.0
Treatment Cycle 2	N	3	5	6
	MEAN	61.6	41.6	41.3
	STD	39.28	28.28	35.45
	MEDIAN	76.1	46.8	39.8
	MINIMUM	17.1	7.7	1.0
	MAXIMUM	91.6	74.8	90.9
Treatment Cycle 3	N	3	5	6
	MEAN	49.4	29.2	46.7
	STD	30.71	34.54	30.14
	MEDIAN	63.1	9.3	60.0
	MINIMUM	14.3	1.4	1.1
	MAXIMUM	71.0	70.4	79.6

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■■■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	4	4	3
	MEAN	70.6	68.8	64.3
	STD	7.51	12.31	12.58
	MEDIAN	70.3	67.7	64.4
	MINIMUM	62.4	55.8	51.7
	MAXIMUM	79.5	84.2	76.8
Treatment Cycle 1	N	4	4	3
	MEAN	40.4	39.2	51.1
	STD	18.05	9.62	3.49
	MEDIAN	43.6	35.2	49.6
	MINIMUM	18.0	33.1	48.7
	MAXIMUM	56.6	53.5	55.1
Treatment Cycle 2	N	4	4	3
	MEAN	30.8	36.5	24.0
	STD	21.03	5.69	6.79
	MEDIAN	28.4	35.4	24.9
	MINIMUM	12.5	30.8	16.9
	MAXIMUM	54.0	44.4	30.4
Treatment Cycle 3	N	4	4	3
	MEAN	27.5	37.8	26.6
	STD	14.66	10.00	12.67
	MEDIAN	27.3	40.7	28.6
	MINIMUM	12.9	23.9	13.1
	MAXIMUM	42.7	45.9	38.2

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	4	7	4
	MEAN	70.2	51.5	55.4
	STD	32.98	23.30	19.58
	MEDIAN	71.1	47.9	50.0
	MINIMUM	39.1	31.8	38.1
	MAXIMUM	99.4	100.0	83.3
Treatment Cycle 1	N	4	7	4
	MEAN	2.5	14.5	57.6
	STD	2.59	12.04	38.18
	MEDIAN	1.3	12.4	59.4
	MINIMUM	1.1	3.2	11.8
	MAXIMUM	6.4	36.1	100.0
Treatment Cycle 2	N	4	6	4
	MEAN	2.6	17.3	23.5
	STD	2.57	29.65	33.31
	MEDIAN	1.3	5.9	10.1
	MINIMUM	1.2	1.8	1.5
	MAXIMUM	6.4	77.6	72.4
Treatment Cycle 3	N	4	6	4
	MEAN	1.9	16.8	68.4
	STD	2.52	16.52	18.35
	MEDIAN	1.0	8.6	67.0
	MINIMUM	0.1	5.1	48.1
	MAXIMUM	5.7	45.6	91.7

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: ■

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	5	4	7
	MEAN	58.5	31.0	49.9
	STD	35.33	7.31	28.04
	MEDIAN	39.4	30.7	42.2
	MINIMUM	23.6	24.0	19.6
	MAXIMUM	96.8	38.7	84.2
Treatment Cycle 1	N	5	4	7
	MEAN	12.7	16.6	32.3
	STD	12.03	13.28	22.55
	MEDIAN	10.9	13.3	31.9
	MINIMUM	1.2	4.8	6.1
	MAXIMUM	33.0	35.1	67.7
Treatment Cycle 2	N	5	4	4
	MEAN	12.1	14.3	17.2
	STD	11.74	12.32	7.75
	MEDIAN	8.3	12.3	16.6
	MINIMUM	1.4	2.0	8.3
	MAXIMUM	29.6	30.9	27.2
Treatment Cycle 3	N	5	4	3
	MEAN	11.4	15.2	18.6
	STD	11.96	5.76	15.64
	MEDIAN	9.5	14.8	23.7
	MINIMUM	0.0	8.7	1.1
	MAXIMUM	31.2	22.7	31.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.8

Summary Statistics for Mean Luteal Phase VAS-Mood Scores
By Centre Group
Per Protocol Population

Centre Grouping - ITT: [REDACTED]

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=74)	Paroxetine CR 12.5 mg (N=99)	Placebo (N=96)
Baseline	N	3	4	5
	MEAN	27.3	42.8	48.7
	STD	11.55	13.68	12.05
	MEDIAN	24.3	36.3	48.7
	MINIMUM	17.6	35.4	32.8
	MAXIMUM	40.1	63.3	65.5
Treatment Cycle 1	N	3	4	5
	MEAN	16.9	19.2	36.2
	STD	17.82	31.73	36.06
	MEDIAN	13.5	3.7	22.3
	MINIMUM	1.1	2.6	6.1
	MAXIMUM	36.2	66.8	96.7
Treatment Cycle 2	N	3	4	4
	MEAN	19.9	20.4	41.8
	STD	28.45	21.11	41.12
	MEDIAN	5.8	18.5	29.0
	MINIMUM	1.2	1.0	10.4
	MAXIMUM	52.6	43.7	98.9
Treatment Cycle 3	N	3	4	4
	MEAN	7.5	12.2	26.2
	STD	12.11	18.54	26.85
	MEDIAN	1.1	3.9	15.5
	MINIMUM	0.0	1.2	8.4
	MAXIMUM	21.5	40.0	65.3

Phase: Luteal Phase (days = -1 - -5)

Table 13.9

Summary of Adjusted Change from Baseline in Luteal Phase VAS Physical Symptoms Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	301	-20.72	2.87	-14.25	2.70
	Paroxetine CR 12.5 mg vs Placebo	301	-22.49	2.67	-14.25	2.70
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	352	-19.17	2.56	-13.89	2.49
	Paroxetine CR 12.5 mg vs Placebo	352	-20.46	2.46	-13.89	2.49

Phase: Luteal Phase (days = -1 - -5)

Table 13.10

Summary of Analysis for Change from Baseline in Luteal Phase VAS Physical Symptoms Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-6.47	[-14.18, 1.24]	0.100
	Parox CR 12.5 mg vs Placebo	-8.25	[-15.69, -0.80]	0.030
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-5.28	[-12.26, 1.69]	0.137
	Parox CR 12.5 mg vs Placebo	-6.57	[-13.42, 0.29]	0.060

* Difference in adjusted least square means are shown
Phase: Luteal Phase (days = -1 - -5)

Table 13.11

Summary Statistics for Luteal Phase VAS Physical Symptoms Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	54.6	57.5	55.4
	STD	28.05	29.13	29.02
	MEDIAN	54.4	60.0	59.4
	MINIMUM	0.2	1.0	1.0
	MAXIMUM	99.6	100.0	100.0
Treatment Cycle 1	N	109	120	116
	MEAN	36.9	40.2	44.0
	STD	29.49	27.85	29.26
	MEDIAN	30.0	34.2	43.2
	MINIMUM	0.4	0.4	0.6
	MAXIMUM	100.0	99.2	100.0
Treatment Cycle 2	N	98	113	109
	MEAN	37.0	34.8	41.9
	STD	30.26	27.86	29.26
	MEDIAN	33.4	29.8	38.8
	MINIMUM	0.2	0.2	0.2
	MAXIMUM	99.8	100.0	100.0
Treatment Cycle 3	N	93	105	104
	MEAN	34.4	33.7	40.6
	STD	29.81	27.34	28.70
	MEDIAN	24.2	28.0	36.9
	MINIMUM	0.0	1.0	0.0
	MAXIMUM	100.0	100.0	99.5

Phase: Luteal Phase (days = -1 - -5)

Table 13.12

Summary of the Percentage of Subjects Responding
(50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score)
Intention-to-Treat Population

	Treatment Group								
	Paroxetine CR 25 mg			Paroxetine CR 12.5 mg			Placebo		
	n	%	N	n	%	N	n	%	N
Cycle									
Treatment Cycle 1	75	68.8	109	80	66.7	120	55	46.6	118
Treatment Cycle 2	71	72.4	98	75	66.4	113	60	55.6	108
Treatment Cycle 3	74	79.6	93	74	70.5	105	56	53.8	104
Treatment Cycle 3 LOCF Endpoint	81	72.3	112	81	66.4	122	59	49.6	119

Phase: Luteal Phase (days = -1 - -5)

Table 13.13.1

Summary of Logistic Regression for Subjects with a
50% Reduction from Baseline Mean Luteal Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Odds Ratio*	95% CI for Odds Ratio	p-value
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	3.93	[1.97, 7.85]	<0.001
	Parox CR 12.5 mg vs Placebo	2.50	[1.33, 4.71]	0.005
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	3.03	[1.66, 5.53]	<0.001
	Parox CR 12.5 mg vs Placebo	2.49	[1.40, 4.45]	0.002

* The odds ratio represents the odds of improving with Paroxetine relative to placebo
Phase: Luteal Phase (days = -1 - -5)

Table 13.13.2

Summary Statistics for Percentage Change from Baseline in Mean Luteal Phase VAS-Mood Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	54.4	52.2	55.7
	STD	24.46	21.35	21.52
	MEDIAN	48.9	47.0	55.4
	MINIMUM	13.6	14.7	13.1
	MAXIMUM	99.4	100.0	96.3
Treatment Cycle 1	N	109	120	118
	MEAN	-54.0	-53.2	-35.2
	STD	46.94	45.37	55.72
	MEDIAN	-70.5	-67.3	-45.4
	MINIMUM	-99.7	-98.5	-98.4
	MAXIMUM	134.5	142.1	233.6
Treatment Cycle 2	N	98	113	108
	MEAN	-58.3	-56.3	-37.4
	STD	54.15	44.65	57.96
	MEDIAN	-81.3	-73.3	-59.5
	MINIMUM	-98.8	-98.9	-99.8
	MAXIMUM	199.7	149.2	214.5
Treatment Cycle 3	N	93	105	104
	MEAN	-67.8	-55.4	-40.3
	STD	36.98	44.41	53.86
	MEDIAN	-80.8	-71.7	-55.1
	MINIMUM	-100.0	-98.9	-100.0
	MAXIMUM	105.9	107.3	192.5

Table 13.14.1

Summary of the Percentage of Subjects Responding
(Return to a score of Less Than or Equal to Baseline Mean Follicular Phase VAS-Mood Score)
Intention-to-Treat Population

	Treatment Group								
	Paroxetine CR 25 mg			Paroxetine CR 12.5 mg			Placebo		
	n	%	N	n	%	N	n	%	N
Cycle									
Treatment Cycle 1	19	17.4	109	21	17.5	120	4	3.4	118
Treatment Cycle 2	29	29.6	98	19	16.8	113	10	9.2	109
Treatment Cycle 3	33	35.5	93	21	20.0	105	7	6.7	105
Treatment Cycle 3 LOCF Endpoint	35	31.3	112	21	17.2	122	8	6.7	120

Phase: Follicular Phase (days = 6 - 10)

Table 13.14.2

Summary of Logistic Regression for Subjects with a
Return to a Score of Less Than or Equal to Baseline Mean Follicular Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Odds Ratio*	95% CI for Odds Ratio	p-value
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	8.31	[3.35, 20.63]	<0.001
	Parox CR 12.5 mg vs Placebo	3.62	[1.43, 9.16]	0.007
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	7.08	[3.03, 16.55]	<0.001
	Parox CR 12.5 mg vs Placebo	2.91	[1.21, 7.01]	0.017

* The odds ratio represents the odds of improving with Paroxetine relative to placebo
Phase: Follicular Phase (days = 6 - 10)

Table 13.15.1

Summary of Adjusted Change from Baseline in Mean Luteal Phase VAS Total Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	302	-313.32	22.46	-214.23	20.96
	Paroxetine CR 12.5 mg vs Placebo	302	-296.52	20.87	-214.23	20.96
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	353	-283.54	20.51	-205.72	19.88
	Paroxetine CR 12.5 mg vs Placebo	353	-278.85	19.64	-205.72	19.88

Phase: Luteal Phase (days = -1 - -5)

Table 13.15.2

Summary of Analysis for Change from Baseline in Mean Luteal Phase VAS Total Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-99.09	[-159.14, -39.05]	0.001
	Parox CR 12.5 mg vs Placebo	-82.29	[-140.22, -24.35]	0.006
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-77.82	[-133.47, -22.16]	0.006
	Parox CR 12.5 mg vs Placebo	-73.13	[-127.91, -18.36]	0.009

* Difference in adjusted least square means are shown
Phase: Luteal Phase (days = -1 - -5)

Table 13.15.3

Summary Statistics for Mean Luteal Phase VAS Total Scores
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	545.2	522.0	539.3
	STD	252.77	232.29	220.67
	MEDIAN	488.2	465.1	490.5
	MINIMUM	135.9	151.0	124.8
	MAXIMUM	1083.4	1046.0	1054.8
Treatment Cycle 1	N	109	120	118
	MEAN	287.7	285.9	348.2
	STD	209.57	226.47	263.24
	MEDIAN	247.0	205.1	289.6
	MINIMUM	16.0	21.4	15.8
	MAXIMUM	978.2	1031.0	1100.0
Treatment Cycle 2	N	98	113	109
	MEAN	268.9	255.5	330.9
	STD	255.80	209.71	245.85
	MEDIAN	185.4	202.4	267.4
	MINIMUM	9.8	11.2	13.8
	MAXIMUM	1052.8	926.0	1048.2
Treatment Cycle 3	N	93	105	105
	MEAN	230.5	242.1	327.8
	STD	209.74	203.52	252.56
	MEDIAN	166.0	189.4	276.6
	MINIMUM	0.0	11.0	0.0
	MAXIMUM	998.4	993.8	965.4

Table 13.15.4

Summary Statistics for Percentage Change from Baseline in Mean Luteal Phase VAS Total Scores
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	545.2	522.0	539.3
	STD	252.77	232.29	220.67
	MEDIAN	488.2	465.1	490.5
	MINIMUM	135.9	151.0	124.8
	MAXIMUM	1083.4	1046.0	1054.8
Treatment Cycle 1	N	109	120	118
	MEAN	-38.4	-39.7	-31.2
	STD	46.95	48.54	50.52
	MEDIAN	-49.3	-55.1	-37.4
	MINIMUM	-98.5	-97.9	-94.9
	MAXIMUM	158.4	122.9	161.0
Treatment Cycle 2	N	98	113	108
	MEAN	-43.6	-47.7	-34.4
	STD	59.09	39.14	49.47
	MEDIAN	-61.3	-57.6	-43.5
	MINIMUM	-98.7	-98.6	-98.2
	MAXIMUM	318.6	115.2	153.2
Treatment Cycle 3	N	93	105	104
	MEAN	-54.5	-48.1	-34.7
	STD	38.31	43.23	50.07
	MEDIAN	-63.5	-58.5	-49.4
	MINIMUM	-100.0	-98.6	-100.0
	MAXIMUM	90.3	152.1	159.7

Table 13.16

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Irritability VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	115	130	119
	MEAN	62.6	58.3	63.8
	STD	23.12	22.22	21.06
	MEDIAN	60.6	54.7	65.6
	MINIMUM	1.0	1.8	0.0
	MAXIMUM	99.8	100.0	100.0
Treatment Cycle 1	N	108	120	116
	MEAN	-38.1	-31.4	-24.7
	STD	31.28	28.71	28.58
	MEDIAN	-40.1	-33.1	-26.6
	MINIMUM	-99.6	-96.8	-88.2
	MAXIMUM	27.9	41.2	45.0
Treatment Cycle 2	N	97	113	108
	MEAN	-39.0	-33.2	-25.3
	STD	33.11	27.58	30.88
	MEDIAN	-42.0	-35.6	-25.1
	MINIMUM	-98.2	-97.6	-97.8
	MAXIMUM	42.4	51.2	40.6
Treatment Cycle 3	N	92	105	104
	MEAN	-44.8	-32.3	-28.5
	STD	28.74	30.30	30.21
	MEDIAN	-42.8	-34.2	-28.6
	MINIMUM	-99.0	-94.6	-96.0
	MAXIMUM	28.0	45.4	35.8

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.17

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Tension VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	118
	MEAN	53.7	50.7	52.0
	STD	27.59	25.28	26.58
	MEDIAN	53.2	47.6	53.3
	MINIMUM	1.0	1.5	0.0
	MAXIMUM	99.8	100.0	96.4
Treatment Cycle 1	N	109	120	117
	MEAN	-30.6	-27.0	-20.5
	STD	32.31	29.01	29.51
	MEDIAN	-31.2	-29.6	-19.1
	MINIMUM	-98.4	-99.0	-85.0
	MAXIMUM	36.6	65.6	68.2
Treatment Cycle 2	N	97	113	107
	MEAN	-33.1	-29.1	-23.0
	STD	34.44	27.71	32.62
	MEDIAN	-31.4	-31.2	-23.4
	MINIMUM	-97.8	-97.4	-87.4
	MAXIMUM	39.8	53.4	54.8
Treatment Cycle 3	N	93	105	103
	MEAN	-38.7	-29.1	-23.7
	STD	31.28	28.84	31.61
	MEDIAN	-35.0	-29.9	-25.0
	MINIMUM	-99.4	-97.6	-88.0
	MAXIMUM	42.6	57.6	53.4

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.18

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Depressed Mood VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	49.0	47.9	52.1
	STD	29.11	24.86	24.27
	MEDIAN	47.9	45.9	53.4
	MINIMUM	0.0	1.3	1.0
	MAXIMUM	99.8	100.0	98.0
Treatment Cycle 1	N	109	120	118
	MEAN	-27.3	-26.8	-21.3
	STD	33.21	27.16	32.14
	MEDIAN	-20.4	-28.5	-18.4
	MINIMUM	-99.4	-99.0	-89.2
	MAXIMUM	56.0	61.2	74.8
Treatment Cycle 2	N	98	113	108
	MEAN	-30.1	-26.9	-26.0
	STD	36.89	24.85	33.69
	MEDIAN	-31.5	-26.4	-30.9
	MINIMUM	-98.8	-97.8	-90.2
	MAXIMUM	67.4	35.4	58.4
Treatment Cycle 3	N	93	105	104
	MEAN	-33.6	-29.4	-25.1
	STD	33.35	26.35	30.39
	MEDIAN	-33.8	-29.8	-26.2
	MINIMUM	-99.8	-99.0	-89.8
	MAXIMUM	57.8	32.2	73.8

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.19

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Affective Lability VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	52.7	51.9	55.1
	STD	27.98	22.92	26.10
	MEDIAN	50.6	48.7	58.8
	MINIMUM	0.0	2.6	1.0
	MAXIMUM	100.0	100.0	98.0
Treatment Cycle 1	N	109	120	118
	MEAN	-30.9	-29.6	-22.3
	STD	31.94	26.30	31.94
	MEDIAN	-30.6	-28.5	-19.8
	MINIMUM	-97.4	-96.6	-94.6
	MAXIMUM	54.8	37.2	73.2
Treatment Cycle 2	N	98	113	108
	MEAN	-33.3	-31.7	-25.7
	STD	34.55	25.86	33.21
	MEDIAN	-33.1	-32.0	-22.2
	MINIMUM	-97.2	-97.2	-90.2
	MAXIMUM	57.8	37.2	74.8
Treatment Cycle 3	N	93	105	104
	MEAN	-38.1	-30.5	-26.5
	STD	31.02	26.79	31.27
	MEDIAN	-36.8	-27.8	-31.1
	MINIMUM	-99.2	-93.0	-90.8
	MAXIMUM	57.6	45.6	72.9

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.20

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Decreased Interest VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	44.2	39.9	43.6
	STD	31.00	26.73	26.84
	MEDIAN	39.6	34.9	45.6
	MINIMUM	0.8	0.8	0.6
	MAXIMUM	100.0	98.8	100.0
Treatment Cycle 1	N	109	120	118
	MEAN	-20.2	-19.3	-17.7
	STD	34.46	30.60	31.87
	MEDIAN	-15.8	-19.4	-19.8
	MINIMUM	-96.4	-92.2	-86.2
	MAXIMUM	67.0	67.6	83.8
Treatment Cycle 2	N	98	113	108
	MEAN	-24.8	-21.8	-20.4
	STD	35.44	28.25	34.16
	MEDIAN	-18.1	-19.0	-17.8
	MINIMUM	-96.4	-90.0	-98.8
	MAXIMUM	50.6	57.6	69.8
Treatment Cycle 3	N	93	105	104
	MEAN	-28.0	-22.6	-17.8
	STD	33.64	27.81	32.56
	MEDIAN	-20.8	-23.0	-16.6
	MINIMUM	-96.4	-91.8	-79.6
	MAXIMUM	55.2	52.0	74.8

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.21

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
 Difficulty Concentrating VAS Item Score
 Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	40.5	38.0	38.0
	STD	30.94	27.19	26.23
	MEDIAN	36.8	36.4	33.6
	MINIMUM	0.0	0.8	0.0
	MAXIMUM	100.0	98.4	95.8
Treatment Cycle 1	N	109	120	118
	MEAN	-18.9	-18.0	-15.6
	STD	31.32	27.82	29.79
	MEDIAN	-12.2	-12.5	-14.3
	MINIMUM	-99.2	-90.4	-85.0
	MAXIMUM	62.2	70.4	60.6
Treatment Cycle 2	N	98	113	108
	MEAN	-22.2	-20.4	-16.2
	STD	33.99	25.11	29.60
	MEDIAN	-14.0	-17.4	-15.5
	MINIMUM	-98.8	-92.2	-94.2
	MAXIMUM	49.2	35.7	58.8
Treatment Cycle 3	N	93	105	104
	MEAN	-25.9	-21.2	-14.5
	STD	33.42	26.02	30.95
	MEDIAN	-19.8	-18.6	-9.9
	MINIMUM	-99.0	-94.6	-84.8
	MAXIMUM	62.4	56.8	78.6

Note: Only subjects with baseline assessments are included
 Phase: Luteal Phase (days = -1 - -5)

Table 13.22

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Lack of Energy VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	50.8	45.9	47.5
	STD	29.59	28.50	28.10
	MEDIAN	50.4	46.6	48.6
	MINIMUM	2.0	1.0	1.0
	MAXIMUM	100.0	99.5	100.0
Treatment Cycle 1	N	109	120	118
	MEAN	-12.9	-14.8	-15.9
	STD	34.28	32.58	28.98
	MEDIAN	-10.8	-14.9	-15.4
	MINIMUM	-99.0	-91.2	-98.0
	MAXIMUM	94.8	84.6	69.4
Treatment Cycle 2	N	98	113	108
	MEAN	-19.1	-18.4	-18.6
	STD	36.68	29.54	29.65
	MEDIAN	-17.5	-19.0	-19.1
	MINIMUM	-98.6	-86.2	-98.6
	MAXIMUM	61.2	76.5	73.4
Treatment Cycle 3	N	93	105	104
	MEAN	-24.1	-21.0	-16.8
	STD	34.16	30.53	30.61
	MEDIAN	-18.8	-22.2	-18.3
	MINIMUM	-99.0	-91.8	-89.6
	MAXIMUM	63.2	58.0	69.2

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.23

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Change in Appetite VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	46.8	47.2	44.5
	STD	29.97	29.44	29.55
	MEDIAN	44.5	45.2	43.2
	MINIMUM	0.0	0.8	0.2
	MAXIMUM	100.0	100.0	99.6
Treatment Cycle 1	N	109	120	118
	MEAN	-18.3	-18.0	-14.0
	STD	29.56	29.04	29.45
	MEDIAN	-16.4	-13.2	-13.6
	MINIMUM	-99.6	-98.2	-81.8
	MAXIMUM	56.8	53.4	90.2
Treatment Cycle 2	N	98	113	108
	MEAN	-19.5	-21.0	-12.6
	STD	33.75	26.45	26.82
	MEDIAN	-16.2	-15.8	-9.2
	MINIMUM	-98.8	-97.0	-73.2
	MAXIMUM	70.0	66.2	71.0
Treatment Cycle 3	N	93	105	104
	MEAN	-23.6	-23.5	-13.8
	STD	32.08	31.67	31.94
	MEDIAN	-17.4	-20.1	-13.5
	MINIMUM	-99.0	-98.6	-73.6
	MAXIMUM	40.8	67.6	97.2

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.24

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Change in Sleep Pattern VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	46.7	43.9	46.6
	STD	31.41	31.04	29.99
	MEDIAN	44.8	39.1	47.8
	MINIMUM	1.0	0.4	0.0
	MAXIMUM	99.8	100.0	100.0
Treatment Cycle 1	N	109	120	118
	MEAN	-6.9	-8.9	-14.3
	STD	34.45	32.03	29.21
	MEDIAN	-4.2	-6.9	-13.6
	MINIMUM	-97.2	-98.0	-84.0
	MAXIMUM	82.8	96.2	68.4
Treatment Cycle 2	N	98	113	107
	MEAN	-12.4	-13.4	-15.5
	STD	32.82	26.41	29.99
	MEDIAN	-6.2	-7.8	-15.4
	MINIMUM	-97.0	-85.6	-95.8
	MAXIMUM	86.6	64.7	57.4
Treatment Cycle 3	N	93	105	104
	MEAN	-19.8	-17.5	-13.0
	STD	30.50	28.84	32.88
	MEDIAN	-12.2	-15.8	-12.0
	MINIMUM	-97.2	-98.2	-98.6
	MAXIMUM	56.4	57.6	95.6

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.25

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Feeling Out of Control VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	43.8	40.8	40.8
	STD	31.07	28.57	30.56
	MEDIAN	41.2	34.3	38.0
	MINIMUM	0.0	0.6	0.0
	MAXIMUM	100.0	100.0	100.0
Treatment Cycle 1	N	109	120	118
	MEAN	-25.4	-23.0	-15.5
	STD	31.61	29.53	31.52
	MEDIAN	-20.6	-19.6	-12.3
	MINIMUM	-99.0	-97.6	-92.2
	MAXIMUM	53.6	53.8	80.0
Treatment Cycle 2	N	98	113	108
	MEAN	-27.6	-24.3	-19.1
	STD	33.51	26.90	33.03
	MEDIAN	-20.5	-21.4	-16.9
	MINIMUM	-98.8	-93.2	-98.4
	MAXIMUM	32.0	59.2	93.2
Treatment Cycle 3	N	93	105	104
	MEAN	-32.1	-26.1	-16.6
	STD	32.74	27.98	30.42
	MEDIAN	-25.3	-21.8	-12.0
	MINIMUM	-99.0	-97.0	-92.8
	MAXIMUM	36.6	42.2	53.2

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.26

Summary Statistics for Baseline and Change from Baseline in Luteal Phase
Physical Symptoms VAS Item Score
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	116	130	119
	MEAN	54.6	57.5	55.4
	STD	28.05	29.13	29.02
	MEDIAN	54.4	60.0	59.4
	MINIMUM	0.2	1.0	1.0
	MAXIMUM	99.6	100.0	100.0
Treatment Cycle 1	N	109	120	116
	MEAN	-17.0	-16.7	-12.0
	STD	29.76	28.99	28.98
	MEDIAN	-12.6	-13.0	-9.3
	MINIMUM	-91.2	-98.0	-91.2
	MAXIMUM	55.4	61.6	67.4
Treatment Cycle 2	N	98	113	108
	MEAN	-17.8	-21.4	-13.1
	STD	34.14	30.41	29.61
	MEDIAN	-16.0	-18.8	-6.8
	MINIMUM	-96.2	-94.6	-93.8
	MAXIMUM	82.0	57.0	79.2
Treatment Cycle 3	N	93	105	103
	MEAN	-21.8	-23.0	-12.7
	STD	34.90	33.62	30.35
	MEDIAN	-15.8	-19.6	-9.2
	MINIMUM	-99.6	-98.6	-79.6
	MAXIMUM	75.0	65.6	51.2

Note: Only subjects with baseline assessments are included
Phase: Luteal Phase (days = -1 - -5)

Table 13.27

Summary of Adjusted Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Social/Leisure

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	Number Used In Analysis	-----Pairwise Comparisons-----			
			Adjusted Mean for Group 1	S.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	S.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	194	-3.23	0.37	-2.65	0.33
	Paroxetine CR 12.5 mg vs Placebo	194	-3.30	0.33	-2.65	0.33
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	274	-2.97	0.31	-2.34	0.28
	Paroxetine CR 12.5 mg vs Placebo	274	-3.07	0.28	-2.34	0.28

Table 13.27

Summary of Adjusted Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Work

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	186	-2.87	0.36	-1.74	0.30
	Paroxetine CR 12.5 mg vs Placebo	186	-2.55	0.31	-1.74	0.30
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	269	-2.57	0.28	-1.71	0.24
	Paroxetine CR 12.5 mg vs Placebo	269	-2.40	0.25	-1.71	0.24

Table 13.27

Summary of Adjusted Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Family/home

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	Number Used In Analysis	-----Pairwise Comparisons-----			
			Adjusted Mean for Group 1	S.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	S.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	194	-3.77	0.37	-2.93	0.33
	Paroxetine CR 12.5 mg vs Placebo	194	-3.70	0.34	-2.93	0.33
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	274	-3.65	0.32	-2.73	0.28
	Paroxetine CR 12.5 mg vs Placebo	274	-3.43	0.28	-2.73	0.28

Table 13.27

Summary of Adjusted Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Total

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	Number Used In Analysis	-----Pairwise Comparisons-----			
			Adjusted Mean for Group 1	S.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	S.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	186	-10.34	1.08	-7.33	0.92
	Paroxetine CR 12.5 mg vs Placebo	186	-9.68	0.94	-7.33	0.92
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	269	-9.40	0.86	-6.66	0.74
	Paroxetine CR 12.5 mg vs Placebo	269	-8.98	0.75	-6.66	0.74

Table 13.28

Summary of Analysis for Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Social/Leisure

		-----Pairwise Comparisons-----			
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference		p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-0.57	[-1.55,	0.40]	0.246
	Parox CR 12.5 mg vs Placebo	-0.65	[-1.56,	0.26]	0.163
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-0.63	[-1.45,	0.18]	0.129
	Parox CR 12.5 mg vs Placebo	-0.72	[-1.49,	0.04]	0.063

* Difference in adjusted least square means are shown

Table 13.28

Summary of Analysis for Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Work

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-1.13	[-2.05, -0.22]	0.016
	Parox CR 12.5 mg vs Placebo	-0.81	[-1.66, 0.03]	0.060
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-0.86	[-1.59, -0.13]	0.021
	Parox CR 12.5 mg vs Placebo	-0.69	[-1.36, -0.01]	0.047

* Difference in adjusted least square means are shown

Table 13.28

Summary of Analysis for Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Family/home

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-0.84	[-1.82, 0.14]	0.091
	Parox CR 12.5 mg vs Placebo	-0.77	[-1.69, 0.15]	0.100
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-0.91	[-1.73, -0.09]	0.029
	Parox CR 12.5 mg vs Placebo	-0.70	[-1.47, 0.07]	0.073

* Difference in adjusted least square means are shown

Table 13.28

Summary of Analysis for Change from Baseline in Sheehan Disability Scale (Individual and Total Scores)
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Score: Total

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-3.01	[-5.79, -0.23]	0.034
	Parox CR 12.5 mg vs Placebo	-2.35	[-4.91, 0.20]	0.071
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-2.74	[-4.97, -0.51]	0.016
	Parox CR 12.5 mg vs Placebo	-2.33	[-4.40, -0.26]	0.028

* Difference in adjusted least square means are shown

Table 13.29

Summary Statistics for Sheehan Disability Scale
(Individual and Total Scores)
Intention-to-Treat Population

Score: Social/Leisure

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	85	110	104
	MEAN	5.9	5.7	6.0
	STD	2.67	2.69	2.79
	MEDIAN	7.0	6.0	7.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	10
Treatment Cycle 1	N	91	101	105
	MEAN	3.2	3.2	3.7
	STD	3.06	2.71	3.12
	MEDIAN	3.0	2.0	2.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	10
Treatment Cycle 2	N	71	86	88
	MEAN	2.9	3.0	3.6
	STD	3.01	2.67	2.75
	MEDIAN	2.0	2.0	3.0
	MINIMUM	0	0	0
	MAXIMUM	10	9	10
Treatment Cycle 3	N	75	77	82
	MEAN	2.7	2.6	3.4
	STD	2.89	2.41	2.85
	MEDIAN	2.0	2.0	3.0
	MINIMUM	0	0	0
	MAXIMUM	10	8	10

Table 13.29

Summary Statistics for Sheehan Disability Scale
(Individual and Total Scores)
Intention-to-Treat Population

Score: Work

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	82	108	104
	MEAN	5.0	4.8	4.8
	STD	2.60	2.74	2.41
	MEDIAN	6.0	5.0	5.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	9
Treatment Cycle 1	N	89	100	104
	MEAN	2.5	2.7	2.9
	STD	2.55	2.52	2.57
	MEDIAN	2.0	2.0	2.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	10
Treatment Cycle 2	N	68	86	86
	MEAN	2.5	2.7	2.8
	STD	2.64	2.51	2.46
	MEDIAN	2.0	2.0	2.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	8
Treatment Cycle 3	N	72	77	81
	MEAN	2.3	2.4	3.2
	STD	2.83	2.28	2.66
	MEDIAN	1.0	2.0	3.0
	MINIMUM	0	0	0
	MAXIMUM	10	8	10

Table 13.29

Summary Statistics for Sheehan Disability Scale
(Individual and Total Scores)
Intention-to-Treat Population

Score: Family/Home

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	85	110	104
	MEAN	7.0	6.1	6.4
	STD	2.34	2.87	2.80
	MEDIAN	8.0	7.0	7.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	10
Treatment Cycle 1	N	91	100	105
	MEAN	3.1	3.2	3.9
	STD	2.87	2.89	3.04
	MEDIAN	2.0	2.0	3.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	10
Treatment Cycle 2	N	71	86	88
	MEAN	2.7	3.0	3.9
	STD	2.95	2.78	2.84
	MEDIAN	2.0	2.0	4.0
	MINIMUM	0	0	0
	MAXIMUM	10	10	10
Treatment Cycle 3	N	75	77	82
	MEAN	2.8	2.7	3.7
	STD	2.89	2.50	2.88
	MEDIAN	2.0	2.0	3.0
	MINIMUM	0	0	0
	MAXIMUM	10	9	10

Table 13.29

Summary Statistics for Sheehan Disability Scale
(Individual and Total Scores)
Intention-to-Treat Population

Score: Total

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	82	108	104
	MEAN	17.6	16.8	17.2
	STD	6.38	7.46	6.88
	MEDIAN	19.0	18.0	19.0
	MINIMUM	0	0	0
	MAXIMUM	30	30	28
Treatment Cycle 1	N	89	100	104
	MEAN	8.6	9.1	10.5
	STD	7.82	7.48	8.25
	MEDIAN	6.0	7.0	8.0
	MINIMUM	0	0	0
	MAXIMUM	28	25	29
Treatment Cycle 2	N	68	86	86
	MEAN	7.9	8.7	10.3
	STD	8.12	7.51	7.60
	MEDIAN	6.0	7.0	9.0
	MINIMUM	0	0	0
	MAXIMUM	30	27	27
Treatment Cycle 3	N	72	77	81
	MEAN	7.8	7.6	10.3
	STD	8.41	6.80	8.16
	MEDIAN	5.0	6.0	9.0
	MINIMUM	0	0	0
	MAXIMUM	30	23	28

Table 13.30

Summary of Adjusted Change from Baseline in PMTS Total Scores
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	Number Used In Analysis	-----Pairwise Comparisons-----			
			Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	209	-11.99	1.03	-8.47	0.92
	Paroxetine CR 12.5 mg vs Placebo	209	-10.63	0.89	-8.47	0.92
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	290	-11.42	0.84	-8.22	0.76
	Paroxetine CR 12.5 mg vs Placebo	290	-10.00	0.74	-8.22	0.76

Table 13.31

Summary of Analysis for Change from Baseline in PMTS Total Scores
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-3.52	[-6.24, -0.79]	0.012
	Parox CR 12.5 mg vs Placebo	-2.15	[-4.66, 0.35]	0.091
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-3.21	[-5.42, -0.99]	0.005
	Parox CR 12.5 mg vs Placebo	-1.78	[-3.86, 0.30]	0.093

* Difference in adjusted least square means are shown

Table 13.32

Summary Statistics for PMTS Total Score
Intention-to-Treat Population

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	93	116	107
	MEAN	21.9	21.9	21.3
	STD	6.39	6.38	5.55
	MEDIAN	22.0	23.0	22.0
	MINIMUM	7.0	4.0	4.0
	MAXIMUM	35.0	33.0	31.0
Treatment Cycle 1	N	93	101	104
	MEAN	10.5	11.5	14.0
	STD	7.30	7.78	7.83
	MEDIAN	9.0	10.0	12.0
	MINIMUM	0.0	0.0	2.0
	MAXIMUM	34.0	31.0	33.0
Treatment Cycle 2	N	71	87	90
	MEAN	10.9	11.7	14.2
	STD	9.08	7.96	8.06
	MEDIAN	8.0	11.0	13.5
	MINIMUM	0.0	0.0	0.0
	MAXIMUM	34.0	30.0	35.0
Treatment Cycle 3	N	75	81	83
	MEAN	9.8	11.1	13.5
	STD	7.89	7.10	8.44
	MEDIAN	8.0	10.0	12.0
	MINIMUM	0.0	0.0	0.0
	MAXIMUM	36.0	28.0	32.0

Table 13.33

Summary Statistics for Baseline and Change from Baseline in CGI Severity of Illness Score
Intention-to-Treat Population

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	93	116	107
	MEAN	4.7	4.7	4.6
	STD	0.98	0.95	0.84
	MEDIAN	5.0	5.0	5.0
	MINIMUM	3.0	3.0	3.0
	MAXIMUM	7.0	7.0	7.0
Treatment Cycle 1	N	80	94	96
	MEAN	-2.4	-1.9	-1.3
	STD	1.62	1.55	1.59
	MEDIAN	-3.0	-2.0	-1.0
	MINIMUM	-6.0	-5.0	-5.0
	MAXIMUM	1.0	2.0	2.0
Treatment Cycle 2	N	57	82	84
	MEAN	-2.4	-2.0	-1.4
	STD	1.79	1.60	1.62
	MEDIAN	-3.0	-2.0	-1.0
	MINIMUM	-6.0	-5.0	-5.0
	MAXIMUM	1.0	1.0	2.0
Treatment Cycle 3	N	58	77	74
	MEAN	-2.4	-2.1	-1.9
	STD	1.66	1.70	1.62
	MEDIAN	-3.0	-2.0	-2.0
	MINIMUM	-5.0	-5.0	-5.0
	MAXIMUM	1.0	2.0	1.0

Note: Only subjects with Baseline assessments are included

Table 13.34.1

Summary of Adjusted Change from Baseline in CGI Severity of Illness Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	209	-2.36	0.20	-1.92	0.18
	Paroxetine CR 12.5 mg vs Placebo	209	-2.09	0.17	-1.92	0.18
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	294	-2.36	0.16	-1.75	0.14
	Paroxetine CR 12.5 mg vs Placebo	294	-2.02	0.14	-1.75	0.14

Table 13.34.2

Summary of Analysis for Change from Baseline in CGI Severity of Illness Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	-0.44	[-0.96, 0.08]	0.094
	Parox CR 12.5 mg vs Placebo	-0.17	[-0.65, 0.30]	0.470
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-0.61	[-1.03, -0.20]	0.004
	Parox CR 12.5 mg vs Placebo	-0.27	[-0.67, 0.12]	0.177

* Difference in adjusted least square means are shown

Table 13.35

Number (%) of Subjects in Each Category of CGI Severity of Illness Score
Intention-to-Treat Population

Visit	Severity	Paroxetine CR 25 mg (N=116)	Treatment Group Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	Normal, not at all ill (1)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Borderline mentally ill (2)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Mildly ill (3)	8 (8.6%)	11 (9.5%)	7 (6.5%)
	Moderately ill (4)	32 (34.4%)	39 (33.6%)	42 (39.3%)
	Markedly ill (5)	32 (34.4%)	41 (35.3%)	42 (39.3%)
	Severely ill (6)	18 (19.4%)	23 (19.8%)	15 (14.0%)
	Among the most extremely ill patients (7)	3 (3.2%)	2 (1.7%)	1 (0.9%)
	Total*	93 (100.0%)	116 (100.0%)	107 (100.0%)
	Not assessed (0)	0	0	0
Treatment Cycle 1	Normal, not at all ill (1)	26 (27.4%)	22 (21.8%)	13 (12.4%)
	Borderline mentally ill (2)	28 (29.5%)	26 (25.7%)	24 (22.9%)
	Mildly ill (3)	23 (24.2%)	22 (21.8%)	22 (21.0%)
	Moderately ill (4)	9 (9.5%)	14 (13.9%)	25 (23.8%)
	Markedly ill (5)	5 (5.3%)	14 (13.9%)	14 (13.3%)
	Severely ill (6)	4 (4.2%)	2 (2.0%)	5 (4.8%)
	Among the most extremely ill patients (7)	0 (0.0%)	1 (1.0%)	2 (1.9%)
	Total*	95 (100.0%)	101 (100.0%)	105 (100.0%)
	Not assessed (0)	1	0	0
Treatment Cycle 2	Normal, not at all ill (1)	29 (40.8%)	25 (28.7%)	13 (14.3%)
	Borderline mentally ill (2)	12 (16.9%)	21 (24.1%)	16 (17.6%)
	Mildly ill (3)	17 (23.9%)	16 (18.4%)	24 (26.4%)
	Moderately ill (4)	6 (8.5%)	10 (11.5%)	22 (24.2%)
	Markedly ill (5)	4 (5.6%)	11 (12.6%)	13 (14.3%)
	Severely ill (6)	3 (4.2%)	4 (4.6%)	3 (3.3%)
	Among the most extremely ill patients (7)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Total*	71 (100.0%)	87 (100.0%)	91 (100.0%)
	Not assessed (0)	0	0	0
Treatment Cycle 3	Normal, not at all ill (1)	27 (36.0%)	24 (29.6%)	19 (23.2%)
	Borderline mentally ill (2)	23 (30.7%)	19 (23.5%)	17 (20.7%)
	Mildly ill (3)	13 (17.3%)	16 (19.8%)	17 (20.7%)
	Moderately ill (4)	7 (9.3%)	14 (17.3%)	19 (23.2%)
	Markedly ill (5)	2 (2.7%)	3 (3.7%)	8 (9.8%)
	Severely ill (6)	2 (2.7%)	5 (6.2%)	2 (2.4%)
	Among the most extremely ill patients (7)	1 (1.3%)	0 (0.0%)	0 (0.0%)
	Total*	75 (100.0%)	81 (100.0%)	82 (100.0%)
	Not assessed (0)	0	0	1

Note: Not Assessed does not include missing values

*Total and % exclude Subjects classified as 'Not Assessed' (i.e. CGI score of zero)

Table 13.36

Number (%) of Subjects by Change in the CGI Severity of Illness Score from Baseline
Intention-to-Treat Population

		Treatment Groups					
		Paroxetine CR 25 mg (N=116)		Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
		n	%	n	%	n	%
Visit	Change from Baseline in SOI						
Treatment Cycle 1	-7	0	0	0	0	0	0
	-6	1	1.3	0	0	0	0
	-5	5	6.3	4	4.3	2	2.1
	-4	16	20.0	14	14.9	7	7.3
	-3	19	23.8	15	16.0	13	13.5
	-2	12	15.0	20	21.3	21	21.9
	-1	16	20.0	23	24.5	21	21.9
	0	8	10.0	15	16.0	22	22.9
	1	3	3.8	2	2.1	6	6.3
	2	0	0	1	1.1	4	4.2
	3	0	0	0	0	0	0
	4	0	0	0	0	0	0
	5	0	0	0	0	0	0
	6	0	0	0	0	0	0
	7	0	0	0	0	0	0
	Total	80	100.0	94	100.0	96	100.0
Treatment Cycle 2	-7	0	0	0	0	0	0
	-6	1	1.8	0	0	0	0

(Continued)

SOI = Severity of Illness

Table 13.36

Number (%) of Subjects by Change in the CGI Severity of Illness Score from Baseline
Intention-to-Treat Population

		Treatment Groups					
		Paroxetine CR 25 mg (N=116)		Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
		n	%	n	%	n	%
Visit	Change from Baseline in SOI						
Treatment Cycle 2							
	-5	6	10.5	5	6.1	1	1.2
	-4	9	15.8	12	14.6	10	11.9
	-3	13	22.8	15	18.3	12	14.3
	-2	11	19.3	14	17.1	15	17.9
	-1	8	14.0	20	24.4	22	26.2
	0	4	7.0	13	15.9	14	16.7
	1	5	8.8	3	3.7	8	9.5
	2	0	0	0	0	2	2.4
	3	0	0	0	0	0	0
	4	0	0	0	0	0	0
	5	0	0	0	0	0	0
	6	0	0	0	0	0	0
	7	0	0	0	0	0	0
	Total	57	100.0	82	100.0	84	100.0
Treatment Cycle 3							
	-7	0	0	0	0	0	0
	-6	0	0	0	0	0	0
	-5	5	8.6	5	6.5	3	4.1
	-4	13	22.4	13	16.9	11	14.9

(Continued)

SOI = Severity of Illness

Table 13.36

Number (%) of Subjects by Change in the CGI Severity of Illness Score from Baseline
Intention-to-Treat Population

		Treatment Groups					
		Paroxetine CR 25 mg (N=116)		Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
		n	%	n	%	n	%
Visit	Change from Baseline in SOI						
Treatment Cycle 3							
	-3	13	22.4	17	22.1	15	20.3
	-2	10	17.2	13	16.9	11	14.9
	-1	10	17.2	12	15.6	16	21.6
	0	3	5.2	13	16.9	14	18.9
	1	4	6.9	3	3.9	4	5.4
	2	0	0	1	1.3	0	0
	3	0	0	0	0	0	0
	4	0	0	0	0	0	0
	5	0	0	0	0	0	0
	6	0	0	0	0	0	0
	7	0	0	0	0	0	0
	Total	58	100.0	77	100.0	74	100.0

SOI = Severity of Illness

Table 13.37

Summary of the Percentage of Subjects Responding on the CGI Global Improvement Item (score of 1 or 2)
Intention-to-Treat Population

	Treatment Group								
	Paroxetine CR 25 mg			Paroxetine CR 12.5 mg			Placebo		
	n	%	N	n	%	N	n	%	N
Visit									
Treatment Cycle 1	60	62.5	96	57	56.4	101	46	43.8	105
Treatment Cycle 2	48	67.6	71	49	56.3	87	37	40.7	91
Treatment Cycle 3	56	74.7	75	48	59.3	81	38	46.3	82
Treatment Cycle 3 LOCF Endpoint	71	67.6	105	66	56.9	116	50	43.1	116

Table 13.38

Summary of Logistic Regression for Subjects Responding on the CGI Global Improvement Item
Adjusted for Centre Group and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Odds Ratio*	95% CI for Odds Ratio	p-value
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	4.65	[2.16, 10.03]	<0.001
	Parox CR 12.5 mg vs Placebo	1.99	[1.00, 3.95]	0.049
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	3.47	[1.87, 6.43]	<0.001
	Parox CR 12.5 mg vs Placebo	1.97	[1.11, 3.50]	0.021

* The odds ratio represents the odds of improving with Paroxetine relative to placebo

Table 13.39

Number (%) of Subjects in Each Category of CGI Global Improvement Item
Intention-to-Treat Population

Visit	Global Improvement	Paroxetine CR 25 mg (N=116)	Treatment Group Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Treatment Cycle 1	Very much improved (1)	28 (29.2%)	29 (28.7%)	13 (12.4%)
	Much Improved (2)	32 (33.3%)	28 (27.7%)	33 (31.4%)
	Minimally improved (3)	23 (24.0%)	26 (25.7%)	28 (26.7%)
	No change (4)	8 (8.3%)	13 (12.9%)	20 (19.0%)
	Minimally worse (5)	3 (3.1%)	3 (3.0%)	7 (6.7%)
	Much worse (6)	2 (2.1%)	2 (2.0%)	3 (2.9%)
	Very much worse (7)	0 (0.0%)	0 (0.0%)	1 (1.0%)
	Total*	96 (100.0%)	101 (100.0%)	105 (100.0%)
	Not assessed (0)	0	0	0
Treatment Cycle 2	Very much improved (1)	29 (40.8%)	23 (26.4%)	15 (16.5%)
	Much Improved (2)	19 (26.8%)	26 (29.9%)	22 (24.2%)
	Minimally improved (3)	12 (16.9%)	23 (26.4%)	22 (24.2%)
	No change (4)	9 (12.7%)	13 (14.9%)	26 (28.6%)
	Minimally worse (5)	1 (1.4%)	2 (2.3%)	4 (4.4%)
	Much worse (6)	1 (1.4%)	0 (0.0%)	2 (2.2%)
	Very much worse (7)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Total*	71 (100.0%)	87 (100.0%)	91 (100.0%)
	Not assessed (0)	0	0	0
Treatment Cycle 3	Very much improved (1)	26 (34.7%)	21 (25.9%)	19 (23.2%)
	Much Improved (2)	30 (40.0%)	27 (33.3%)	19 (23.2%)
	Minimally improved (3)	9 (12.0%)	16 (19.8%)	17 (20.7%)
	No change (4)	8 (10.7%)	13 (16.0%)	25 (30.5%)
	Minimally worse (5)	2 (2.7%)	3 (3.7%)	0 (0.0%)
	Much worse (6)	0 (0.0%)	1 (1.2%)	2 (2.4%)
	Very much worse (7)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Total*	75 (100.0%)	81 (100.0%)	82 (100.0%)
	Not assessed (0)	0	0	1

Note: Not Assessed does not include missing values

*Total and % exclude Subjects classified as 'Not Assessed' (i.e. CGI score of zero)

Table 13.40

Summary of the Percentage of Subjects Responding on the Patient Global Evaluation (score of 1 or 2)
Intention-to-Treat Population

	Treatment Groups								
	Paroxetine CR 25 mg			Paroxetine CR 12.5 mg			Placebo		
	n	%	N	n	%	N	n	%	N
Visit									
Treatment Cycle 1	48	53.9	89	44	46.3	95	39	37.1	105
Treatment Cycle 2	36	51.4	70	41	50.0	82	22	25.3	87
Treatment Cycle 3	41	54.7	75	42	54.5	77	25	30.9	81
Treatment Cycle 3 LOCF Endpoint	49	48.0	102	59	51.8	114	33	28.7	115

Patient Global Evaluation Responders are defined as having a global improvement score of 1 (very much improved) or 2 (much improved)

Table 13.41

Summary of Logistic Regression for Subjects Responding on Patient Global Evaluation
Adjusted for Centre Group and Age
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison	-----Pairwise Comparisons-----		
		Odds Ratio*	95% CI for Odds Ratio	p-value
Treatment Cycle 3 OC	Parox CR 25.0 mg vs Placebo	3.49	[1.67, 7.30]	<0.001
	Parox CR 12.5 mg vs Placebo	3.21	[1.55, 6.62]	0.002
Treatment Cycle 3 LOCF Endpoint	Parox CR 25.0 mg vs Placebo	2.67	[1.44, 4.94]	0.002
	Parox CR 12.5 mg vs Placebo	3.07	[1.69, 5.58]	<0.001

* The odds ratio represents the odds of improving with Paroxetine relative to placebo

Table 13.42

Number (%) of Subjects in Each Category of Patient Global Evaluation
Intention-to-Treat Population

Visit	Patient Global Evaluation	Paroxetine CR 25 mg (N=116)	Treatment Group Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Treatment Cycle 1	Very much improved	21 (23.6%)	20 (21.1%)	9 (8.6%)
	Much improved	27 (30.3%)	24 (25.3%)	30 (28.6%)
	Minimally improved	26 (29.2%)	29 (30.5%)	31 (29.5%)
	No change	8 (9.0%)	13 (13.7%)	22 (21.0%)
	Minimally worse	2 (2.2%)	5 (5.3%)	9 (8.6%)
	Much worse	4 (4.5%)	3 (3.2%)	3 (2.9%)
	Very much worse	1 (1.1%)	1 (1.1%)	1 (1.0%)
	Total *	89 (100.0%)	95 (100.0%)	105 (100.0%)
	Not assessed	2	6	1
Treatment Cycle 2	Very much improved	16 (22.9%)	19 (23.2%)	6 (6.9%)
	Much improved	20 (28.6%)	22 (26.8%)	16 (18.4%)
	Minimally improved	13 (18.6%)	21 (25.6%)	22 (25.3%)
	No change	14 (20.0%)	13 (15.9%)	32 (36.8%)
	Minimally worse	4 (5.7%)	6 (7.3%)	7 (8.0%)
	Much worse	3 (4.3%)	1 (1.2%)	3 (3.4%)
	Very much worse	0 (0.0%)	0 (0.0%)	1 (1.1%)
	Total *	70 (100.0%)	82 (100.0%)	87 (100.0%)
	Not assessed	1	4	1
Treatment Cycle 3	Very much improved	20 (26.7%)	17 (22.1%)	12 (14.8%)
	Much improved	21 (28.0%)	25 (32.5%)	13 (16.0%)
	Minimally improved	21 (28.0%)	15 (19.5%)	29 (35.8%)
	No change	8 (10.7%)	15 (19.5%)	23 (28.4%)
	Minimally worse	2 (2.7%)	4 (5.2%)	3 (3.7%)
	Much worse	2 (2.7%)	1 (1.3%)	1 (1.2%)
	Very much worse	1 (1.3%)	0 (0.0%)	0 (0.0%)
	Total *	75 (100.0%)	77 (100.0%)	81 (100.0%)
	Not assessed	1	0	1

Note: Not Assessed does not include missing values

*Total and % exclude Subjects classified as 'Not Assessed' (i.e. Patient Global Evaluation score of zero)

Table 13.43

Summary of Adjusted Change from Baseline of AUC Daily Luteal Phase VAS-Mood Score
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

		-----Pairwise Comparisons-----				
Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
2	Paroxetine CR 25 mg vs Placebo	353	-26.32	1.52	-18.19	1.48
	Paroxetine CR 12.5 mg vs Placebo	353	-25.00	1.46	-18.19	1.48

Phase: Luteal Phase (days = -1 - -5)

Table 13.44

Summary of Analysis for Change from Baseline for AUC Daily Luteal Phase VAS-Mood Scores
Adjusted for Centre Group, Baseline Score and Age
Intention-to-Treat Population

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Phase LOCF Endpoint	Parox CR 25.0 mg vs Placebo	-8.13	[-12.26, -3.99]	<0.001
	Parox CR 12.5 mg vs Placebo	-6.81	[-10.88, -2.73]	<0.001

* Difference in adjusted least square means are shown
Phase: Luteal Phase (days = -1 - -5)

Table 13.45

Summary Statistics for AUC Daily Luteal Phase VAS-Mood Scores
Intention-to-Treat Population

Cycle	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	116	130	119
	MEAN	43.7	41.8	44.8
	STD	19.91	17.32	17.54
	MEDIAN	39.3	37.1	45.3
	MINIMUM	9.2	11.1	9.2
	MAXIMUM	79.6	80.0	77.2
Treatment Phase	N	112	122	120
	MEAN	16.9	18.3	25.6
	STD	17.60	15.45	18.09
	MEDIAN	8.3	13.5	22.2
	MINIMUM	0.6	1.1	0.3
	MAXIMUM	69.6	68.7	77.1

Phase: Luteal Phase (days = -1 - -5)

Table 13.46

Number (%) of Subjects in Each Category of Patient Evaluation of Study Medication
Intention-to-Treat Population

Patient Evaluation	Reason	Treatment Group				Total (N=361)	
		Paroxetine CR 25 mg (N=114)	Paroxetine CR 12.5 mg (N=128)	Placebo (N=119)			
TOTAL	TOTAL	114 (100.0%)	128 (100.0%)	119 (100.0%)		361	(100.0%)
Yes	TOTAL	69 (60.5%)	73 (57.0%)	62 (52.1%)		204	(56.5%)
No	TOTAL	28 (24.6%)	32 (25.0%)	45 (37.8%)		105	(29.1%)
	Lack of Efficacy	11 (39.3%)	23 (71.9%)	41 (91.1%)		75	(71.4%)
	Side effects	16 (57.1%)	9 (28.1%)	2 (4.4%)		27	(25.7%)
	Other	1 (3.6%)	0 (0.0%)	2 (4.4%)		3	(2.9%)
Not sure	TOTAL	17 (14.9%)	23 (18.0%)	12 (10.1%)		52	(14.4%)
	Lack of Efficacy	7 (41.2%)	15 (65.2%)	6 (50.0%)		28	(53.8%)
	Side effects	3 (17.6%)	2 (8.7%)	2 (16.7%)		7	(13.5%)
	Anti-medication (i.e	1 (5.9%)	1 (4.3%)	0 (0.0%)		2	(3.8%)
	Other	6 (35.3%)	5 (21.7%)	4 (33.3%)		15	(28.8%)

Note: The column counts denote the number of Subjects with Patient Evaluation of Study Medication

Table 13.47

Number (%) of Subjects with a Missing Luteal VAS-Mood Score
Intention-to-Treat Population

Cycle	Treatment Groups							
	Parox CR 25.0 mg (N=116)		Parox CR 12.5 mg (N=130)		Placebo (N=120)		Total (N=366)	
	n	%	n	%	n	%	n	%
Reference Cycle 1	0		0		0		0	
Reference Cycle 1A	0		0		1	0.8	1	0.3
Reference Cycle 1B	0		0		0		0	
Baseline	0		0		1	0.8	1	0.3
Treatment Cycle 1	7	6	9	6.9	2	1.7	18	4.9
Treatment Cycle 2	4	3.4	5	3.8	8	6.7	17	4.6
Treatment Cycle 3	3	2.6	7	5.4	1	0.8	11	3

Table 13.48

Number (%) of Subjects with Missing Mean Luteal Phase VAS Scores for the Core PMDD Symptoms
Intention-to-Treat Population

----- Treatment Group=Paroxetine CR 25 mg (N=116) -----

Cycle	Items Missing	Affective Lability		Depressed Mood		Luteal Phase VAS Items Irritability		Tension		Total+	
		n	%	n	%	n	%	n	%	n	%
RC1	0									115	99.1
RC1A	0									28	24.1
RC1B	0									2	1.7
Baseline	0									115	99.1
	1					1	0.9			1	0.9
TC1	0									109	94.0
	4	7	6.0	7	6.0	7	6.0	7	6.0	7	6.0
TC2	0									97	83.6
	1							1	0.9	1	0.9
	4	4	3.4	4	3.4	4	3.4	4	3.4	4	3.4
TC3	0									93	80.2
	4	3	2.6	3	2.6	3	2.6	3	2.6	3	2.6

RC = Reference Cycle, TC = Treatment Cycle
+ Total number of subjects with missing Mean Luteal Phase VAS symptom scores

Table 13.48

Number (%) of Subjects with Missing Mean Luteal Phase VAS Scores for the Core PMDD Symptoms
Intention-to-Treat Population

----- Treatment Group=Paroxetine CR 12.5 mg (N=130) -----

Cycle	Items Missing	Affective Lability		Depressed Mood		Luteal Phase VAS Items Irritability		Tension		Total+	
		n	%	n	%	n	%	n	%	n	%
RC1	0									129	99.2
RC1A	0									16	12.3
Baseline	0									130	100.0
TC1	0									120	92.3
	4	9	6.9	9	6.9	9	6.9	9	6.9	9	6.9
TC2	0									113	86.9
	4	5	3.8	5	3.8	5	3.8	5	3.8	5	3.8
TC3	0									105	80.8
	4	7	5.4	7	5.4	7	5.4	7	5.4	7	5.4

RC = Reference Cycle, TC = Treatment Cycle
+ Total number of subjects with missing Mean Luteal Phase VAS symptom scores

Table 13.48

Number (%) of Subjects with Missing Mean Luteal Phase VAS Scores for the Core PMDD Symptoms
Intention-to-Treat Population

----- Treatment Group=Placebo (N=120) -----

Cycle	Items Missing	Affective Lability		Depressed Mood		Luteal Phase VAS Items Irritability		Tension		Total+	
		n	%	n	%	n	%	n	%	n	%
RC1	0									120	100.0
RC1A	0									31	25.8
	4	1	0.8	1	0.8	1	0.8	1	0.8	1	0.8
Baseline	0									118	98.3
	1							1	0.8	1	0.8
	4	1	0.8	1	0.8	1	0.8	1	0.8	1	0.8
TC1	0									116	96.7
	1					2	1.7			2	1.7
	4	2	1.7	2	1.7	2	1.7	2	1.7	2	1.7
TC2	0									109	90.8
	4	8	6.7	8	6.7	8	6.7	8	6.7	8	6.7
TC3	0									104	86.7
	1	1	0.8							1	0.8
	4	1	0.8	1	0.8	1	0.8	1	0.8	1	0.8

RC = Reference Cycle, TC = Treatment Cycle
+ Total number of subjects with missing Mean Luteal Phase VAS symptom scores

Table 13.49

Number (%) of Subjects with Missing Daily Luteal Phase VAS Scores for the Core PMDD Symptoms
Intention-to-Treat Population

----- Treatment Group=Paroxetine CR 25 mg (N=116) -----

Cycle	Days Missing	Luteal Phase VAS Items							
		Affective n	Lability %	Depressed n	Mood %	Irritability n		Tension n	%
RC1	1	5	4.3	4	3.4	5	4.3	5	4.3
RC1A	1	1	0.9	1	0.9	1	0.9	1	0.9
Baseline	1	5	4.3	5	4.3	3	2.6	5	4.3
	2					1	0.9		
TC1	1	3	2.6	3	2.6	5	4.3	3	2.6
	3	1	0.9	1	0.9	1	0.9	1	0.9
	5	2	1.7	2	1.7	2	1.7	2	1.7
TC2	1	6	5.2	5	4.3	7	6.0	6	5.2
	2	1	0.9	1	0.9	1	0.9	2	1.7
TC3	1	2	1.7	2	1.7	3	2.6	2	1.7

RC = Reference Cycle, TC = Treatment Cycle

Table 13.49

Number (%) of Subjects with Missing Daily Luteal Phase VAS Scores for the Core PMDD Symptoms
Intention-to-Treat Population

----- Treatment Group=Paroxetine CR 12.5 mg (N=130) -----

Cycle	Days Missing	Luteal Phase VAS Items							
		Affective n	Lability %	Depressed n	Mood %	Irritability n		Tension n	%
RC1	1	2	1.5	2	1.5	3	2.3	4	3.1
Baseline	1	5	3.8	3	2.3	6	4.6	7	5.4
TC1	1	1	0.8			1	0.8	1	0.8
	2	1	0.8	1	0.8	1	0.8	1	0.8
TC2	1	4	3.1	4	3.1	3	2.3	3	2.3
TC3	1	5	3.8	3	2.3	4	3.1	5	3.8
	2	1	0.8	1	0.8	1	0.8	1	0.8

RC = Reference Cycle, TC = Treatment Cycle

Table 13.49

Number (%) of Subjects with Missing Daily Luteal Phase VAS Scores for the Core PMDD Symptoms
Intention-to-Treat Population

----- Treatment Group=Placebo (N=120) -----

Cycle	Days Missing	Luteal Phase VAS Items							
		Affective n	Lability %	Depressed n	Mood %	Irritability n	%	Tension n	%
RC1	1	6	5.0	8	6.7	5	4.2	6	5.0
RC1A	1	2	1.7	2	1.7	3	2.5	2	1.7
Baseline	1	5	4.2	5	4.2	5	4.2	3	2.5
	2							1	0.8
TC1	1	6	5.0	5	4.2	7	5.8	6	5.0
	2	1	0.8	1	0.8	2	1.7	1	0.8
TC2	1	4	3.3	3	2.5	4	3.3	3	2.5
	2	1	0.8	1	0.8	1	0.8	1	0.8
	3	1	0.8	1	0.8	1	0.8	1	0.8
TC3	1	13	10.8	11	9.2	11	9.2	11	9.2
	2	1	0.8						

RC = Reference Cycle, TC = Treatment Cycle

14. DATA SOURCE TABLES: QUALITY OF LIFE

	Page
Table 14.1 Summary of Adjusted Change from Baseline in EQ-5D Visual Analogue Scale Adjusted for Centre Group, Baseline Score, Age and Employment Status Intention-to-Treat Population	451
Table 14.2 Summary of Analysis for Change from Baseline in EQ-5D Visual Analogue Scale Adjusted for Centre Group, Baseline Score, Age and Employment Status Intention-to-Treat Population	452
Table 14.3 Summary Statistics for Baseline and Change from Baseline in EQ-5D Visual Analogue Scale Intention-to-Treat Population	453
Table 14.4 Number (%) of Subjects in Each Category of EQ-5D Health Profile Intention-to-Treat Population	454
Table 14.5 Summary Statistics for Baseline, Treatment Cycle 3 and Change from Baseline for EQ-5D Utility Score Intention-to-Treat Population	458
Table 14.6 Number (%) of Subjects in Each Category of the ISCO-88 Intention-to-Treat Population.	459
Table 14.7 Number (%) of Subjects in Each Category of the WPAI Employed/Unemployed Question Intention-to-Treat Population.	460
Table 14.8 Summary Statistics for the Number of Hours Missed from Work for Health Reasons (from the WPAI) Intention-to-Treat Population	461
Table 14.9 Summary Statistics for the Number of Hours Missed from Work for Other Reasons (from the WPAI) Intention-to-Treat Population	462
Table 14.10 Summary Statistics for the Number of Hours Worked (from the WPAI) Intention-to-Treat Population	463
Table 14.11 Number (%) of Subjects with Health Problems Affecting Productivity While Working Categorised by Response (from the WPAI) Intention-to-Treat Population.	464
Table 14.12 Number (%) of Subjects with Health Problems Affecting Regular Daily Activities Categorised by Response (from the WPAI) Intention-to-Treat Population.	466

Table 14.1

Summary of Adjusted Change from Baseline in EQ-5D Visual Analogue Scale
Adjusted for Centre Group, Baseline Score, Age and Employment Status
Intention-to-Treat Population

Change from Baseline to:	Treatment Comparison (Group 1 vs Group 2)	-----Pairwise Comparisons-----				
		Number Used In Analysis	Adjusted Mean for Group 1	s.e. of Adjusted Mean for Group 1	Adjusted Mean for Group 2	s.e. of Adjusted Mean for Group 2
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	191	23.64	3.21	16.74	3.06
	Paroxetine CR 12.5 mg vs Placebo	191	20.32	2.98	16.74	3.06
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	272	21.64	2.95	13.33	2.77
	Paroxetine CR 12.5 mg vs Placebo	272	17.19	2.73	13.33	2.77

Table 14.2

Summary of Analysis for Change from Baseline in EQ-5D Visual Analogue Scale
Adjusted for Centre Group, Baseline Score, Age and Employment Status
Intention-to-Treat Population

		-----Pairwise Comparisons-----		
Change from Baseline to:	Treatment Comparison	Treatment Difference*	95% CI for Treatment Difference	p-value for Treatment Difference
Treatment Cycle 3 OC	Paroxetine CR 25 mg vs Placebo	6.91	[-0.96, 14.77]	0.085
	Paroxetine CR 12.5 mg vs Placebo	3.58	[-3.76, 10.92]	0.337
Treatment Cycle 3 LOCF Endpoint	Paroxetine CR 25 mg vs Placebo	8.31	[1.19, 15.43]	0.022
	Paroxetine CR 12.5 mg vs Placebo	3.86	[-2.80, 10.52]	0.254

* Difference in adjusted least square means are shown

Table 14.3

Summary Statistics for Baseline and Change from Baseline in EQ-5D Visual Analogue Scale
Intention-to-Treat Population

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	86	110	102
	MEAN	54.1	52.2	54.2
	STD	31.59	30.35	30.77
	MEDIAN	65.0	42.0	50.0
	MINIMUM	0	0	2
	MAXIMUM	100	100	100
Treatment Cycle 1	N	71	88	92
	MEAN	20.3	17.8	13.2
	STD	31.10	35.09	31.49
	MEDIAN	10.0	10.5	5.0
	MINIMUM	-75	-99	-75
	MAXIMUM	85	90	80
Treatment Cycle 2	N	54	75	76
	MEAN	19.4	23.8	12.0
	STD	34.46	29.96	32.37
	MEDIAN	10.0	11.0	5.0
	MINIMUM	-81	-40	-85
	MAXIMUM	91	98	83
Treatment Cycle 3	N	54	69	69
	MEAN	22.0	22.9	20.7
	STD	32.88	30.59	32.66
	MEDIAN	10.0	20.0	15.0
	MINIMUM	-37	-71	-71
	MAXIMUM	95	80	95

Table 14.4

Number (%) of Subjects in Each Category of EQ-5D Health Profile
Intention-to-Treat Population

Visit: Baseline

Category	Question	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	TOTAL	86 (74.1%)	111 (85.4%)	104 (86.7%)	301 (82.2%)	
Anxiety/Depression	TOTAL	86 (74.1%)	111 (85.4%)	104 (86.7%)	301 (82.2%)	
	I am extremely anxious or depressed	14 (12.1%)	23 (17.7%)	18 (15.0%)	55 (15.0%)	
	I am moderately anxious or depressed	36 (31.0%)	50 (38.5%)	45 (37.5%)	131 (35.8%)	
	I am not anxious or depressed	36 (31.0%)	38 (29.2%)	41 (34.2%)	115 (31.4%)	
Mobility	TOTAL	86 (74.1%)	111 (85.4%)	104 (86.7%)	301 (82.2%)	
	I am confined to bed	2 (1.7%)	0 (0.0%)	0 (0.0%)	2 (0.5%)	
	I have no problems in walking about	75 (64.7%)	102 (78.5%)	90 (75.0%)	267 (73.0%)	
	I have some problems in walking about	9 (7.8%)	9 (6.9%)	14 (11.7%)	32 (8.7%)	
Pain/Discomfort	TOTAL	84 (72.4%)	111 (85.4%)	104 (86.7%)	299 (81.7%)	
	I have extreme pain or discomfort	8 (6.9%)	15 (11.5%)	14 (11.7%)	37 (10.1%)	
	I have moderate pain or discomfort	38 (32.8%)	57 (43.8%)	45 (37.5%)	140 (38.3%)	
	I have no pain or discomfort	38 (32.8%)	39 (30.0%)	45 (37.5%)	122 (33.3%)	
Self-Care	TOTAL	86 (74.1%)	111 (85.4%)	104 (86.7%)	301 (82.2%)	
	I have no problems with self-care	83 (71.6%)	110 (84.6%)	100 (83.3%)	293 (80.1%)	
	I have some problems washing or dressing myself	3 (2.6%)	1 (0.8%)	4 (3.3%)	8 (2.2%)	
Usual Activities	TOTAL	86 (74.1%)	111 (85.4%)	104 (86.7%)	301 (82.2%)	
	I am unable to perform my usual activities	3 (2.6%)	3 (2.3%)	1 (0.8%)	7 (1.9%)	
	I have no problems with performing my usual activities	55 (47.4%)	65 (50.0%)	64 (53.3%)	184 (50.3%)	
	I have some problems with performing my usual activities	28 (24.1%)	43 (33.1%)	39 (32.5%)	110 (30.1%)	

Only questions with a response within a category are included

Table 14.4

Number (%) of Subjects in Each Category of EQ-5D Health Profile
Intention-to-Treat Population

Visit: Treatment Cycle 1

Category	Question	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	TOTAL	91 (78.4%)	100 (76.9%)	104 (86.7%)	295 (80.6%)	
Anxiety/Depression	TOTAL	91 (78.4%)	100 (76.9%)	104 (86.7%)	295 (80.6%)	
	I am extremely anxious or depressed	7 (6.0%)	1 (0.8%)	7 (5.8%)	15 (4.1%)	
	I am moderately anxious or depressed	15 (12.9%)	28 (21.5%)	36 (30.0%)	79 (21.6%)	
	I am not anxious or depressed	69 (59.5%)	71 (54.6%)	61 (50.8%)	201 (54.9%)	
Mobility	TOTAL	90 (77.6%)	99 (76.2%)	104 (86.7%)	293 (80.1%)	
	I have no problems in walking about	85 (73.3%)	94 (72.3%)	95 (79.2%)	274 (74.9%)	
	I have some problems in walking about	5 (4.3%)	5 (3.8%)	9 (7.5%)	19 (5.2%)	
Pain/Discomfort	TOTAL	91 (78.4%)	100 (76.9%)	104 (86.7%)	295 (80.6%)	
	I have extreme pain or discomfort	3 (2.6%)	3 (2.3%)	7 (5.8%)	13 (3.6%)	
	I have moderate pain or discomfort	29 (25.0%)	35 (26.9%)	51 (42.5%)	115 (31.4%)	
	I have no pain or discomfort	59 (50.9%)	62 (47.7%)	46 (38.3%)	167 (45.6%)	
Self-Care	TOTAL	91 (78.4%)	99 (76.2%)	104 (86.7%)	294 (80.3%)	
	I have no problems with self-care	90 (77.6%)	98 (75.4%)	101 (84.2%)	289 (79.0%)	
	I have some problems washing or dressing myself	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)	
Usual Activities	TOTAL	91 (78.4%)	100 (76.9%)	104 (86.7%)	295 (80.6%)	
	I am unable to perform my usual activities	2 (1.7%)	2 (1.5%)	2 (1.7%)	6 (1.6%)	
	I have no problems with performing my usual activities	69 (59.5%)	81 (62.3%)	81 (67.5%)	231 (63.1%)	
	I have some problems with performing my usual activities	20 (17.2%)	17 (13.1%)	21 (17.5%)	58 (15.8%)	

Only questions with a response within a category are included

Table 14.4

Number (%) of Subjects in Each Category of EQ-5D Health Profile
Intention-to-Treat Population

Visit: Treatment Cycle 2

Category	Question	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
TOTAL	TOTAL	70 (60.3%)	84 (64.6%)	88 (73.3%)	242 (66.1%)
Anxiety/Depression	TOTAL	69 (59.5%)	84 (64.6%)	88 (73.3%)	241 (65.8%)
	I am extremely anxious or depressed	4 (3.4%)	1 (0.8%)	8 (6.7%)	13 (3.6%)
	I am moderately anxious or depressed	15 (12.9%)	26 (20.0%)	28 (23.3%)	69 (18.9%)
	I am not anxious or depressed	50 (43.1%)	57 (43.8%)	52 (43.3%)	159 (43.4%)
Mobility	TOTAL	69 (59.5%)	84 (64.6%)	88 (73.3%)	241 (65.8%)
	I have no problems in walking about	64 (55.2%)	79 (60.8%)	82 (68.3%)	225 (61.5%)
	I have some problems in walking about	5 (4.3%)	5 (3.8%)	6 (5.0%)	16 (4.4%)
Pain/Discomfort	TOTAL	69 (59.5%)	84 (64.6%)	88 (73.3%)	241 (65.8%)
	I have extreme pain or discomfort	4 (3.4%)	2 (1.5%)	5 (4.2%)	11 (3.0%)
	I have moderate pain or discomfort	22 (19.0%)	35 (26.9%)	37 (30.8%)	94 (25.7%)
	I have no pain or discomfort	43 (37.1%)	47 (36.2%)	46 (38.3%)	136 (37.2%)
Self-Care	TOTAL	70 (60.3%)	84 (64.6%)	88 (73.3%)	242 (66.1%)
	I have no problems with self-care	69 (59.5%)	83 (63.8%)	85 (70.8%)	237 (64.8%)
	I have some problems washing or dressing myself	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)
Usual Activities	TOTAL	70 (60.3%)	84 (64.6%)	88 (73.3%)	242 (66.1%)
	I am unable to perform my usual activities	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)
	I have no problems with performing my usual activities	53 (45.7%)	69 (53.1%)	71 (59.2%)	193 (52.7%)
	I have some problems with performing my usual activities	15 (12.9%)	14 (10.8%)	16 (13.3%)	45 (12.3%)

Only questions with a response within a category are included

Table 14.4

Number (%) of Subjects in Each Category of EQ-5D Health Profile
Intention-to-Treat Population

Visit: Treatment Cycle 3

Category	Question	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
TOTAL	TOTAL	75 (64.7%)	77 (59.2%)	81 (67.5%)	233 (63.7%)	
Anxiety/Depression	TOTAL	75 (64.7%)	76 (58.5%)	80 (66.7%)	231 (63.1%)	
	I am extremely anxious or depressed	4 (3.4%)	1 (0.8%)	5 (4.2%)	10 (2.7%)	
	I am moderately anxious or depressed	15 (12.9%)	19 (14.6%)	25 (20.8%)	59 (16.1%)	
	I am not anxious or depressed	56 (48.3%)	56 (43.1%)	50 (41.7%)	162 (44.3%)	
Mobility	TOTAL	75 (64.7%)	77 (59.2%)	81 (67.5%)	233 (63.7%)	
	I have no problems in walking about	71 (61.2%)	71 (54.6%)	73 (60.8%)	215 (58.7%)	
	I have some problems in walking about	4 (3.4%)	6 (4.6%)	8 (6.7%)	18 (4.9%)	
Pain/Discomfort	TOTAL	75 (64.7%)	76 (58.5%)	81 (67.5%)	232 (63.4%)	
	I have extreme pain or discomfort	2 (1.7%)	1 (0.8%)	2 (1.7%)	5 (1.4%)	
	I have moderate pain or discomfort	23 (19.8%)	32 (24.6%)	38 (31.7%)	93 (25.4%)	
	I have no pain or discomfort	50 (43.1%)	43 (33.1%)	41 (34.2%)	134 (36.6%)	
Self-Care	TOTAL	75 (64.7%)	77 (59.2%)	81 (67.5%)	233 (63.7%)	
	I am unable to wash or dress myself	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	I have no problems with self-care	73 (62.9%)	76 (58.5%)	78 (65.0%)	227 (62.0%)	
	I have some problems washing or dressing myself	1 (0.9%)	1 (0.8%)	3 (2.5%)	5 (1.4%)	
Usual Activities	TOTAL	74 (63.8%)	76 (58.5%)	81 (67.5%)	231 (63.1%)	
	I am unable to perform my usual activities	2 (1.7%)	1 (0.8%)	1 (0.8%)	4 (1.1%)	
	I have no problems with performing my usual activities	62 (53.4%)	61 (46.9%)	58 (48.3%)	181 (49.5%)	
	I have some problems with performing my usual activities	10 (8.6%)	14 (10.8%)	22 (18.3%)	46 (12.6%)	

Only questions with a response within a category are included

Table 14.5

Summary Statistics for Baseline, Treatment Cycle 3 and Change from Baseline for EQ-5D Utility Score
Intention-to-Treat Population

Visit	Statistic	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Baseline	N	84	111	104
	MEAN	0.693	0.650	0.670
	STD	0.324	0.323	0.328
	MEDIAN	0.796	0.689	0.725
	MINIMUM	-0.221	-0.077	-0.181
	MAXIMUM	1.000	1.000	1.000
Treatment Cycle 3	N	74	76	80
	MEAN	0.848	0.859	0.805
	STD	0.238	0.173	0.225
	MEDIAN	1.000	0.848	0.796
	MINIMUM	-0.066	0.101	0.030
	MAXIMUM	1.000	1.000	1.000
Change from Baseline	N	53	69	69
	MEAN	0.179	0.195	0.163
	STD	0.331	0.304	0.303
	MEDIAN	0.152	0.107	0.036
	MINIMUM	-0.564	-0.624	-0.590
	MAXIMUM	1.221	0.843	0.972

Table 14.6

Number (%) of Subjects in Each Category of the ISCO-88
Intention-to-Treat Population

Occupation	Treatment Group			Total (N=366)
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Legislator, senior official or manager	4 (3.4%)	4 (3.1%)	3 (2.5%)	11 (3.0%)
Professional	28 (24.1%)	28 (21.5%)	33 (27.5%)	89 (24.3%)
Technician or associate professional	26 (22.4%)	36 (27.7%)	24 (20.0%)	86 (23.5%)
Clerk	19 (16.4%)	21 (16.2%)	30 (25.0%)	70 (19.1%)
Service/Shop/Sales worker	14 (12.1%)	18 (13.8%)	16 (13.3%)	48 (13.1%)
Skilled (agricultural/fishery)	1 (0.9%)	0 (0.0%)	3 (2.5%)	4 (1.1%)
Craft and related trades worker (e.g. miner, builder)	1 (0.9%)	2 (1.5%)	0 (0.0%)	3 (0.8%)
Machine operator/assembler	2 (1.7%)	5 (3.8%)	1 (0.8%)	8 (2.2%)
Military	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
Elementary occupation	1 (0.9%)	1 (0.8%)	0 (0.0%)	2 (0.5%)
Not applicable	20 (17.2%)	14 (10.8%)	10 (8.3%)	44 (12.0%)

Table 14.7

Number (%) of Subjects in Each Category of the WPAI Employed/Unemployed Question
Intention-to-Treat Population

Visit	Employment Status	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
TOTAL	TOTAL	110 (94.8%)	127 (97.7%)	120 (100.0%)	357 (97.5%)
Baseline	TOTAL	86 (100.0%)	110 (100.0%)	104 (100.0%)	300 (100.0%)
	Employed	70 (81.4%)	91 (82.7%)	90 (86.5%)	251 (83.7%)
	Unemployed	16 (18.6%)	19 (17.3%)	14 (13.5%)	49 (16.3%)
Treatment Cycle 1	TOTAL	91 (100.0%)	101 (100.0%)	105 (100.0%)	297 (100.0%)
	Employed	68 (74.7%)	83 (82.2%)	88 (83.8%)	239 (80.5%)
	Unemployed	23 (25.3%)	18 (17.8%)	17 (16.2%)	58 (19.5%)
Treatment Cycle 2	TOTAL	70 (100.0%)	85 (100.0%)	88 (100.0%)	243 (100.0%)
	Employed	54 (77.1%)	74 (87.1%)	76 (86.4%)	204 (84.0%)
	Unemployed	16 (22.9%)	11 (12.9%)	12 (13.6%)	39 (16.0%)
Treatment Cycle 3	TOTAL	74 (100.0%)	77 (100.0%)	80 (100.0%)	231 (100.0%)
	Employed	55 (74.3%)	62 (80.5%)	68 (85.0%)	185 (80.1%)
	Unemployed	19 (25.7%)	15 (19.5%)	12 (15.0%)	46 (19.9%)

Table 14.8

Summary Statistics for the Number of Hours Missed from Work for Health Reasons (from the WPAI)
Intention-to-Treat Population

Visit	Statistic	Paroxetine CR 25 mg (N=116)	Treatment Group Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	70	89	89
	MEAN	1.6	2.7	2.1
	STD	5.20	7.31	6.85
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	37	40	42
Treatment Cycle 1	N	65	83	86
	MEAN	3.1	1.4	3.0
	STD	10.02	5.55	9.86
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	56	38	76
Treatment Cycle 2	N	53	74	75
	MEAN	4.3	5.3	2.0
	STD	11.25	12.93	7.31
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	60	65	43
Treatment Cycle 3	N	54	61	68
	MEAN	1.8	2.4	3.5
	STD	7.07	6.18	9.44
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	40	30	40

Note: Time missed from work for health reasons does not include time missed from work to participate in the study

Table 14.9

Summary Statistics for the Number of Hours Missed from Work for Other Reasons (from the WPAI)
Intention-to-Treat Population

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	70	89	89
	MEAN	3.5	3.6	4.7
	STD	8.52	8.31	9.45
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	49	40	40
Treatment Cycle 1	N	65	83	85
	MEAN	3.1	5.6	3.2
	STD	9.39	11.75	8.36
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	48	42	40
Treatment Cycle 2	N	53	72	75
	MEAN	7.3	3.4	3.6
	STD	12.95	9.61	7.82
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	48	56	40
Treatment Cycle 3	N	54	61	66
	MEAN	4.4	5.1	6.5
	STD	10.79	10.46	11.86
	MEDIAN	0.0	0.0	0.0
	MINIMUM	0	0	0
	MAXIMUM	46	40	41

Note: Where no reply to employed/unemployed question hours missed from work not included in table

Table 14.10

Summary Statistics for the Number of Hours Worked (from the WPAI)
Intention-to-Treat Population

Visit	Statistic	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Baseline	N	69	89	90
	MEAN	28.1	28.8	27.6
	STD	15.31	15.76	15.86
	MEDIAN	30.0	32.0	30.0
	MINIMUM	0	0	0
	MAXIMUM	60	60	84
Treatment Cycle 1	N	66	82	87
	MEAN	26.3	29.7	30.9
	STD	16.23	16.68	14.44
	MEDIAN	28.5	35.0	35.0
	MINIMUM	0	0	0
	MAXIMUM	60	80	70
Treatment Cycle 2	N	53	74	74
	MEAN	24.3	30.2	27.7
	STD	16.65	14.58	15.81
	MEDIAN	25.0	32.0	34.0
	MINIMUM	0	0	0
	MAXIMUM	60	56	70
Treatment Cycle 3	N	55	62	67
	MEAN	28.1	28.5	26.3
	STD	15.30	15.59	17.27
	MEDIAN	30.0	31.5	32.0
	MINIMUM	0	0	0
	MAXIMUM	60	57	63

Note: Where no reply to employed/unemployed question hours worked not included in table

Table 14.11

Number (%) of Subjects with Health Problems Affecting Productivity While Working
Categorised by Response (from the WPAI)
Intention-to-Treat Population

Visit	Response	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Baseline	TOTAL	66 (56.9%)	87 (66.9%)	86 (71.7%)	239 (65.3%)
	0	7 (6.0%)	10 (7.7%)	10 (8.3%)	27 (7.4%)
	1	3 (2.6%)	4 (3.1%)	5 (4.2%)	12 (3.3%)
	2	6 (5.2%)	13 (10.0%)	14 (11.7%)	33 (9.0%)
	3	6 (5.2%)	10 (7.7%)	14 (11.7%)	30 (8.2%)
	4	6 (5.2%)	4 (3.1%)	5 (4.2%)	15 (4.1%)
	5	7 (6.0%)	9 (6.9%)	11 (9.2%)	27 (7.4%)
	6	10 (8.6%)	11 (8.5%)	10 (8.3%)	31 (8.5%)
	7	6 (5.2%)	16 (12.3%)	8 (6.7%)	30 (8.2%)
	8	11 (9.5%)	5 (3.8%)	7 (5.8%)	23 (6.3%)
	9	3 (2.6%)	2 (1.5%)	1 (0.8%)	6 (1.6%)
	10	1 (0.9%)	3 (2.3%)	1 (0.8%)	5 (1.4%)
Treatment Cycle 1	TOTAL	66 (56.9%)	80 (61.5%)	85 (70.8%)	231 (63.1%)
	0	19 (16.4%)	18 (13.8%)	19 (15.8%)	56 (15.3%)
	1	8 (6.9%)	18 (13.8%)	8 (6.7%)	34 (9.3%)
	2	6 (5.2%)	10 (7.7%)	24 (20.0%)	40 (10.9%)
	3	7 (6.0%)	14 (10.8%)	10 (8.3%)	31 (8.5%)
	4	4 (3.4%)	7 (5.4%)	5 (4.2%)	16 (4.4%)
	5	6 (5.2%)	6 (4.6%)	5 (4.2%)	17 (4.6%)
	6	5 (4.3%)	4 (3.1%)	4 (3.3%)	13 (3.6%)
	7	7 (6.0%)	1 (0.8%)	5 (4.2%)	13 (3.6%)
	8	1 (0.9%)	2 (1.5%)	2 (1.7%)	5 (1.4%)
	9	2 (1.7%)	0 (0.0%)	2 (1.7%)	4 (1.1%)
	10	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)
Treatment Cycle 2	TOTAL	52 (44.8%)	71 (54.6%)	73 (60.8%)	196 (53.6%)
	0	19 (16.4%)	18 (13.8%)	18 (15.0%)	55 (15.0%)
	1	6 (5.2%)	11 (8.5%)	13 (10.8%)	30 (8.2%)
	2	10 (8.6%)	11 (8.5%)	10 (8.3%)	31 (8.5%)
	3	1 (0.9%)	8 (6.2%)	5 (4.2%)	14 (3.8%)
	4	3 (2.6%)	7 (5.4%)	7 (5.8%)	17 (4.6%)
	5	4 (3.4%)	4 (3.1%)	8 (6.7%)	16 (4.4%)
	6	5 (4.3%)	2 (1.5%)	1 (0.8%)	8 (2.2%)
	7	2 (1.7%)	5 (3.8%)	4 (3.3%)	11 (3.0%)
	8	1 (0.9%)	3 (2.3%)	6 (5.0%)	10 (2.7%)
	9	1 (0.9%)	1 (0.8%)	1 (0.8%)	3 (0.8%)
	10	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
Treatment Cycle 3	TOTAL	53 (45.7%)	60 (46.2%)	63 (52.5%)	176 (48.1%)
	0	21 (18.1%)	14 (10.8%)	19 (15.8%)	54 (14.8%)
	1	7 (6.0%)	12 (9.2%)	9 (7.5%)	28 (7.7%)
	2	10 (8.6%)	14 (10.8%)	2 (1.7%)	26 (7.1%)

Response on a scale of 0-10. 0 - no effect on productivity, to 10 - Subject was completely prevented from working
Note: Where no reply to employed/unemployed question response not included in table

Table 14.11

Number (%) of Subjects with Health Problems Affecting Productivity While Working
Categorised by Response (from the WPAI)
Intention-to-Treat Population

Visit	Response	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
Treatment Cycle 3	3	2 (1.7%)	6 (4.6%)	6 (5.0%)	14 (3.8%)	
	4	1 (0.9%)	3 (2.3%)	6 (5.0%)	10 (2.7%)	
	5	1 (0.9%)	4 (3.1%)	5 (4.2%)	10 (2.7%)	
	6	2 (1.7%)	1 (0.8%)	5 (4.2%)	8 (2.2%)	
	7	5 (4.3%)	4 (3.1%)	5 (4.2%)	14 (3.8%)	
	8	2 (1.7%)	2 (1.5%)	5 (4.2%)	9 (2.5%)	
	9	1 (0.9%)	0 (0.0%)	1 (0.8%)	2 (0.5%)	
	10	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	

Response on a scale of 0-10. 0 - no effect on productivity, to 10 - Subject was completely prevented from working
Note: Where no reply to employed/unemployed question response not included in table

Table 14.12

Number (%) of Subjects with Health Problems Affecting Regular Daily Activities
Categorised by Response (from the WPAI)
Intention-to-Treat Population

Visit	Response	Treatment Group				Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)		
Baseline	TOTAL	86 (74.1%)	109 (83.8%)	104 (86.7%)	299 (81.7%)	
	0	5 (4.3%)	7 (5.4%)	4 (3.3%)	16 (4.4%)	
	1	1 (0.9%)	5 (3.8%)	9 (7.5%)	15 (4.1%)	
	2	5 (4.3%)	10 (7.7%)	5 (4.2%)	20 (5.5%)	
	3	6 (5.2%)	6 (4.6%)	8 (6.7%)	20 (5.5%)	
	4	7 (6.0%)	7 (5.4%)	10 (8.3%)	24 (6.6%)	
	5	8 (6.9%)	15 (11.5%)	9 (7.5%)	32 (8.7%)	
	6	8 (6.9%)	9 (6.9%)	13 (10.8%)	30 (8.2%)	
	7	20 (17.2%)	21 (16.2%)	15 (12.5%)	56 (15.3%)	
	8	16 (13.8%)	18 (13.8%)	21 (17.5%)	55 (15.0%)	
	9	6 (5.2%)	7 (5.4%)	10 (8.3%)	23 (6.3%)	
Treatment Cycle 1	10	4 (3.4%)	4 (3.1%)	0 (0.0%)	8 (2.2%)	
	TOTAL	88 (75.9%)	100 (76.9%)	105 (87.5%)	293 (80.1%)	
	0	22 (19.0%)	15 (11.5%)	13 (10.8%)	50 (13.7%)	
	1	7 (6.0%)	17 (13.1%)	13 (10.8%)	37 (10.1%)	
	2	11 (9.5%)	12 (9.2%)	14 (11.7%)	37 (10.1%)	
	3	8 (6.9%)	10 (7.7%)	14 (11.7%)	32 (8.7%)	
	4	8 (6.9%)	15 (11.5%)	9 (7.5%)	32 (8.7%)	
	5	10 (8.6%)	6 (4.6%)	5 (4.2%)	21 (5.7%)	
	6	2 (1.7%)	8 (6.2%)	11 (9.2%)	21 (5.7%)	
	7	10 (8.6%)	7 (5.4%)	11 (9.2%)	28 (7.7%)	
	8	5 (4.3%)	8 (6.2%)	9 (7.5%)	22 (6.0%)	
Treatment Cycle 2	9	5 (4.3%)	1 (0.8%)	4 (3.3%)	10 (2.7%)	
	10	0 (0.0%)	1 (0.8%)	2 (1.7%)	3 (0.8%)	
	TOTAL	70 (60.3%)	85 (65.4%)	88 (73.3%)	243 (66.4%)	
	0	17 (14.7%)	15 (11.5%)	12 (10.0%)	44 (12.0%)	
	1	9 (7.8%)	15 (11.5%)	11 (9.2%)	35 (9.6%)	
	2	11 (9.5%)	14 (10.8%)	12 (10.0%)	37 (10.1%)	
	3	5 (4.3%)	7 (5.4%)	12 (10.0%)	24 (6.6%)	
	4	3 (2.6%)	12 (9.2%)	5 (4.2%)	20 (5.5%)	
	5	8 (6.9%)	7 (5.4%)	13 (10.8%)	28 (7.7%)	
	6	2 (1.7%)	2 (1.5%)	5 (4.2%)	9 (2.5%)	
	7	5 (4.3%)	4 (3.1%)	5 (4.2%)	14 (3.8%)	
Treatment Cycle 3	8	7 (6.0%)	6 (4.6%)	10 (8.3%)	23 (6.3%)	
	9	2 (1.7%)	3 (2.3%)	3 (2.5%)	8 (2.2%)	
	10	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
	TOTAL	75 (64.7%)	77 (59.2%)	80 (66.7%)	232 (63.4%)	
	0	20 (17.2%)	16 (12.3%)	16 (13.3%)	52 (14.2%)	
	1	14 (12.1%)	10 (7.7%)	8 (6.7%)	32 (8.7%)	

Response on a scale of 0-10. 0 - no effect on regular daily activity, to 10 - Subject was completely prevented from carrying out regular daily activities

Table 14.12

Number (%) of Subjects with Health Problems Affecting Regular Daily Activities
Categorised by Response (from the WPAI)
Intention-to-Treat Population

Visit	Response	Treatment Group			Total (N=366)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	
Treatment Cycle 3	2	15 (12.9%)	18 (13.8%)	9 (7.5%)	42 (11.5%)
	3	5 (4.3%)	9 (6.9%)	9 (7.5%)	23 (6.3%)
	4	2 (1.7%)	5 (3.8%)	4 (3.3%)	11 (3.0%)
	5	3 (2.6%)	7 (5.4%)	9 (7.5%)	19 (5.2%)
	6	2 (1.7%)	4 (3.1%)	5 (4.2%)	11 (3.0%)
	7	8 (6.9%)	5 (3.8%)	7 (5.8%)	20 (5.5%)
	8	4 (3.4%)	3 (2.3%)	6 (5.0%)	13 (3.6%)
	9	0 (0.0%)	0 (0.0%)	6 (5.0%)	6 (1.6%)
	10	2 (1.7%)	0 (0.0%)	1 (0.8%)	3 (0.8%)

Response on a scale of 0-10. 0 - no effect on regular daily activity, to 10 - Subject was completely prevented from carrying out regular daily activities

15. DATA SOURCE TABLES: SAFETY RESULTS

	Page
Table 15.1 Number (%) of Subjects with Baseline Adverse Events By Body System and Preferred Term Screening Only Population	471
Table 15.2 Number (%) of Subjects with Baseline Adverse Events By Body System and Preferred Term Randomised (non-ITT) Population	473
Table 15.3 Number (%) of Subjects with Baseline Adverse Events By Body System and Preferred Term Intention-to-Treat Population	474
Table 15.4 Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase By Body System and Preferred Term Intention-to-Treat Population	476
Table 15.5 Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or more of the Population During the Treatment Phase In Descending Order Intention-to-Treat Population	480
Table 15.6 Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase By Body System and Preferred Term Intention-to-Treat Population (with Follow-up)	483
Table 15.7 Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or more of the Population During the Follow-up Phase In Descending Order Intention-to-Treat Population (with Follow-up)	485
Table 15.8 Number (%) of Subjects with Serious Adverse Events By Study Phase By Body System and Preferred Term Intention-to-Treat Population	486
Table 15.9 Number (%) of Subjects with Serious Adverse Events Occurring in 1% or more of the Population By Study Phase In Descending Order Intention-to-Treat Population	489
Table 15.10 Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity By Body System and Preferred Term Intention-to-Treat Population	492
Table 15.11 Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase By Severity in Descending Order Intention-to-Treat Population	501
Table 15.12 Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Severity By Body System and Preferred Term Intention-to-Treat Population (with Follow-up)	506
Table 15.13 Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Follow-up Phase By Severity in Descending Order Intention-to-Treat Population (with Follow-up)	510
Table 15.14 Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events During the Treatment Phase By Body System and Preferred Term Intention-to-Treat Population	513
Table 15.15 Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events Occurring in 1% or more of the Population During the Treatment Phase In Descending Order Intention-to-Treat Population	516

Table 15.16 Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events During the Follow-up Phase By Body System and Preferred Term Intention-to-Treat Population (with Follow-up)	518
Table 15.17 Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events Occurring in 1% or more of the Population During the Follow-up Phase In Descending Order Intention-to-Treat Population	519
Table 15.18 Number (%) of Subjects with Adverse Events Leading to Withdrawal from the Study By Body System and Preferred Term Intention-to-Treat Population	520
Table 15.19 Number (%) of Subjects with Adverse Events Leading to Withdrawal from Study Occurring in 1% or More of the Population During the Treatment Phase In Descending Order Intention-to-Treat Population	522
Table 15.20 Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence By Body System and Preferred Term Intention-to-Treat Population	523
Table 15.21 Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase By Time of First Occurrence In Descending Order Intention-to-Treat Population	531
Table 15.22 Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity By Body System and Preferred Term Intention-to-Treat Population	537
Table 15.23 Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Maximum Severity By Body System and Preferred Term Intention-to-Treat Population (with Follow-up).	546
Table 15.24 Summary Statistics For Baseline and Change from Baseline for Vital Signs by Visit Intention-to-Treat Population	550
Table 15.25 Number (%) of Subjects with Vital Signs of Potential Clinical Concern During the Treatment or Follow-up Phase Intention-to-Treat Population	553
Table 15.26 Number (%) of Subjects with Vital Sign Transitions from Baseline to Endpoint and/or Follow-up Intention-to-Treat Population	557
Table 15.27 Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase Intention-to-Treat Population	560
Table 15.29 Criteria for Clinical Concern Flagging of Laboratory Parameters	579
Table 15.30 Number (%) of Subjects with Transitions from Baseline to Endpoint By Laboratory Parameter Intention-to-Treat Population	580
Table 15.31 Number (%) of Subjects with Positive Serum Pregnancy Test Results During the Treatment or Follow-up Phase Intention-to-Treat Population	635
Table 15.33 Summary Statistics for Visit and Change from Baseline for Laboratory Parameters By Treatment Group and Visit Intention-to-Treat Population	636

Table 15.34 Number (%) of Subjects Exposed to Study Medication By Treatment Group and Time Intervals Intention-to-Treat Population	645
Table 15.35 Narrative Locator Table	646
Table 15.36 Narratives for Subjects with Serious Adverse Events	647
Table 15.37 Narratives for Subjects with Adverse Events Leading to Withdrawal from the Study	656
Table 15.38 Narratives for Subjects with Laboratory Values of Potential Clinical Concern	685
Supplementary Table 15.1 Number (%) of Subjects with Treatment Emergent Adverse Events Occurring in 5% or More of the Paroxetine CR Subjects and at Least Twice the Incidence of Placebo By Body System and Preferred Term	693
Supplementary Table 15.2 Number (%) of Subjects with Treatment Emergent Adverse Events by Selected Concomitant Medications Intention- to- Treat Population	694
Supplementary Table 15.3 Number (%) of Subjects with Treatment Emergent Adverse Events by Selected Active Conditions Intention- to- Treat Population	714
Supplementary Table 15.4 Comparative Summary of Treatment Emergent Adverse Events between North America and Europe By Body System and Preferred Term Intention- to- Treat Population	734
Supplementary Table 15.5 Comparative Summary of Treatment Emergent Adverse Events with PMDD CR Continuous Dosing By Body System and Preferred Term Intention- to- Treat Population	738
Supplementary Table 15.6 Comparative Summary of Follow- up Phase Emergent Adverse Events with PMDD CR Continuous Dosing By Body System and Preferred Term Intention- to- Treat Population (with Follow-Up)	743
Supplementary Table 15.7 Summary of Paroxetine CR Treatment Emergent Adverse Events Unique to Intermittent PMDD By Body System and Preferred Term Intention- to- Treat Population	746
Supplementary Table 15.8 Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods By Severity Intention- to- Treat Population	747

Table 15.1

Number (%) of Subjects with Baseline Adverse Events
By Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Total Number of Subjects (N=1242)	
TOTAL	TOTAL	96	(7.7%)
Body as a Whole	TOTAL	42	(3.4%)
	ABDOMINAL PAIN	6	(0.5%)
	ASTHENIA	6	(0.5%)
	BACK PAIN	2	(0.2%)
	HEADACHE	21	(1.7%)
	INFECTION	7	(0.6%)
	TRAUMA	2	(0.2%)
Cardiovascular System	TOTAL	3	(0.2%)
	HEMORRHAGE	1	(0.1%)
	MIGRAINE	2	(0.2%)
	PALPITATION	1	(0.1%)
Digestive System	TOTAL	20	(1.6%)
	CONSTIPATION	3	(0.2%)
	DECREASED APPETITE	1	(0.1%)
	DIARRHEA	4	(0.3%)
	DRY MOUTH	4	(0.3%)
	DYSPEPSIA	1	(0.1%)
	FLATULENCE	2	(0.2%)
	GASTROINTESTINAL DISORDER	1	(0.1%)
	INCREASED APPETITE	2	(0.2%)
	NAUSEA	5	(0.4%)
	TOOTH CARIES	1	(0.1%)
Metabolic and Nutritional Disorders	TOTAL	1	(0.1%)
	BILIRUBINEMIA	1	(0.1%)
Musculoskeletal System	TOTAL	3	(0.2%)
	BURSITIS	1	(0.1%)
	MYALGIA	2	(0.2%)
Nervous System	TOTAL	10	(0.8%)
	ANXIETY	1	(0.1%)
	CONCENTRATION IMPAIRED	1	(0.1%)
	DEPRESSION	1	(0.1%)
	DIZZINESS	2	(0.2%)
	INSOMNIA	3	(0.2%)

Screening only population contains both screening failures and placebo run-in failures

Total Number of Subjects 1242

Total Number of Subjects with AEs 96

Table 15.1

Number (%) of Subjects with Baseline Adverse Events
By Body System and Preferred Term
Screening Only Population

Body System	Preferred Term	Total Number of Subjects (N=1242)	
Nervous System	LIBIDO DECREASED	1	(0.1%)
	NERVOUSNESS	1	(0.1%)
	NEURALGIA	1	(0.1%)
	PARESTHESIA	1	(0.1%)
	SOMNOLENCE	1	(0.1%)
	THINKING ABNORMAL	1	(0.1%)
Respiratory System	TOTAL	23	(1.9%)
	BRONCHITIS	2	(0.2%)
	COUGH INCREASED	1	(0.1%)
	HYPERVENTILATION	1	(0.1%)
	PHARYNGITIS	2	(0.2%)
	PNEUMONIA	3	(0.2%)
	RESPIRATORY DISORDER	13	(1.0%)
	SINUSITIS	2	(0.2%)
Skin and Appendages	TOTAL	6	(0.5%)
	ACNE	1	(0.1%)
	HERPES SIMPLEX	1	(0.1%)
	NAIL DISORDER	1	(0.1%)
	PRURITUS	2	(0.2%)
	SWEATING	1	(0.1%)
Special Senses	TOTAL	3	(0.2%)
	ABNORMAL VISION	2	(0.2%)
	OTITIS MEDIA	1	(0.1%)
Urogenital System	TOTAL	10	(0.8%)
	AMENORRHEA	2	(0.2%)
	DYSMENORRHEA	6	(0.5%)
	PYELONEPHRITIS	1	(0.1%)
	UNINTENDED PREGNANCY	1	(0.1%)

Screening only population contains both screening failures and placebo run-in failures
Total Number of Subjects 1242
Total Number of Subjects with AEs 96

Table 15.2

Number (%) of Subjects with Baseline Adverse Events
By Body System and Preferred Term
Randomised (non-ITT) Population

Body System	Preferred Term	Total Number of Subjects (N=7)

TOTAL	TOTAL	3 (42.9%)
Body as a Whole	TOTAL	1 (14.3%)
	ABDOMINAL PAIN	1 (14.3%)
Digestive System	TOTAL	1 (14.3%)
	FLATULENCE	1 (14.3%)
	NAUSEA	1 (14.3%)
Nervous System	TOTAL	2 (28.6%)
	INSOMNIA	1 (14.3%)
	NEURALGIA	1 (14.3%)
Urogenital System	TOTAL	1 (14.3%)
	DYSMENORRHEA	1 (14.3%)

Onset date prior to start of randomised study medication
Total Number of Subjects 7
Total Number of Subjects with AEs 3

Table 15.3

Number (%) of Subjects with Baseline Adverse Events
By Body System and Preferred Term
Intention-to-Treat Population

		Total Number of Subjects (N=366)	
Body System	Preferred Term		

TOTAL	TOTAL	96	(26.2%)
Body as a Whole	TOTAL	51	(13.9%)
	ABDOMINAL PAIN	5	(1.4%)
	ALLERGIC REACTION	1	(0.3%)
	ASTHENIA	4	(1.1%)
	BACK PAIN	1	(0.3%)
	FEVER	1	(0.3%)
	FLU SYNDROME	1	(0.3%)
	HEADACHE	25	(6.8%)
	INFECTION	14	(3.8%)
	MONILIASIS	1	(0.3%)
	PAIN	3	(0.8%)
	TRAUMA	2	(0.5%)
Cardiovascular System	TOTAL	4	(1.1%)
	ARRHYTHMIA	1	(0.3%)
	HYPERTENSION	1	(0.3%)
	MIGRAINE	2	(0.5%)
Digestive System	TOTAL	15	(4.1%)
	CONSTIPATION	1	(0.3%)
	DIARRHEA	3	(0.8%)
	DRY MOUTH	1	(0.3%)
	DYSPEPSIA	2	(0.5%)
	GASTROENTERITIS	2	(0.5%)
	GINGIVITIS	1	(0.3%)
	NAUSEA	6	(1.6%)
Endocrine System	VOMITING	1	(0.3%)
	TOTAL	1	(0.3%)
Hemic and Lymphatic System	OVARY DISORDER	1	(0.3%)
	TOTAL	1	(0.3%)
Metabolic and Nutritional Disorders	ANEMIA	1	(0.3%)
	TOTAL	1	(0.3%)
	WEIGHT LOSS	1	(0.3%)

Onset date prior to start of randomised study medication
Total Number of Subjects 366
Total Number of Subjects with AEs 96

Table 15.3

Number (%) of Subjects with Baseline Adverse Events
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Total Number of Subjects (N=366)	
Musculoskeletal System	TOTAL	3	(0.8%)
	ARTHRALGIA	2	(0.5%)
	MYALGIA	1	(0.3%)
Nervous System	TOTAL	12	(3.3%)
	AGITATION	1	(0.3%)
	AMNESIA	1	(0.3%)
	CONFUSION	1	(0.3%)
	DIZZINESS	3	(0.8%)
	HYPERKINESIA	2	(0.5%)
	HYPERTONIA	1	(0.3%)
	INSOMNIA	5	(1.4%)
	NEUROVASCULAR COMPRESSION	1	(0.3%)
	SOMNOLENCE	1	(0.3%)
Respiratory System	TOTAL	22	(6.0%)
	BRONCHITIS	2	(0.5%)
	COUGH INCREASED	1	(0.3%)
	PHARYNGITIS	2	(0.5%)
	RESPIRATORY DISORDER	12	(3.3%)
	RHINITIS	1	(0.3%)
	SINUSITIS	5	(1.4%)
Skin and Appendages	TOTAL	2	(0.5%)
	ACNE	1	(0.3%)
	SWEATING	1	(0.3%)
Special Senses	TOTAL	3	(0.8%)
	EAR PAIN	2	(0.5%)
	EYE DISORDER	1	(0.3%)
Urogenital System	TOTAL	15	(4.1%)
	BREAST PAIN	1	(0.3%)
	DYSMENORRHEA	8	(2.2%)
	MENORRHAGIA	1	(0.3%)
	MENSTRUAL DISORDER	1	(0.3%)
	UNINTENDED PREGNANCY	1	(0.3%)
	VAGINAL MONILIASIS	3	(0.8%)

Onset date prior to start of randomised study medication
Total Number of Subjects 366
Total Number of Subjects with AEs 96

Table 15.4

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	89 (76.7%)	88 (67.7%)	68 (56.7%)
Body as a Whole	TOTAL	50 (43.1%)	42 (32.3%)	37 (30.8%)
	ABDOMINAL PAIN	4 (3.4%)	4 (3.1%)	0 (0.0%)
	ALLERGIC REACTION	1 (0.9%)	2 (1.5%)	3 (2.5%)
	ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ASTHENIA	22 (19.0%)	16 (12.3%)	5 (4.2%)
	BACK PAIN	2 (1.7%)	4 (3.1%)	5 (4.2%)
	CHEST PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CHILLS	1 (0.9%)	1 (0.8%)	0 (0.0%)
	FEVER	2 (1.7%)	0 (0.0%)	1 (0.8%)
	FLU SYNDROME	1 (0.9%)	1 (0.8%)	0 (0.0%)
	HEADACHE	18 (15.5%)	16 (12.3%)	17 (14.2%)
	INFECTION	10 (8.6%)	5 (3.8%)	8 (6.7%)
	MONILIASIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NEOPLASM	1 (0.9%)	1 (0.8%)	0 (0.0%)
	PAIN	2 (1.7%)	2 (1.5%)	2 (1.7%)
	SHOCK	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TRAUMA	2 (1.7%)	3 (2.3%)	4 (3.3%)
Cardiovascular System	TOTAL	3 (2.6%)	7 (5.4%)	4 (3.3%)
	ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	HAEMATOMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MIGRAINE	0 (0.0%)	1 (0.8%)	3 (2.5%)
	MYOCARDIAL INFARCT	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PALPITATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	POSTURAL HYPOTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PULMONARY EMBOLUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VASCULAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	VASODILATATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Digestive System	TOTAL	43 (37.1%)	33 (25.4%)	11 (9.2%)
	COLITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	CONSTIPATION	3 (2.6%)	1 (0.8%)	1 (0.8%)
	DECREASED APPETITE	4 (3.4%)	1 (0.8%)	0 (0.0%)
	DIARRHEA	8 (6.9%)	7 (5.4%)	0 (0.0%)
	DRY MOUTH	3 (2.6%)	3 (2.3%)	1 (0.8%)
	DYSPEPSIA	3 (2.6%)	2 (1.5%)	2 (1.7%)
	DYSPHAGIA	0 (0.0%)	2 (1.5%)	0 (0.0%)
	FLATULENCE	0 (0.0%)	1 (0.8%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.4

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Digestive System	GASTRITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GASTROENTERITIS	1 (0.9%)	1 (0.8%)	0 (0.0%)
	GASTROINTESTINAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)
	GINGIVITIS	2 (1.7%)	1 (0.8%)	0 (0.0%)
	INCREASED APPETITE	1 (0.9%)	0 (0.0%)	1 (0.8%)
	NAUSEA	27 (23.3%)	16 (12.3%)	2 (1.7%)
	TOOTH DISORDER	1 (0.9%)	1 (0.8%)	2 (1.7%)
	VOMITING	1 (0.9%)	1 (0.8%)	1 (0.8%)
Endocrine System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	OVARY DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)
	ANEMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	LYMPHADENOPATHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
Metabolic and Nutritional Disorders	TOTAL	4 (3.4%)	3 (2.3%)	3 (2.5%)
	EDEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	GENERALIZED EDEMA	1 (0.9%)	2 (1.5%)	1 (0.8%)
	THIRST	0 (0.0%)	0 (0.0%)	1 (0.8%)
	WEIGHT GAIN	3 (2.6%)	0 (0.0%)	1 (0.8%)
	TOTAL	2 (1.7%)	3 (2.3%)	7 (5.8%)
Musculoskeletal System	ARTHRALGIA	1 (0.9%)	1 (0.8%)	2 (1.7%)
	MYALGIA	1 (0.9%)	2 (1.5%)	3 (2.5%)
	TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	2 (1.7%)
	TOTAL	37 (31.9%)	38 (29.2%)	17 (14.2%)
Nervous System	ABNORMAL DREAMS	1 (0.9%)	1 (0.8%)	0 (0.0%)
	ALCOHOL ABUSE	1 (0.9%)	0 (0.0%)	0 (0.0%)
	AMNESIA	3 (2.6%)	0 (0.0%)	0 (0.0%)
	ANXIETY	2 (1.7%)	2 (1.5%)	3 (2.5%)
	CONCENTRATION IMPAIRED	1 (0.9%)	2 (1.5%)	0 (0.0%)
	CONFUSION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DEPRESSION	2 (1.7%)	3 (2.3%)	1 (0.8%)
	DIZZINESS	8 (6.9%)	7 (5.4%)	3 (2.5%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HYPESTHESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
	INCOORDINATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	4 (3.4%)	13 (10.0%)	3 (2.5%)
	TOTAL	37 (31.9%)	38 (29.2%)	17 (14.2%)
	ABNORMAL DREAMS	1 (0.9%)	1 (0.8%)	0 (0.0%)
	ALCOHOL ABUSE	1 (0.9%)	0 (0.0%)	0 (0.0%)
	AMNESIA	3 (2.6%)	0 (0.0%)	0 (0.0%)
	ANXIETY	2 (1.7%)	2 (1.5%)	3 (2.5%)
	CONCENTRATION IMPAIRED	1 (0.9%)	2 (1.5%)	0 (0.0%)
	CONFUSION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DEPRESSION	2 (1.7%)	3 (2.3%)	1 (0.8%)
	DIZZINESS	8 (6.9%)	7 (5.4%)	3 (2.5%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HYPESTHESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
	INCOORDINATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	4 (3.4%)	13 (10.0%)	3 (2.5%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.4

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Nervous System	LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	15 (12.9%)	7 (5.4%)	7 (5.8%)
	MYOCLONUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NERVOUSNESS	1 (0.9%)	6 (4.6%)	2 (1.7%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	SOMNOLENCE	5 (4.3%)	3 (2.3%)	1 (0.8%)
	THINKING ABNORMAL	1 (0.9%)	1 (0.8%)	0 (0.0%)
	TREMOR	7 (6.0%)	4 (3.1%)	0 (0.0%)
	VERTIGO	2 (1.7%)	3 (2.3%)	1 (0.8%)
Respiratory System	TOTAL	13 (11.2%)	20 (15.4%)	18 (15.0%)
	ASTHMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BRONCHITIS	1 (0.9%)	3 (2.3%)	0 (0.0%)
	COUGH INCREASED	0 (0.0%)	0 (0.0%)	2 (1.7%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	PHARYNGITIS	3 (2.6%)	0 (0.0%)	5 (4.2%)
	PNEUMONIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	5 (4.3%)	9 (6.9%)	13 (10.8%)
	SINUSITIS	3 (2.6%)	7 (5.4%)	2 (1.7%)
	YAWN	0 (0.0%)	2 (1.5%)	0 (0.0%)
Skin and Appendages	TOTAL	12 (10.3%)	10 (7.7%)	9 (7.5%)
	ACNE	0 (0.0%)	2 (1.5%)	1 (0.8%)
	CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	ECZEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FURUNCULOSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	HERPES SIMPLEX	1 (0.9%)	1 (0.8%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PRURITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)
	PUSTULAR RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	RASH	1 (0.9%)	0 (0.0%)	1 (0.8%)
	SKIN BENIGN NEOPLASM	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SWEATING	10 (8.6%)	4 (3.1%)	1 (0.8%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Searches	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PUNCTURE SITE REACTION	0 (0.0%)	1 (0.8%)	0 (0.0%)
Special Senses	TOTAL	4 (3.4%)	5 (3.8%)	2 (1.7%)
	ABNORMAL VISION	3 (2.6%)	0 (0.0%)	0 (0.0%)
	ABNORMALITY OF	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ACCOMMODATION			

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.4

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Special Senses	EAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	EAR PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	OTITIS MEDIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
	TASTE PERVERSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TINNITUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	16 (13.8%)	13 (10.0%)	13 (10.8%)
	AMENORRHEA	0 (0.0%)	1 (0.8%)	1 (0.8%)
	BREAST ATROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST NEOPLASM	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)
	CYSTITIS	2 (1.7%)	1 (0.8%)	3 (2.5%)
	DYSMENORRHEA	4 (3.4%)	4 (3.1%)	4 (3.3%)
	FEMALE GENITAL DISORDERS	3 (2.6%)	2 (1.5%)	0 (0.0%)
	FEMALE LACTATION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	LEUKORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	1 (0.9%)	1 (0.8%)	1 (0.8%)
	MENSTRUAL DISORDER	2 (1.7%)	1 (0.8%)	0 (0.0%)
	METrorrhagia	1 (0.9%)	0 (0.0%)	0 (0.0%)
	URINARY TRACT INFECTION	1 (0.9%)	1 (0.8%)	2 (1.7%)
	VAGINAL MONILIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VAGINITIS	1 (0.9%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.5

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or more of the Population During the Treatment Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	85 (73.3%)	82 (63.1%)	62 (51.7%)
NAUSEA	27 (23.3%)	16 (12.3%)	2 (1.7%)
ASTHENIA	22 (19.0%)	16 (12.3%)	5 (4.2%)
HEADACHE	18 (15.5%)	16 (12.3%)	17 (14.2%)
LIBIDO DECREASED	15 (12.9%)	7 (5.4%)	7 (5.8%)
INFECTION	10 (8.6%)	5 (3.8%)	8 (6.7%)
SWEATING	10 (8.6%)	4 (3.1%)	1 (0.8%)
DIARRHEA	8 (6.9%)	7 (5.4%)	0 (0.0%)
DIZZINESS	8 (6.9%)	7 (5.4%)	3 (2.5%)
TREMOR	7 (6.0%)	4 (3.1%)	0 (0.0%)
RESPIRATORY DISORDER	5 (4.3%)	9 (6.9%)	13 (10.8%)
SOMNOLENCE	5 (4.3%)	3 (2.3%)	1 (0.8%)
ABDOMINAL PAIN	4 (3.4%)	4 (3.1%)	0 (0.0%)
DECREASED APPETITE	4 (3.4%)	1 (0.8%)	0 (0.0%)
DYSMENORRHEA	4 (3.4%)	4 (3.1%)	4 (3.3%)
INSOMNIA	4 (3.4%)	13 (10.0%)	3 (2.5%)
ABNORMAL VISION	3 (2.6%)	0 (0.0%)	0 (0.0%)
AMNESIA	3 (2.6%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	3 (2.6%)	1 (0.8%)	1 (0.8%)
DRY MOUTH	3 (2.6%)	3 (2.3%)	1 (0.8%)
DYSPEPSIA	3 (2.6%)	2 (1.5%)	2 (1.7%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.5

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or more of the Population During the Treatment Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Treatment Group Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
FEMALE GENITAL DISORDERS	3 (2.6%)	2 (1.5%)	0 (0.0%)
PHARYNGITIS	3 (2.6%)	0 (0.0%)	5 (4.2%)
SINUSITIS	3 (2.6%)	7 (5.4%)	2 (1.7%)
WEIGHT GAIN	3 (2.6%)	0 (0.0%)	1 (0.8%)
ANXIETY	2 (1.7%)	2 (1.5%)	3 (2.5%)
BACK PAIN	2 (1.7%)	4 (3.1%)	5 (4.2%)
CYSTITIS	2 (1.7%)	1 (0.8%)	3 (2.5%)
DEPRESSION	2 (1.7%)	3 (2.3%)	1 (0.8%)
FEVER	2 (1.7%)	0 (0.0%)	1 (0.8%)
GINGIVITIS	2 (1.7%)	1 (0.8%)	0 (0.0%)
HYPESTHESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)
MENSTRUAL DISORDER	2 (1.7%)	1 (0.8%)	0 (0.0%)
PAIN	2 (1.7%)	2 (1.5%)	2 (1.7%)
TRAUMA	2 (1.7%)	3 (2.3%)	4 (3.3%)
VERTIGO	2 (1.7%)	3 (2.3%)	1 (0.8%)
ALLERGIC REACTION	1 (0.9%)	2 (1.5%)	3 (2.5%)
ARTHRALGIA	1 (0.9%)	1 (0.8%)	2 (1.7%)
BRONCHITIS	1 (0.9%)	3 (2.3%)	0 (0.0%)
CONCENTRATION IMPAIRED	1 (0.9%)	2 (1.5%)	0 (0.0%)
GENERALIZED EDEMA	1 (0.9%)	2 (1.5%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.5

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or more of the Population During the Treatment Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
MYALGIA	1 (0.9%)	2 (1.5%)	3 (2.5%)
NERVOUSNESS	1 (0.9%)	6 (4.6%)	2 (1.7%)
TOOTH DISORDER	1 (0.9%)	1 (0.8%)	2 (1.7%)
URINARY TRACT INFECTION	1 (0.9%)	1 (0.8%)	2 (1.7%)
ACNE	0 (0.0%)	2 (1.5%)	1 (0.8%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	2 (1.7%)
DYSPHAGIA	0 (0.0%)	2 (1.5%)	0 (0.0%)
MIGRAINE	0 (0.0%)	1 (0.8%)	3 (2.5%)
OTITIS MEDIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
PRURITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	2 (1.7%)
YAWN	0 (0.0%)	2 (1.5%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.6

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	
TOTAL	TOTAL	19 (16.4%)	29 (22.5%)	15 (12.5%)
Body as a Whole	TOTAL	9 (7.8%)	13 (10.1%)	6 (5.0%)
	ABDOMINAL PAIN	0 (0.0%)	1 (0.8%)	1 (0.8%)
	ALLERGIC REACTION	1 (0.9%)	0 (0.0%)	1 (0.8%)
	ASTHENIA	2 (1.7%)	1 (0.8%)	0 (0.0%)
	BACK PAIN	1 (0.9%)	1 (0.8%)	0 (0.0%)
	FEVER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FLU SYNDROME	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	2 (1.7%)	5 (3.9%)	2 (1.7%)
	INFECTION	3 (2.6%)	2 (1.6%)	2 (1.7%)
	MALaise	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NEOPLASM	1 (0.9%)	0 (0.0%)	0 (0.0%)
	TRAUMA	0 (0.0%)	2 (1.6%)	0 (0.0%)
Cardiovascular System	TOTAL	2 (1.7%)	3 (2.3%)	1 (0.8%)
	HYPERTENSION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	MIGRAINE	1 (0.9%)	0 (0.0%)	1 (0.8%)
	PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
Digestive System	TOTAL	2 (1.7%)	3 (2.3%)	2 (1.7%)
	DIARRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSPEPSIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	GASTROENTERITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NAUSEA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	VOMITING	0 (0.0%)	1 (0.8%)	1 (0.8%)
Hemic and Lymphatic System	TOTAL	1 (0.9%)	0 (0.0%)	3 (2.5%)
	ANEMIA	1 (0.9%)	0 (0.0%)	3 (2.5%)
	LEUKOPENIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Metabolic and Nutritional Disorders	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	LIPODYSTROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SGPT INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
Musculoskeletal System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ARTHRITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.6

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	
Nervous System	TOTAL	3 (2.6%)	6 (4.7%)	2 (1.7%)
	DEPRESSION	1 (0.9%)	3 (2.3%)	1 (0.8%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	INSOMNIA	1 (0.9%)	2 (1.6%)	0 (0.0%)
	LIBIDO DECREASED	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)
Respiratory System	TOTAL	2 (1.7%)	2 (1.6%)	1 (0.8%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	RESPIRATORY DISORDER	1 (0.9%)	2 (1.6%)	1 (0.8%)
Skin and Appendages	TOTAL	0 (0.0%)	2 (1.6%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SKIN DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Senses	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)
	ABNORMAL VISION	1 (0.9%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	3 (2.6%)	4 (3.1%)	2 (1.7%)
	ABORTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)
	BREAST PAIN	0 (0.0%)	2 (1.6%)	0 (0.0%)
	CREATININE CLEARANCE DECREASED	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DYSMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MENSTRUAL DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VAGINAL MONILIASIS	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.7

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or more of the Population During the Follow-up Phase
In Descending Order
Intention-to-Treat Population (with Follow-up)

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	10 (8.6%)	22 (17.1%)	8 (6.7%)
INFECTION	3 (2.6%)	2 (1.6%)	2 (1.7%)
ASTHENIA	2 (1.7%)	1 (0.8%)	0 (0.0%)
HEADACHE	2 (1.7%)	5 (3.9%)	2 (1.7%)
ANEMIA	1 (0.9%)	0 (0.0%)	3 (2.5%)
DEPRESSION	1 (0.9%)	3 (2.3%)	1 (0.8%)
INSOMNIA	1 (0.9%)	2 (1.6%)	0 (0.0%)
RESPIRATORY DISORDER	1 (0.9%)	2 (1.6%)	1 (0.8%)
BREAST PAIN	0 (0.0%)	2 (1.6%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	2 (1.6%)	0 (0.0%)
PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.6%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.8

Number (%) of Subjects with Serious Adverse Events By Study Phase
By Body System and Preferred Term
Intention-to-Treat Population

Study Phase : Pre-Treatment Phase

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	UNINTENDED PREGNANCY	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with Serious AEs 1

Table 15.8

Number (%) of Subjects with Serious Adverse Events By Study Phase
By Body System and Preferred Term
Intention-to-Treat Population

Study Phase : Treatment Phase

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	1 (0.9%)	2 (1.5%)	2 (1.7%)
Body as a Whole	TOTAL	1 (0.9%)	0 (0.0%)	2 (1.7%)
	ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	TRAUMA	0 (0.0%)	0 (0.0%)	2 (1.7%)
Cardiovascular System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PULMONARY EMBOLUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
Nervous System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with Serious AEs 5

Table 15.8

Number (%) of Subjects with Serious Adverse Events By Study Phase
By Body System and Preferred Term
Intention-to-Treat Population

Study Phase : Follow-Up Phase

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)
Nervous System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	DEPRESSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ABORTION	1 (0.9%)	0 (0.0%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with Serious AEs 2

Table 15.9

Number (%) of Subjects with Serious Adverse Events Occurring in 1% or more of the Population By Study Phase
In Descending Order

Intention-to-Treat Population

Study Phase : Pre-Treatment Phase

NO DATA AVAILABLE FOR THIS REPORT

Total Number of Subjects 366
Total Number of Subjects with Serious AEs 1

Table 15.9

Number (%) of Subjects with Serious Adverse Events Occurring in 1% or more of the Population By Study Phase
In Descending Order

Intention-to-Treat Population

Study Phase : Treatment Phase

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	0 (0.0%)	0 (0.0%)	2 (1.7%)
TRAUMA	0 (0.0%)	0 (0.0%)	2 (1.7%)

Total Number of Subjects 366
Total Number of Subjects with Serious AEs 5

Table 15.9

Number (%) of Subjects with Serious Adverse Events Occurring in 1% or more of the Population By Study Phase
In Descending Order

Intention-to-Treat Population

Study Phase : Follow-Up Phase

NO DATA AVAILABLE FOR THIS REPORT

Total Number of Subjects 365
Total Number of Subjects with Serious AEs 2

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Unknown

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	1 (0.9%)	2 (1.5%)	0 (0.0%)
Digestive System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NAUSEA	0 (0.0%)	1 (0.8%)	0 (0.0%)
Nervous System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	AMENORRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Mild

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
TOTAL	TOTAL	56 (48.3%)	47 (36.2%)	33 (27.5%)
Body as a Whole	TOTAL	25 (21.6%)	16 (12.3%)	11 (9.2%)
	ABDOMINAL PAIN	2 (1.7%)	1 (0.8%)	0 (0.0%)
	ALLERGIC REACTION	1 (0.9%)	0 (0.0%)	1 (0.8%)
	ASTHENIA	11 (9.5%)	7 (5.4%)	1 (0.8%)
	BACK PAIN	1 (0.9%)	0 (0.0%)	2 (1.7%)
	CHEST PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CHILLS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	FLU SYNDROME	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	7 (6.0%)	2 (1.5%)	4 (3.3%)
	INFECTION	2 (1.7%)	2 (1.5%)	2 (1.7%)
	MONILIASIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PAIN	0 (0.0%)	1 (0.8%)	1 (0.8%)
	TRAUMA	2 (1.7%)	2 (1.5%)	1 (0.8%)
Cardiovascular System	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)
	ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	PALPITATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Digestive System	TOTAL	25 (21.6%)	18 (13.8%)	4 (3.3%)
	COLITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	CONSTIPATION	2 (1.7%)	1 (0.8%)	0 (0.0%)
	DECREASED APPETITE	3 (2.6%)	0 (0.0%)	0 (0.0%)
	DIARRHEA	4 (3.4%)	5 (3.8%)	0 (0.0%)
	DRY MOUTH	2 (1.7%)	1 (0.8%)	0 (0.0%)
	DYSPEPSIA	2 (1.7%)	1 (0.8%)	1 (0.8%)
	DYSPHAGIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FLATULENCE	0 (0.0%)	1 (0.8%)	0 (0.0%)
	GINGIVITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	INCREASED APPETITE	1 (0.9%)	0 (0.0%)	1 (0.8%)
	NAUSEA	14 (12.1%)	9 (6.9%)	2 (1.7%)
Metabolic and Nutritional Disorders	TOTAL	3 (2.6%)	2 (1.5%)	2 (1.7%)
	GENERALIZED EDEMA	0 (0.0%)	2 (1.5%)	0 (0.0%)
	THIRST	0 (0.0%)	0 (0.0%)	1 (0.8%)
	WEIGHT GAIN	3 (2.6%)	0 (0.0%)	1 (0.8%)
Musculoskeletal System	TOTAL	1 (0.9%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Mild

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
Musculoskeletal System	ARTHRALGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	17 (14.7%)	15 (11.5%)	10 (8.3%)
	ABNORMAL DREAMS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ANXIETY	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CONCENTRATION IMPAIRED	0 (0.0%)	1 (0.8%)	0 (0.0%)
	CONFUSION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DIZZINESS	3 (2.6%)	3 (2.3%)	2 (1.7%)
	HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INCOORDINATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	2 (1.7%)	6 (4.6%)	3 (2.5%)
	LACK OF EMOTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	4 (3.4%)	1 (0.8%)	4 (3.3%)
	NERVOUSNESS	1 (0.9%)	3 (2.3%)	2 (1.7%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	TREMOR	6 (5.2%)	4 (3.1%)	0 (0.0%)
	VERTIGO	1 (0.9%)	1 (0.8%)	0 (0.0%)
Respiratory System	TOTAL	3 (2.6%)	7 (5.4%)	7 (5.8%)
	BRONCHITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	COUGH INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	PHARYNGITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	2 (1.7%)	2 (1.5%)	6 (5.0%)
	SINUSITIS	0 (0.0%)	2 (1.5%)	0 (0.0%)
	YAWN	0 (0.0%)	2 (1.5%)	0 (0.0%)
Skin and Appendages	TOTAL	3 (2.6%)	3 (2.3%)	4 (3.3%)
	ACNE	0 (0.0%)	1 (0.8%)	1 (0.8%)
	CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	FURUNCULOSIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	HERPES SIMPLEX	1 (0.9%)	0 (0.0%)	0 (0.0%)
	RASH	0 (0.0%)	0 (0.0%)	1 (0.8%)
	SKIN BENIGN NEOPLASM	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SWEATING	2 (1.7%)	1 (0.8%)	0 (0.0%)
Special Searches	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PUNCTURE SITE REACTION	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Mild

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Special Senses	TOTAL	0 (0.0%)	3 (2.3%)	0 (0.0%)
	EAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TASTE PERVERSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TINNITUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	8 (6.9%)	3 (2.3%)	4 (3.3%)
	AMENORRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	BREAST ATROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST NEOPLASM	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)
	CYSTITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DYSMENORRHEA	2 (1.7%)	0 (0.0%)	0 (0.0%)
	FEMALE LACTATION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	LEUKORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MENSTRUAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)
	METrorrhagia	1 (0.9%)	0 (0.0%)	0 (0.0%)
	URINARY TRACT INFECTION	1 (0.9%)	1 (0.8%)	1 (0.8%)
	VAGINITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Moderate

Body System	Preferred Term	Paroxetine CR 25 mg (N=116)		Treatment Group Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
TOTAL	TOTAL	63	(54.3%)	62	(47.7%)	51	(42.5%)
Body as a Whole	TOTAL	28	(24.1%)	26	(20.0%)	23	(19.2%)
	ABDOMINAL PAIN	1	(0.9%)	2	(1.5%)	0	(0.0%)
	ALLERGIC REACTION	0	(0.0%)	2	(1.5%)	2	(1.7%)
	ASTHENIA	12	(10.3%)	7	(5.4%)	4	(3.3%)
	BACK PAIN	0	(0.0%)	3	(2.3%)	3	(2.5%)
	CHILLS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	FEVER	2	(1.7%)	0	(0.0%)	1	(0.8%)
	FLU SYNDROME	1	(0.9%)	1	(0.8%)	0	(0.0%)
	HEADACHE	10	(8.6%)	12	(9.2%)	12	(10.0%)
	INFECTION	6	(5.2%)	2	(1.5%)	3	(2.5%)
	NEOPLASM	1	(0.9%)	1	(0.8%)	0	(0.0%)
	PAIN	2	(1.7%)	0	(0.0%)	1	(0.8%)
	SHOCK	0	(0.0%)	1	(0.8%)	0	(0.0%)
	TRAUMA	0	(0.0%)	1	(0.8%)	1	(0.8%)
Cardiovascular System	TOTAL	2	(1.7%)	6	(4.6%)	0	(0.0%)
	HAEMATOMA	0	(0.0%)	1	(0.8%)	0	(0.0%)
	HYPERTENSION	0	(0.0%)	1	(0.8%)	0	(0.0%)
	MIGRAINE	0	(0.0%)	1	(0.8%)	0	(0.0%)
	MYOCARDIAL INFARCT	0	(0.0%)	1	(0.8%)	0	(0.0%)
	POSTURAL HYPOTENSION	0	(0.0%)	1	(0.8%)	0	(0.0%)
	PULMONARY EMBOLUS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	TACHYCARDIA	1	(0.9%)	0	(0.0%)	0	(0.0%)
	VASODILATATION	1	(0.9%)	0	(0.0%)	0	(0.0%)
Digestive System	TOTAL	25	(21.6%)	13	(10.0%)	8	(6.7%)
	CONSTIPATION	3	(2.6%)	0	(0.0%)	1	(0.8%)
	DECREASED APPETITE	1	(0.9%)	1	(0.8%)	0	(0.0%)
	DIARRHEA	4	(3.4%)	2	(1.5%)	0	(0.0%)
	DRY MOUTH	0	(0.0%)	2	(1.5%)	1	(0.8%)
	DYSPEPSIA	1	(0.9%)	1	(0.8%)	1	(0.8%)
	DYSPHAGIA	0	(0.0%)	1	(0.8%)	0	(0.0%)
	FLATULENCE	0	(0.0%)	1	(0.8%)	1	(0.8%)
	GASTRITIS	0	(0.0%)	0	(0.0%)	1	(0.8%)
	GASTROENTERITIS	1	(0.9%)	1	(0.8%)	0	(0.0%)
	GASTROINTESTINAL DISORDER	1	(0.9%)	0	(0.0%)	0	(0.0%)
	GINGIVITIS	2	(1.7%)	0	(0.0%)	0	(0.0%)
	INCREASED APPETITE	1	(0.9%)	0	(0.0%)	0	(0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Digestive System	NAUSEA	14 (12.1%)	4 (3.1%)	0 (0.0%)
	TOOTH DISORDER	1 (0.9%)	1 (0.8%)	2 (1.7%)
	VOMITING	0 (0.0%)	0 (0.0%)	1 (0.8%)
Endocrine System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	OVARY DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)
	ANEMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	LYMPHADENOPATHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
Metabolic and Nutritional Disorders	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Musculoskeletal System	TOTAL	1 (0.9%)	3 (2.3%)	5 (4.2%)
	ARTHRALGIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
	MYALGIA	1 (0.9%)	2 (1.5%)	2 (1.7%)
	TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	22 (19.0%)	24 (18.5%)	9 (7.5%)
	ABNORMAL DREAMS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ANXIETY	2 (1.7%)	0 (0.0%)	2 (1.7%)
	CONCENTRATION IMPAIRED	1 (0.9%)	1 (0.8%)	0 (0.0%)
	DEPRESSION	0 (0.0%)	2 (1.5%)	1 (0.8%)
	DIZZINESS	4 (3.4%)	4 (3.1%)	1 (0.8%)
	HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	2 (1.7%)	10 (7.7%)	0 (0.0%)
	LACK OF EMOTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	7 (6.0%)	5 (3.8%)	2 (1.7%)
	NERVOUSNESS	0 (0.0%)	3 (2.3%)	1 (0.8%)
	SOMNOLENCE	4 (3.4%)	3 (2.3%)	1 (0.8%)
	THINKING ABNORMAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	TREMOR	2 (1.7%)	1 (0.8%)	0 (0.0%)
	VERTIGO	1 (0.9%)	1 (0.8%)	1 (0.8%)
Respiratory System	TOTAL	7 (6.0%)	14 (10.8%)	10 (8.3%)
	ASTHMA	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Respiratory System	BRONCHITIS	0 (0.0%)	2 (1.5%)	0 (0.0%)
	COUGH INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
	PHARYNGITIS	3 (2.6%)	0 (0.0%)	3 (2.5%)
	PNEUMONIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	3 (2.6%)	7 (5.4%)	5 (4.2%)
	SINUSITIS	1 (0.9%)	5 (3.8%)	2 (1.7%)
Skin and Appendages	TOTAL	7 (6.0%)	7 (5.4%)	3 (2.5%)
	ACNE	0 (0.0%)	1 (0.8%)	0 (0.0%)
	ECZEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HERPES SIMPLEX	0 (0.0%)	1 (0.8%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PRURITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)
	PUSTULAR RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SWEATING	6 (5.2%)	3 (2.3%)	0 (0.0%)
Special Senses	TOTAL	2 (1.7%)	2 (1.5%)	2 (1.7%)
	ABNORMAL VISION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	EAR PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	OTITIS MEDIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
Urogenital System	TOTAL	7 (6.0%)	6 (4.6%)	8 (6.7%)
	CYSTITIS	2 (1.7%)	1 (0.8%)	2 (1.7%)
	DYSMENORRHEA	3 (2.6%)	3 (2.3%)	4 (3.3%)
	FEMALE GENITAL DISORDERS	1 (0.9%)	1 (0.8%)	0 (0.0%)
	MENORRHAGIA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VAGINAL MONILIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VAGINITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Severe

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	29 (25.0%)	26 (20.0%)	17 (14.2%)
Body as a Whole	TOTAL	11 (9.5%)	11 (8.5%)	11 (9.2%)
	ABDOMINAL PAIN	1 (0.9%)	1 (0.8%)	0 (0.0%)
	ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ASTHENIA	4 (3.4%)	4 (3.1%)	0 (0.0%)
	BACK PAIN	1 (0.9%)	1 (0.8%)	1 (0.8%)
	HEADACHE	3 (2.6%)	3 (2.3%)	4 (3.3%)
	INFECTION	2 (1.7%)	1 (0.8%)	3 (2.5%)
	PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TRAUMA	0 (0.0%)	0 (0.0%)	3 (2.5%)
Cardiovascular System	TOTAL	0 (0.0%)	1 (0.8%)	3 (2.5%)
	MIGRAINE	0 (0.0%)	0 (0.0%)	3 (2.5%)
	VASCULAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
Digestive System	TOTAL	8 (6.9%)	5 (3.8%)	0 (0.0%)
	DIARRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DRY MOUTH	2 (1.7%)	0 (0.0%)	0 (0.0%)
	DYSPHAGIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NAUSEA	5 (4.3%)	3 (2.3%)	0 (0.0%)
	VOMITING	1 (0.9%)	1 (0.8%)	0 (0.0%)
Metabolic and Nutritional Disorders	TOTAL	1 (0.9%)	1 (0.8%)	0 (0.0%)
	EDEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	GENERALIZED EDEMA	1 (0.9%)	0 (0.0%)	0 (0.0%)
Musculoskeletal System	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MYALGIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	13 (11.2%)	12 (9.2%)	2 (1.7%)
	ALCOHOL ABUSE	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ANXIETY	0 (0.0%)	2 (1.5%)	1 (0.8%)
	DEPRESSION	2 (1.7%)	1 (0.8%)	0 (0.0%)
	DIZZINESS	2 (1.7%)	0 (0.0%)	0 (0.0%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	INSOMNIA	0 (0.0%)	2 (1.5%)	0 (0.0%)
	LIBIDO DECREASED	6 (5.2%)	3 (2.3%)	1 (0.8%)
	MYOCLONUS	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.10

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Severe

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Nervous System	SOMNOLENCE	2 (1.7%)	1 (0.8%)	0 (0.0%)
	THINKING ABNORMAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TREMOR	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VERTIGO	0 (0.0%)	1 (0.8%)	0 (0.0%)
Respiratory System	TOTAL	3 (2.6%)	0 (0.0%)	2 (1.7%)
	BRONCHITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	PHARYNGITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	0 (0.0%)	0 (0.0%)	2 (1.7%)
	SINUSITIS	2 (1.7%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	TOTAL	6 (5.2%)	1 (0.8%)	2 (1.7%)
	RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SWEATING	5 (4.3%)	1 (0.8%)	1 (0.8%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Senses	TOTAL	3 (2.6%)	0 (0.0%)	0 (0.0%)
	ABNORMAL VISION	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ABNORMALITY OF ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	3 (2.6%)	3 (2.3%)	1 (0.8%)
	CYSTITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSMENORRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FEMALE GENITAL DISORDERS	2 (1.7%)	1 (0.8%)	0 (0.0%)
	MENSTRUAL DISORDER	1 (0.9%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.11

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Severity in Descending Order
Intention-to-Treat Population

Severity : Mild

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	47 (40.5%)	39 (30.0%)	24 (20.0%)
NAUSEA	14 (12.1%)	9 (6.9%)	2 (1.7%)
ASTHENIA	11 (9.5%)	7 (5.4%)	1 (0.8%)
HEADACHE	7 (6.0%)	2 (1.5%)	4 (3.3%)
TREMOR	6 (5.2%)	4 (3.1%)	0 (0.0%)
DIARRHEA	4 (3.4%)	5 (3.8%)	0 (0.0%)
LIBIDO DECREASED	4 (3.4%)	1 (0.8%)	4 (3.3%)
DECREASED APPETITE	3 (2.6%)	0 (0.0%)	0 (0.0%)
DIZZINESS	3 (2.6%)	3 (2.3%)	2 (1.7%)
WEIGHT GAIN	3 (2.6%)	0 (0.0%)	1 (0.8%)
ABDOMINAL PAIN	2 (1.7%)	1 (0.8%)	0 (0.0%)
AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	2 (1.7%)	1 (0.8%)	0 (0.0%)
DRY MOUTH	2 (1.7%)	1 (0.8%)	0 (0.0%)
DYSMENORRHEA	2 (1.7%)	0 (0.0%)	0 (0.0%)
DYSPEPSIA	2 (1.7%)	1 (0.8%)	1 (0.8%)
INFECTION	2 (1.7%)	2 (1.5%)	2 (1.7%)
INSOMNIA	2 (1.7%)	6 (4.6%)	3 (2.5%)
RESPIRATORY DISORDER	2 (1.7%)	2 (1.5%)	6 (5.0%)
SWEATING	2 (1.7%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.11

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Severity in Descending Order
Intention-to-Treat Population

Severity : Mild

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TRAUMA	2 (1.7%)	2 (1.5%)	1 (0.8%)
BACK PAIN	1 (0.9%)	0 (0.0%)	2 (1.7%)
NERVOUSNESS	1 (0.9%)	3 (2.3%)	2 (1.7%)
GENERALIZED EDEMA	0 (0.0%)	2 (1.5%)	0 (0.0%)
SINUSITIS	0 (0.0%)	2 (1.5%)	0 (0.0%)
YAWN	0 (0.0%)	2 (1.5%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.11

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Severity in Descending Order
Intention-to-Treat Population

Severity : Moderate

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	56 (48.3%)	52 (40.0%)	43 (35.8%)
NAUSEA	14 (12.1%)	4 (3.1%)	0 (0.0%)
ASTHENIA	12 (10.3%)	7 (5.4%)	4 (3.3%)
HEADACHE	10 (8.6%)	12 (9.2%)	12 (10.0%)
LIBIDO DECREASED	7 (6.0%)	5 (3.8%)	2 (1.7%)
INFECTION	6 (5.2%)	2 (1.5%)	3 (2.5%)
SWEATING	6 (5.2%)	3 (2.3%)	0 (0.0%)
DIARRHEA	4 (3.4%)	2 (1.5%)	0 (0.0%)
DIZZINESS	4 (3.4%)	4 (3.1%)	1 (0.8%)
SOMNOLENCE	4 (3.4%)	3 (2.3%)	1 (0.8%)
CONSTIPATION	3 (2.6%)	0 (0.0%)	1 (0.8%)
DYSMENORRHEA	3 (2.6%)	3 (2.3%)	4 (3.3%)
PHARYNGITIS	3 (2.6%)	0 (0.0%)	3 (2.5%)
RESPIRATORY DISORDER	3 (2.6%)	7 (5.4%)	5 (4.2%)
AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
ANXIETY	2 (1.7%)	0 (0.0%)	2 (1.7%)
CYSTITIS	2 (1.7%)	1 (0.8%)	2 (1.7%)
FEVER	2 (1.7%)	0 (0.0%)	1 (0.8%)
GINGIVITIS	2 (1.7%)	0 (0.0%)	0 (0.0%)
INSOMNIA	2 (1.7%)	10 (7.7%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

503

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Table 15.11

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Severity in Descending Order
Intention-to-Treat Population

Severity : Moderate

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
PAIN	2 (1.7%)	0 (0.0%)	1 (0.8%)
TREMOR	2 (1.7%)	1 (0.8%)	0 (0.0%)
ABDOMINAL PAIN	1 (0.9%)	2 (1.5%)	0 (0.0%)
MYALGIA	1 (0.9%)	2 (1.5%)	2 (1.7%)
SINUSITIS	1 (0.9%)	5 (3.8%)	2 (1.7%)
TOOTH DISORDER	1 (0.9%)	1 (0.8%)	2 (1.7%)
ALLERGIC REACTION	0 (0.0%)	2 (1.5%)	2 (1.7%)
ARTHRALGIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
BACK PAIN	0 (0.0%)	3 (2.3%)	3 (2.5%)
BRONCHITIS	0 (0.0%)	2 (1.5%)	0 (0.0%)
DEPRESSION	0 (0.0%)	2 (1.5%)	1 (0.8%)
DRY MOUTH	0 (0.0%)	2 (1.5%)	1 (0.8%)
NERVOUSNESS	0 (0.0%)	3 (2.3%)	1 (0.8%)
OTITIS MEDIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
PRURITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.11

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Severity in Descending Order
Intention-to-Treat Population

Severity : Severe

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	23 (19.8%)	19 (14.6%)	15 (12.5%)
LIBIDO DECREASED	6 (5.2%)	3 (2.3%)	1 (0.8%)
NAUSEA	5 (4.3%)	3 (2.3%)	0 (0.0%)
SWEATING	5 (4.3%)	1 (0.8%)	1 (0.8%)
ASTHENIA	4 (3.4%)	4 (3.1%)	0 (0.0%)
HEADACHE	3 (2.6%)	3 (2.3%)	4 (3.3%)
ABNORMAL VISION	2 (1.7%)	0 (0.0%)	0 (0.0%)
DEPRESSION	2 (1.7%)	1 (0.8%)	0 (0.0%)
DIZZINESS	2 (1.7%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	2 (1.7%)	0 (0.0%)	0 (0.0%)
FEMALE GENITAL DISORDERS	2 (1.7%)	1 (0.8%)	0 (0.0%)
INFECTION	2 (1.7%)	1 (0.8%)	3 (2.5%)
SINUSITIS	2 (1.7%)	0 (0.0%)	0 (0.0%)
SOMNOLENCE	2 (1.7%)	1 (0.8%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (1.5%)	1 (0.8%)
INSOMNIA	0 (0.0%)	2 (1.5%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	3 (2.5%)
RESPIRATORY DISORDER	0 (0.0%)	0 (0.0%)	2 (1.7%)
TRAUMA	0 (0.0%)	0 (0.0%)	3 (2.5%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.12

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Mild

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	
TOTAL	TOTAL	8 (6.9%)	6 (4.7%)	6 (5.0%)
Body as a Whole	TOTAL	4 (3.4%)	3 (2.3%)	1 (0.8%)
	ABDOMINAL PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BACK PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FEVER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FLU SYNDROME	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	1 (0.9%)	0 (0.0%)	1 (0.8%)
	INFECTION	1 (0.9%)	1 (0.8%)	0 (0.0%)
	NEOPLASM	1 (0.9%)	0 (0.0%)	0 (0.0%)
Cardiovascular System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MIGRAINE	1 (0.9%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	0 (0.0%)	3 (2.5%)
	ANEMIA	0 (0.0%)	0 (0.0%)	3 (2.5%)
	LEUKOPENIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Metabolic and Nutritional Disorders	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	LIPODYSTROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SGPT INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
Respiratory System	TOTAL	2 (1.7%)	0 (0.0%)	1 (0.8%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	RESPIRATORY DISORDER	1 (0.9%)	0 (0.0%)	1 (0.8%)
Skin and Appendages	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Senses	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ABNORMAL VISION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)
	BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CREATININE CLEARANCE DECREASED	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VAGINAL MONILIASIS	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.12

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	TOTAL	9 (7.8%)	18 (14.0%)	7 (5.8%)
Body as a Whole	TOTAL	2 (1.7%)	8 (6.2%)	3 (2.5%)
	ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)
	ASTHENIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	BACK PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	0 (0.0%)	5 (3.9%)	1 (0.8%)
	INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MALAISE	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TRAUMA	0 (0.0%)	2 (1.6%)	0 (0.0%)
Cardiovascular System	TOTAL	1 (0.9%)	3 (2.3%)	0 (0.0%)
	HYPERTENSION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
Digestive System	TOTAL	2 (1.7%)	3 (2.3%)	2 (1.7%)
	DIARRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSPEPSIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	GASTROENTERITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NAUSEA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	VOMITING	0 (0.0%)	1 (0.8%)	1 (0.8%)
Hemic and Lymphatic System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ANEMIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
Musculoskeletal System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ARTHRITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
Nervous System	TOTAL	3 (2.6%)	4 (3.1%)	2 (1.7%)
	DEPRESSION	1 (0.9%)	1 (0.8%)	1 (0.8%)
	INSOMNIA	1 (0.9%)	2 (1.6%)	0 (0.0%)
	LIBIDO DECREASED	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)
Respiratory System	TOTAL	0 (0.0%)	2 (1.6%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.12

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
Respiratory System	RESPIRATORY DISORDER	0 (0.0%)	2 (1.6%)	0 (0.0%)
Skin and Appendages	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SKIN DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
Special Senses	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	ABNORMAL VISION	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)
	BREAST PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	DYSMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.12

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Severe

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	TOTAL	6 (5.2%)	7 (5.4%)	3 (2.5%)
Body as a Whole	TOTAL	5 (4.3%)	2 (1.6%)	2 (1.7%)
	ALLERGIC REACTION	1 (0.9%)	0 (0.0%)	1 (0.8%)
	ASTHENIA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	HEADACHE	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INFECTION	2 (1.7%)	1 (0.8%)	1 (0.8%)
Cardiovascular System	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MIGRAINE	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	0 (0.0%)	2 (1.6%)	0 (0.0%)
	DEPRESSION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	2 (1.6%)	0 (0.0%)
	ABORTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	BREAST PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MENSTRUAL DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.13

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Follow-up Phase
By Severity in Descending Order
Intention-to-Treat Population (with Follow-up)

Severity : Mild

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	0 (0.0%)	0 (0.0%)	3 (2.5%)
ANEMIA	0 (0.0%)	0 (0.0%)	3 (2.5%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.13

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Follow-up Phase
By Severity in Descending Order
Intention-to-Treat Population (with Follow-up)

Severity : Moderate

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	1 (0.9%)	14 (10.9%)	1 (0.8%)
INSOMNIA	1 (0.9%)	2 (1.6%)	0 (0.0%)
HEADACHE	0 (0.0%)	5 (3.9%)	1 (0.8%)
HYPERTENSION	0 (0.0%)	2 (1.6%)	0 (0.0%)
PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)
RESPIRATORY DISORDER	0 (0.0%)	2 (1.6%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.6%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.13

Number (%) of Subjects with Emergent Adverse Events Occurring in 1% or More of the Population During the Follow-up Phase
By Severity in Descending Order
Intention-to-Treat Population (with Follow-up)

Severity : Severe

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	2 (1.7%)	3 (2.3%)	1 (0.8%)
INFECTION	2 (1.7%)	1 (0.8%)	1 (0.8%)
DEPRESSION	0 (0.0%)	2 (1.6%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.14

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	
TOTAL	TOTAL	69 (59.5%)	56 (43.1%)	25 (20.8%)
Body as a Whole	TOTAL	27 (23.3%)	25 (19.2%)	10 (8.3%)
	ABDOMINAL PAIN	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ASTHENIA	19 (16.4%)	15 (11.5%)	4 (3.3%)
	BACK PAIN	0 (0.0%)	2 (1.5%)	1 (0.8%)
	CHEST PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CHILLS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FLU SYNDROME	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HEADACHE	8 (6.9%)	8 (6.2%)	6 (5.0%)
	PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
Cardiovascular System	TOTAL	2 (1.7%)	5 (3.8%)	1 (0.8%)
	ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	HAEMATOMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MYOCARDIAL INFARCT	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PALPITATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	POSTURAL HYPOTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	VASCULAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	VASODILATATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Digestive System	TOTAL	37 (31.9%)	25 (19.2%)	7 (5.8%)
	COLITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	CONSTIPATION	3 (2.6%)	1 (0.8%)	1 (0.8%)
	DECREASED APPETITE	3 (2.6%)	1 (0.8%)	0 (0.0%)
	DIARRHEA	6 (5.2%)	6 (4.6%)	0 (0.0%)
	DRY MOUTH	3 (2.6%)	3 (2.3%)	1 (0.8%)
	DYSPEPSIA	1 (0.9%)	0 (0.0%)	1 (0.8%)
	DYSPHAGIA	0 (0.0%)	2 (1.5%)	0 (0.0%)
	FLATULENCE	0 (0.0%)	1 (0.8%)	1 (0.8%)
	INCREASED APPETITE	1 (0.9%)	0 (0.0%)	1 (0.8%)
	NAUSEA	25 (21.6%)	13 (10.0%)	2 (1.7%)
	VOMITING	1 (0.9%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	ANEMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
Metabolic and Nutritional Disorders	TOTAL	3 (2.6%)	2 (1.5%)	2 (1.7%)

Total Number of Subjects 366

Total Number of Subjects with Related or Possibly Related AEs 150

Table 15.14

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Metabolic and Nutritional Disorders	EDEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	GENERALIZED EDEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	THIRST	0 (0.0%)	0 (0.0%)	1 (0.8%)
	WEIGHT GAIN	3 (2.6%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	36 (31.0%)	28 (21.5%)	13 (10.8%)
	ABNORMAL DREAMS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	AMNESIA	3 (2.6%)	0 (0.0%)	0 (0.0%)
	ANXIETY	2 (1.7%)	0 (0.0%)	2 (1.7%)
	CONCENTRATION IMPAIRED	1 (0.9%)	2 (1.5%)	0 (0.0%)
	CONFUSION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DEPRESSION	2 (1.7%)	1 (0.8%)	0 (0.0%)
	DIZZINESS	8 (6.9%)	6 (4.6%)	2 (1.7%)
	HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INCOORDINATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	2 (1.7%)	10 (7.7%)	2 (1.7%)
	LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	15 (12.9%)	7 (5.4%)	6 (5.0%)
	MYOCLONUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NERVOUSNESS	1 (0.9%)	4 (3.1%)	2 (1.7%)
	SOMNOLENCE	5 (4.3%)	3 (2.3%)	1 (0.8%)
	THINKING ABNORMAL	1 (0.9%)	1 (0.8%)	0 (0.0%)
	TREMOR	7 (6.0%)	4 (3.1%)	0 (0.0%)
	VERTIGO	2 (1.7%)	3 (2.3%)	0 (0.0%)
Respiratory System	TOTAL	2 (1.7%)	2 (1.5%)	0 (0.0%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SINUSITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	YAWN	0 (0.0%)	2 (1.5%)	0 (0.0%)
Skin and Appendages	TOTAL	10 (8.6%)	7 (5.4%)	2 (1.7%)
	ACNE	0 (0.0%)	1 (0.8%)	1 (0.8%)
	ECZEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PRURITUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SWEATING	9 (7.8%)	4 (3.1%)	1 (0.8%)
Special Senses	TOTAL	4 (3.4%)	1 (0.8%)	0 (0.0%)
	ABNORMAL VISION	3 (2.6%)	0 (0.0%)	0 (0.0%)

Total Number of Subjects 366

Total Number of Subjects with Related or Possibly Related AEs 150

Table 15.14

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events During the Treatment Phase
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Special Senses	ABNORMALITY OF	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MYDRIASIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TINNITUS			
Urogenital System	TOTAL	5 (4.3%)	4 (3.1%)	0 (0.0%)
	AMENORRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST ATROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FEMALE GENITAL DISORDERS	3 (2.6%)	2 (1.5%)	0 (0.0%)
	MENORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENSTRUAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with Related or Possibly Related AEs 150

Table 15.15

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events Occurring in 1% or more of the Population
During the Treatment Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Paroxetine CR 25 mg (N=116)	Treatment Group Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	64 (55.2%)	51 (39.2%)	22 (18.3%)
NAUSEA	25 (21.6%)	13 (10.0%)	2 (1.7%)
ASTHENIA	19 (16.4%)	15 (11.5%)	4 (3.3%)
LIBIDO DECREASED	15 (12.9%)	7 (5.4%)	6 (5.0%)
SWEATING	9 (7.8%)	4 (3.1%)	1 (0.8%)
DIZZINESS	8 (6.9%)	6 (4.6%)	2 (1.7%)
HEADACHE	8 (6.9%)	8 (6.2%)	6 (5.0%)
TREMOR	7 (6.0%)	4 (3.1%)	0 (0.0%)
DIARRHEA	6 (5.2%)	6 (4.6%)	0 (0.0%)
SOMNOLENCE	5 (4.3%)	3 (2.3%)	1 (0.8%)
ABNORMAL VISION	3 (2.6%)	0 (0.0%)	0 (0.0%)
AMNESIA	3 (2.6%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	3 (2.6%)	1 (0.8%)	1 (0.8%)
DECREASED APPETITE	3 (2.6%)	1 (0.8%)	0 (0.0%)
DRY MOUTH	3 (2.6%)	3 (2.3%)	1 (0.8%)
FEMALE GENITAL DISORDERS	3 (2.6%)	2 (1.5%)	0 (0.0%)
WEIGHT GAIN	3 (2.6%)	0 (0.0%)	1 (0.8%)
ABDOMINAL PAIN	2 (1.7%)	0 (0.0%)	0 (0.0%)
ANXIETY	2 (1.7%)	0 (0.0%)	2 (1.7%)
DEPRESSION	2 (1.7%)	1 (0.8%)	0 (0.0%)
INSOMNIA	2 (1.7%)	10 (7.7%)	2 (1.7%)

Total Number of Subjects 366
Total Number of Subjects with Related or Possibly Related AEs 150

Table 15.15

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events Occurring in 1% or more of the Population
During the Treatment Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)
VERTIGO	2 (1.7%)	3 (2.3%)	0 (0.0%)
CONCENTRATION IMPAIRED	1 (0.9%)	2 (1.5%)	0 (0.0%)
NERVOUSNESS	1 (0.9%)	4 (3.1%)	2 (1.7%)
BACK PAIN	0 (0.0%)	2 (1.5%)	1 (0.8%)
DYSPHAGIA	0 (0.0%)	2 (1.5%)	0 (0.0%)
YAWN	0 (0.0%)	2 (1.5%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with Related or Possibly Related AEs 150

Table 15.16

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events During the Follow-up Phase
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	TOTAL	5 (4.3%)	8 (6.2%)	1 (0.8%)
Body as a Whole	TOTAL	2 (1.7%)	5 (3.9%)	0 (0.0%)
	ALLERGIC REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ASTHENIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	0 (0.0%)	3 (2.3%)	0 (0.0%)
	INFECTION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MALAISE	0 (0.0%)	1 (0.8%)	0 (0.0%)
Cardiovascular System	TOTAL	0 (0.0%)	2 (1.6%)	0 (0.0%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)
Digestive System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NAUSEA	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	ANEMIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Metabolic and Nutritional Disorders	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	SGPT INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	2 (1.7%)	1 (0.8%)	0 (0.0%)
	DEPRESSION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	0 (0.0%)	1 (0.8%)	0 (0.0%)
	VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)
Respiratory System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
Special Senses	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	ABNORMAL VISION	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with Related or Possibly Related AEs 14

Table 15.17

Number (%) of Subjects with Related or Possibly Related Emergent Adverse Events Occurring in 1% or more of the Population
During the Follow-up Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	0 (0.0%)	5 (3.9%)	0 (0.0%)
HEADACHE	0 (0.0%)	3 (2.3%)	0 (0.0%)
PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with Related or Possibly Related AEs 14

Table 15.18

Number (%) of Subjects with Adverse Events Leading to Withdrawal from the Study
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	16 (13.8%)	13 (10.0%)	5 (4.2%)
Body as a Whole	TOTAL	3 (2.6%)	3 (2.3%)	2 (1.7%)
	ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ASTHENIA	1 (0.9%)	2 (1.5%)	0 (0.0%)
	HEADACHE	1 (0.9%)	1 (0.8%)	1 (0.8%)
	TRAUMA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Cardiovascular System	TOTAL	0 (0.0%)	3 (2.3%)	0 (0.0%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MYOCARDIAL INFARCT	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PULMONARY EMBOLUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
Digestive System	TOTAL	6 (5.2%)	5 (3.8%)	1 (0.8%)
	DECREASED APPETITE	1 (0.9%)	1 (0.8%)	0 (0.0%)
	DIARRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DRY MOUTH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	GASTRITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NAUSEA	4 (3.4%)	3 (2.3%)	0 (0.0%)
	TOOTH DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	VOMITING	1 (0.9%)	0 (0.0%)	0 (0.0%)
Nervous System	TOTAL	8 (6.9%)	8 (6.2%)	1 (0.8%)
	ANXIETY	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DEPRESSION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DIZZINESS	3 (2.6%)	1 (0.8%)	0 (0.0%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	INSOMNIA	2 (1.7%)	4 (3.1%)	0 (0.0%)
	LACK OF EMOTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	1 (0.9%)	0 (0.0%)	0 (0.0%)
	NERVOUSNESS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SOMNOLENCE	1 (0.9%)	1 (0.8%)	1 (0.8%)
	THINKING ABNORMAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TREMOR	2 (1.7%)	1 (0.8%)	0 (0.0%)
	VERTIGO	1 (0.9%)	1 (0.8%)	0 (0.0%)
Skin and Appendages	TOTAL	2 (1.7%)	1 (0.8%)	0 (0.0%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SWEATING	1 (0.9%)	0 (0.0%)	0 (0.0%)

Withdrawals based on subjects who had an action of 'Drug Stopped' on the Adverse Event panel of the eCRF

Total Number of Subjects 366

Total Number of Subjects with AEs Leading to Withdrawal 34

Table 15.18

Number (%) of Subjects with Adverse Events Leading to Withdrawal from the Study
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Special Senses	TOTAL	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ABNORMAL VISION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ABNORMALITY OF ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	2 (1.7%)	2 (1.5%)	1 (0.8%)
	AMENORRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	FEMALE GENITAL DISORDERS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MENORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENSTRUAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)
	UNINTENDED PREGNANCY	0 (0.0%)	1 (0.8%)	0 (0.0%)

Withdrawals based on subjects who had an action of 'Drug Stopped' on the Adverse Event panel of the eCRF
Total Number of Subjects 366
Total Number of Subjects with AEs Leading to Withdrawal 34

Table 15.19

Number (%) of Subjects with Adverse Events Leading to Withdrawal from Study
Occurring in 1% or More of the Population During the Treatment Phase
In Descending Order
Intention-to-Treat Population

Preferred Term	Treatment Group		
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	6 (5.2%)	7 (5.4%)	0 (0.0%)
NAUSEA	4 (3.4%)	3 (2.3%)	0 (0.0%)
DIZZINESS	3 (2.6%)	1 (0.8%)	0 (0.0%)
INSOMNIA	2 (1.7%)	4 (3.1%)	0 (0.0%)
TREMOR	2 (1.7%)	1 (0.8%)	0 (0.0%)
ASTHENIA	1 (0.9%)	2 (1.5%)	0 (0.0%)

Withdrawals based on subjects who had an action of 'Drug Stopped' on the Adverse Event panel of the eCRF
Total Number of Subjects 366
Total Number of Subjects with AEs Leading to Withdrawal 34

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Parox CR 25.0 mg / (N = 116)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
TOTAL	TOTAL	65 (56.0%)	18 (15.5%)	16 (13.8%)	5 (4.3%)	35 (30.2%)	8 (6.9%)	89 (76.7%)
Body as a Whole	ABDOMINAL PAIN	2 (1.7%)	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)
	ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	ASTHENIA	18 (15.5%)	2 (1.7%)	1 (0.9%)	0 (0.0%)	3 (2.6%)	0 (0.0%)	22 (19.0%)
	BACK PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
	CHILLS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
	FLU SYNDROME	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	HEADACHE	6 (5.2%)	3 (2.6%)	2 (1.7%)	1 (0.9%)	4 (3.4%)	2 (1.7%)	18 (15.5%)
	INFECTION	3 (2.6%)	0 (0.0%)	4 (3.4%)	0 (0.0%)	3 (2.6%)	0 (0.0%)	10 (8.6%)
	NEOPLASM	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
	TRAUMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
Cardiovascular System	PALPITATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Digestive System	VASODILATATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	COLITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	CONSTIPATION	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.6%)
	DECREASED APPETITE	4 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)
	DIARRHEA	5 (4.3%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	8 (6.9%)
	DRY MOUTH	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
	DYSPEPSIA	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	3 (2.6%)
	GASTROENTERITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	GASTROINTESTINAL DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	GINGIVITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
	INCREASED APPETITE	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	NAUSEA	23 (19.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)	0 (0.0%)	27 (23.3%)
	TOOTH DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	VOMITING	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Parox CR 25.0 mg / (N = 116)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
Metabolic and Nutritional Disorders	GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	WEIGHT GAIN	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
Musculoskeletal System	ARTHRALGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	MYALGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Nervous System	ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	ALCOHOL ABUSE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.6%)
	ANXIETY	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
	CONCENTRATION IMPAIRED	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	DEPRESSION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
	DIZZINESS	6 (5.2%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	8 (6.9%)
	HYESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
	INCOORDINATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	INSOMNIA	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	4 (3.4%)
	LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
	LIBIDO DECREASED	12 (10.3%)	1 (0.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	15 (12.9%)
	NERVOUSNESS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	SOMNOLENCE	4 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	5 (4.3%)
	THINKING ABNORMAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	TREMOR	6 (5.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	7 (6.0%)
	VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
Respiratory System	BRONCHITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	EPISTAXIS	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	PHARYNGITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.6%)
	RESPIRATORY DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	4 (3.4%)	0 (0.0%)	5 (4.3%)
	SINUSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	2 (1.7%)	3 (2.6%)
Skin and Appendages	HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	PUSTULAR RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	SWEATING	7 (6.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	10 (8.6%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Parox CR 25.0 mg / (N = 116)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
Special Senses	ABNORMAL VISION	2 (1.7%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
	ABNORMALITY OF ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Urogenital System	BREAST PAIN	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	CYSTITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
	DYSMENORRHEA	0 (0.0%)	1 (0.9%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)
	FEMALE GENITAL DISORDERS	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.6%)
	LEUKORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	MENORRHAGIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	MENSTRUAL DISORDER	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
	METrorrhagia	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	URINARY TRACT INFECTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
	VAGINAL MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)
	VAGINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Parox CR 12.5 mg / (N = 130)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
TOTAL	TOTAL	48 (36.9%)	12 (9.2%)	12 (9.2%)	9 (6.9%)	37 (28.5%)	12 (9.2%)	88 (67.7%)
Body as a Whole	ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	4 (3.1%)
	ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
	ASTHENIA	10 (7.7%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	16 (12.3%)
	BACK PAIN	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	4 (3.1%)
	CHILLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
	FLU SYNDROME	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	HEADACHE	7 (5.4%)	2 (1.5%)	0 (0.0%)	2 (1.5%)	4 (3.1%)	1 (0.8%)	16 (12.3%)
	INFECTION	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	5 (3.8%)
	MONILIASIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (1.5%)
	SHOCK	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	TRAUMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
Cardiovascular System	HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	HYPERTENSION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	MYOCARDIAL INFARCT	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
Digestive System	CONSTIPATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	DECREASED APPETITE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DIARRHEA	5 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	7 (5.4%)
	DRY MOUTH	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
	DYSPEPSIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (1.5%)
	DYSPHAGIA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
	FLATULENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GASTROENTERITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GINGIVITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NAUSEA	11 (8.5%)	2 (1.5%)	1 (0.8%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	16 (12.3%)
	TOOTH DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Parox CR 12.5 mg / (N = 130)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
Digestive System	VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
Endocrine System	OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
Hemic and Lymphatic System	ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
Metabolic and Nutritional Disorders	EDEMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GENERALIZED EDEMA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
Musculoskeletal System	ARTHRALGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MYALGIA	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
Nervous System	ABNORMAL DREAMS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	ANXIETY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (1.5%)
	CONCENTRATION IMPAIRED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.5%)
	DEPRESSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
	DIZZINESS	5 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	7 (5.4%)
	EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	INSOMNIA	9 (6.9%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	13 (10.0%)
	LIBIDO DECREASED	4 (3.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	7 (5.4%)
	MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NERVOUSNESS	5 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	6 (4.6%)
	SOMNOLENCE	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.3%)
	THINKING ABNORMAL	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	TREMOR	4 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.1%)
	VERTIGO	2 (1.5%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
Respiratory System	ASTHMA	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	BRONCHITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	3 (2.3%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Parox CR 12.5 mg / (N = 130)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
Respiratory System	RESPIRATORY DISORDER	3 (2.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	4 (3.1%)	1 (0.8%)	9 (6.9%)
	SINUSITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	4 (3.1%)	1 (0.8%)	7 (5.4%)
	YAWN	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
Skin and Appendages	ACNE	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
	ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	PRURITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	SWEATING	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	4 (3.1%)
Special Senses	EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	EAR PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	TASTE PERVERSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	TINNITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
Urogenital System	AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CYSTITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSMENORRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	2 (1.5%)	4 (3.1%)
	FEMALE GENITAL DISORDERS	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
	MENORRHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	MENSTRUAL DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
Special Searches	PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Placebo / (N = 120)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
TOTAL	TOTAL	21 (17.5%)	17 (14.2%)	9 (7.5%)	8 (6.7%)	42 (35.0%)	9 (7.5%)	68 (56.7%)
Body as a Whole	ALLERGIC REACTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	3 (2.5%)
	ASTHENIA	2 (1.7%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	5 (4.2%)
	BACK PAIN	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	5 (4.2%)
	CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
	HEADACHE	3 (2.5%)	5 (4.2%)	2 (1.7%)	1 (0.8%)	4 (3.3%)	2 (1.7%)	17 (14.2%)
	INFECTION	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	3 (2.5%)	2 (1.7%)	8 (6.7%)
	PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	2 (1.7%)
	TRAUMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	4 (3.3%)
Cardiovascular System	ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	MIGRAINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
Digestive System	CONSTIPATION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DRY MOUTH	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSPEPSIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
	FLATULENCE	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GASTRITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	INCREASED APPETITE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	NAUSEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
	TOOTH DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
	VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
Metabolic and Nutritional Disorders	GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	THIRST	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	WEIGHT GAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
Musculoskeletal System	ARTHRALGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (1.7%)
	MYALGIA	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.5%)
	TENDINOUS DISORDER	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
Nervous System	ANXIETY	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.5%)
	CONFUSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.20

Number (%) of Subjects reporting Emergent Adverse Events During the Treatment Phase by Time of First Occurrence
By Body System and Preferred Term
Intention-to-Treat Population

Treatment Group : Placebo / (N = 120)

Body System	Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
Nervous System	DEPRESSION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DIZZINESS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
	INSOMNIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	3 (2.5%)
	LIBIDO DECREASED	3 (2.5%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	7 (5.8%)
	NERVOUSNESS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	SOMNOLENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VERTIGO	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
Respiratory System	COUGH INCREASED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
	PHARYNGITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	5 (4.2%)
	PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	2 (1.7%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	9 (7.5%)	0 (0.0%)	13 (10.8%)
	SINUSITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
Skin and Appendages	ACNE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	PRURITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
	RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	SWEATING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)
Special Senses	OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
Urogenital System	AMENORRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CYSTITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
	DYSMENORRHEA	0 (0.0%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	4 (3.3%)
	FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
	MENORRHAGIA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
	VAGINITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.21

Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Time of First Occurrence

In Descending Order
Intention-to-Treat Population
Treatment Group : Parox CR 25.0 mg / (N = 116)

Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
TOTAL	63 (54.3%)	14 (12.1%)	14 (12.1%)	4 (3.4%)	34 (29.3%)	7 (6.0%)	85 (73.3%)
NAUSEA	23 (19.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)	0 (0.0%)	27 (23.3%)
ASTHENIA	18 (15.5%)	2 (1.7%)	1 (0.9%)	0 (0.0%)	3 (2.6%)	0 (0.0%)	22 (19.0%)
HEADACHE	6 (5.2%)	3 (2.6%)	2 (1.7%)	1 (0.9%)	4 (3.4%)	2 (1.7%)	18 (15.5%)
LIBIDO DECREASED	12 (10.3%)	1 (0.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	15 (12.9%)
INFECTION	3 (2.6%)	0 (0.0%)	4 (3.4%)	0 (0.0%)	3 (2.6%)	0 (0.0%)	10 (8.6%)
SWEATING	7 (6.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	10 (8.6%)
DIARRHEA	5 (4.3%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	8 (6.9%)
DIZZINESS	6 (5.2%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	8 (6.9%)
TREMOR	6 (5.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	7 (6.0%)
RESPIRATORY DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	4 (3.4%)	0 (0.0%)	5 (4.3%)
SOMNOLENCE	4 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	5 (4.3%)
ABDOMINAL PAIN	2 (1.7%)	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)
DECREASED APPETITE	4 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)
DYSMENORRHEA	0 (0.0%)	1 (0.9%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.4%)
INSOMNIA	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	4 (3.4%)
ABNORMAL VISION	2 (1.7%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.6%)
CONSTIPATION	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.6%)
DRY MOUTH	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
DYSPEPSIA	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	3 (2.6%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.21

Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Time of First Occurrence

In Descending Order
Intention-to-Treat Population
Treatment Group : Parox CR 25.0 mg / (N = 116)

Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
FEMALE GENITAL DISORDERS	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.6%)
PHARYNGITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.6%)
SINUSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	2 (1.7%)	3 (2.6%)
WEIGHT GAIN	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
ANXIETY	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
BACK PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
CYSTITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
DEPRESSION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
GINGIVITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
MENSTRUAL DISORDER	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)
TRAUMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.21

Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Time of First Occurrence

In Descending Order
Intention-to-Treat Population
Treatment Group : Parox CR 12.5 mg / (N = 130)

Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
TOTAL	47 (36.2%)	10 (7.7%)	9 (6.9%)	8 (6.2%)	30 (23.1%)	10 (7.7%)	82 (63.1%)
ASTHENIA	10 (7.7%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	16 (12.3%)
HEADACHE	7 (5.4%)	2 (1.5%)	0 (0.0%)	2 (1.5%)	4 (3.1%)	1 (0.8%)	16 (12.3%)
NAUSEA	11 (8.5%)	2 (1.5%)	1 (0.8%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	16 (12.3%)
INSOMNIA	9 (6.9%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	13 (10.0%)
RESPIRATORY DISORDER	3 (2.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	4 (3.1%)	1 (0.8%)	9 (6.9%)
DIARRHEA	5 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	7 (5.4%)
DIZZINESS	5 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	7 (5.4%)
LIBIDO DECREASED	4 (3.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	7 (5.4%)
SINUSITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	4 (3.1%)	1 (0.8%)	7 (5.4%)
NERVOUSNESS	5 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	6 (4.6%)
INFECTION	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	5 (3.8%)
ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	4 (3.1%)
BACK PAIN	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	4 (3.1%)
DYSMENORRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	2 (1.5%)	4 (3.1%)
SWEATING	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	4 (3.1%)
TREMOR	4 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.1%)
BRONCHITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	3 (2.3%)
DEPRESSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
DRY MOUTH	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
SOMNOLENCE	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.3%)
TRAUMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	3 (2.3%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.21

Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
By Time of First Occurrence

In Descending Order
Intention-to-Treat Population
Treatment Group : Parox CR 12.5 mg / (N = 130)

Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
VERTIGO	2 (1.5%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
ACNE	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
ANXIETY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (1.5%)
CONCENTRATION IMPAIRED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.5%)
DYSPEPSIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (1.5%)
DYSPHAGIA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
FEMALE GENITAL DISORDERS	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
GENERALIZED EDEMA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
MYALGIA	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)
PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	2 (1.5%)
YAWN	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.21

Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
 By Time of First Occurrence
 In Descending Order
 Intention-to-Treat Population
 Treatment Group : Placebo / (N = 120)

Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
TOTAL	18 (15.0%)	15 (12.5%)	8 (6.7%)	8 (6.7%)	36 (30.0%)	8 (6.7%)	62 (51.7%)
HEADACHE	3 (2.5%)	5 (4.2%)	2 (1.7%)	1 (0.8%)	4 (3.3%)	2 (1.7%)	17 (14.2%)
RESPIRATORY DISORDER	2 (1.7%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	9 (7.5%)	0 (0.0%)	13 (10.8%)
INFECTION	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	3 (2.5%)	2 (1.7%)	8 (6.7%)
LIBIDO DECREASED	3 (2.5%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	7 (5.8%)
ASTHENIA	2 (1.7%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	5 (4.2%)
BACK PAIN	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	5 (4.2%)
PHARYNGITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	5 (4.2%)
DYSMENORRHEA	0 (0.0%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	4 (3.3%)
TRAUMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	4 (3.3%)
ALLERGIC REACTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	3 (2.5%)
ANXIETY	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.5%)
CYSTITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
DIZZINESS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
INSOMNIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	3 (2.5%)
MIGRAINE	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
MYALGIA	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.5%)
ARTHRALGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (1.7%)
COUGH INCREASED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
DYSPEPSIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
NAUSEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
NERVOUSNESS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.7%)

Total Number of Subjects 366
 Total Number of Subjects with AEs 245

Table 15.21

Number (%) of Subjects reporting Emergent Adverse Events Occurring in 1% or More of the Population During the Treatment Phase
 By Time of First Occurrence
 In Descending Order
 Intention-to-Treat Population
 Treatment Group : Placebo / (N = 120)

Preferred Term	1-7 Days	8-14 Days	15-21 Days	22-28 Days	29-60 Days	>=61 Days	Total
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	2 (1.7%)
PRURITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
SINUSITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
TENDINOUS DISORDER	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
TOOTH DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.7%)
URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)

Total Number of Subjects 366
 Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Unknown

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	1 (0.9%)	2 (1.5%)	0 (0.0%)
Digestive System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	NAUSEA	0 (0.0%)	1 (0.8%)	0 (0.0%)
Nervous System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	AMENORRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Mild

Body System	Preferred Term	Paroxetine CR 25 mg (N=116)		Treatment Group Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
TOTAL	TOTAL	47	(40.5%)	41	(31.5%)	32	(26.7%)
Body as a Whole	TOTAL	21	(18.1%)	13	(10.0%)	9	(7.5%)
	ABDOMINAL PAIN	2	(1.7%)	1	(0.8%)	0	(0.0%)
	ALLERGIC REACTION	1	(0.9%)	0	(0.0%)	1	(0.8%)
	ASTHENIA	7	(6.0%)	5	(3.8%)	1	(0.8%)
	BACK PAIN	1	(0.9%)	0	(0.0%)	1	(0.8%)
	CHEST PAIN	0	(0.0%)	0	(0.0%)	1	(0.8%)
	CHILLS	1	(0.9%)	0	(0.0%)	0	(0.0%)
	HEADACHE	5	(4.3%)	1	(0.8%)	3	(2.5%)
	INFECTION	2	(1.7%)	2	(1.5%)	2	(1.7%)
	MONILIASIS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	PAIN	0	(0.0%)	1	(0.8%)	1	(0.8%)
	TRAUMA	2	(1.7%)	2	(1.5%)	1	(0.8%)
Cardiovascular System	TOTAL	1	(0.9%)	0	(0.0%)	1	(0.8%)
	ARRHYTHMIA	0	(0.0%)	0	(0.0%)	1	(0.8%)
	PALPITATION	1	(0.9%)	0	(0.0%)	0	(0.0%)
Digestive System	TOTAL	18	(15.5%)	17	(13.1%)	4	(3.3%)
	COLITIS	1	(0.9%)	0	(0.0%)	0	(0.0%)
	CONSTIPATION	0	(0.0%)	1	(0.8%)	0	(0.0%)
	DECREASED APPETITE	3	(2.6%)	0	(0.0%)	0	(0.0%)
	DIARRHEA	3	(2.6%)	5	(3.8%)	0	(0.0%)
	DRY MOUTH	1	(0.9%)	1	(0.8%)	0	(0.0%)
	DYSPEPSIA	2	(1.7%)	1	(0.8%)	1	(0.8%)
	DYSPHAGIA	0	(0.0%)	1	(0.8%)	0	(0.0%)
	GINGIVITIS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	INCREASED APPETITE	0	(0.0%)	0	(0.0%)	1	(0.8%)
	NAUSEA	10	(8.6%)	8	(6.2%)	2	(1.7%)
Metabolic and Nutritional Disorders	TOTAL	3	(2.6%)	2	(1.5%)	2	(1.7%)
	GENERALIZED EDEMA	0	(0.0%)	2	(1.5%)	0	(0.0%)
	THIRST	0	(0.0%)	0	(0.0%)	1	(0.8%)
	WEIGHT GAIN	3	(2.6%)	0	(0.0%)	1	(0.8%)
Musculoskeletal System	TOTAL	1	(0.9%)	0	(0.0%)	1	(0.8%)
	ARTHRALGIA	1	(0.9%)	0	(0.0%)	0	(0.0%)
	TENDINOUS DISORDER	0	(0.0%)	0	(0.0%)	1	(0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Mild

Body System	Preferred Term	Paroxetine CR 25 mg (N=116)		Treatment Group Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
Nervous System	TOTAL	13	(11.2%)	11	(8.5%)	9	(7.5%)
	ABNORMAL DREAMS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	AMNESIA	1	(0.9%)	0	(0.0%)	0	(0.0%)
	ANXIETY	0	(0.0%)	0	(0.0%)	1	(0.8%)
	CONCENTRATION IMPAIRED	0	(0.0%)	1	(0.8%)	0	(0.0%)
	CONFUSION	0	(0.0%)	0	(0.0%)	1	(0.8%)
	DIZZINESS	3	(2.6%)	3	(2.3%)	2	(1.7%)
	HYPESTHESIA	1	(0.9%)	0	(0.0%)	0	(0.0%)
	INCOORDINATION	1	(0.9%)	0	(0.0%)	0	(0.0%)
	INSOMNIA	2	(1.7%)	1	(0.8%)	3	(2.5%)
	LACK OF EMOTION	1	(0.9%)	0	(0.0%)	0	(0.0%)
	LIBIDO DECREASED	2	(1.7%)	0	(0.0%)	4	(3.3%)
	NERVOUSNESS	1	(0.9%)	3	(2.3%)	1	(0.8%)
	PARESTHESIA	0	(0.0%)	0	(0.0%)	1	(0.8%)
	TREMOR	4	(3.4%)	3	(2.3%)	0	(0.0%)
	VERTIGO	1	(0.9%)	1	(0.8%)	0	(0.0%)
Respiratory System	TOTAL	3	(2.6%)	7	(5.4%)	7	(5.8%)
	BRONCHITIS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	COUGH INCREASED	0	(0.0%)	0	(0.0%)	1	(0.8%)
	EPISTAXIS	1	(0.9%)	0	(0.0%)	0	(0.0%)
	PHARYNGITIS	0	(0.0%)	0	(0.0%)	1	(0.8%)
	RESPIRATORY DISORDER	2	(1.7%)	2	(1.5%)	6	(5.0%)
	SINUSITIS	0	(0.0%)	2	(1.5%)	0	(0.0%)
	YAWN	0	(0.0%)	2	(1.5%)	0	(0.0%)
Skin and Appendages	TOTAL	2	(1.7%)	3	(2.3%)	4	(3.3%)
	ACNE	0	(0.0%)	1	(0.8%)	1	(0.8%)
	CONTACT DERMATITIS	0	(0.0%)	0	(0.0%)	1	(0.8%)
	FURUNCULOSIS	0	(0.0%)	0	(0.0%)	1	(0.8%)
	HERPES SIMPLEX	1	(0.9%)	0	(0.0%)	0	(0.0%)
	RASH	0	(0.0%)	0	(0.0%)	1	(0.8%)
	SKIN BENIGN NEOPLASM	0	(0.0%)	1	(0.8%)	0	(0.0%)
	SWEATING	1	(0.9%)	1	(0.8%)	0	(0.0%)
Special Searches	TOTAL	0	(0.0%)	1	(0.8%)	0	(0.0%)
	PUNCTURE SITE REACTION	0	(0.0%)	1	(0.8%)	0	(0.0%)
Special Senses	TOTAL	0	(0.0%)	3	(2.3%)	0	(0.0%)
	EAR DISORDER	0	(0.0%)	1	(0.8%)	0	(0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Mild

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Special Senses	TASTE PERVERSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TINNITUS	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	7 (6.0%)	3 (2.3%)	4 (3.3%)
	AMENORRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	BREAST ATROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST NEOPLASM	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BREAST PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)
	DYSMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	FEMALE LACTATION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	LEUKORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MENSTRUAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)
	METORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	URINARY TRACT INFECTION	1 (0.9%)	1 (0.8%)	1 (0.8%)
	VAGINITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Moderate

Body System	Preferred Term	Paroxetine CR 25 mg (N=116)		Treatment Group Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
TOTAL	TOTAL	61	(52.6%)	61	(46.9%)	50	(41.7%)
Body as a Whole	TOTAL	27	(23.3%)	26	(20.0%)	21	(17.5%)
	ABDOMINAL PAIN	1	(0.9%)	2	(1.5%)	0	(0.0%)
	ALLERGIC REACTION	0	(0.0%)	2	(1.5%)	2	(1.7%)
	ASTHENIA	11	(9.5%)	7	(5.4%)	4	(3.3%)
	BACK PAIN	0	(0.0%)	3	(2.3%)	3	(2.5%)
	CHILLS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	FEVER	2	(1.7%)	0	(0.0%)	1	(0.8%)
	FLU SYNDROME	1	(0.9%)	1	(0.8%)	0	(0.0%)
	HEADACHE	10	(8.6%)	12	(9.2%)	10	(8.3%)
	INFECTION	6	(5.2%)	2	(1.5%)	3	(2.5%)
	NEOPLASM	1	(0.9%)	1	(0.8%)	0	(0.0%)
	PAIN	2	(1.7%)	0	(0.0%)	1	(0.8%)
	SHOCK	0	(0.0%)	1	(0.8%)	0	(0.0%)
	TRAUMA	0	(0.0%)	1	(0.8%)	0	(0.0%)
Cardiovascular System	TOTAL	2	(1.7%)	6	(4.6%)	0	(0.0%)
	HAEMATOMA	0	(0.0%)	1	(0.8%)	0	(0.0%)
	HYPERTENSION	0	(0.0%)	1	(0.8%)	0	(0.0%)
	MIGRAINE	0	(0.0%)	1	(0.8%)	0	(0.0%)
	MYOCARDIAL INFARCT	0	(0.0%)	1	(0.8%)	0	(0.0%)
	POSTURAL HYPOTENSION	0	(0.0%)	1	(0.8%)	0	(0.0%)
	PULMONARY EMBOLUS	0	(0.0%)	1	(0.8%)	0	(0.0%)
	TACHYCARDIA	1	(0.9%)	0	(0.0%)	0	(0.0%)
	VASODILATATION	1	(0.9%)	0	(0.0%)	0	(0.0%)
Digestive System	TOTAL	23	(19.8%)	12	(9.2%)	8	(6.7%)
	CONSTIPATION	3	(2.6%)	0	(0.0%)	1	(0.8%)
	DECREASED APPETITE	1	(0.9%)	1	(0.8%)	0	(0.0%)
	DIARRHEA	4	(3.4%)	2	(1.5%)	0	(0.0%)
	DRY MOUTH	0	(0.0%)	2	(1.5%)	1	(0.8%)
	DYSPEPSIA	1	(0.9%)	1	(0.8%)	1	(0.8%)
	FLATULENCE	0	(0.0%)	1	(0.8%)	1	(0.8%)
	GASTRITIS	0	(0.0%)	0	(0.0%)	1	(0.8%)
	GASTROENTERITIS	1	(0.9%)	1	(0.8%)	0	(0.0%)
	GASTROINTESTINAL DISORDER	1	(0.9%)	0	(0.0%)	0	(0.0%)
	GINGIVITIS	2	(1.7%)	0	(0.0%)	0	(0.0%)
	INCREASED APPETITE	1	(0.9%)	0	(0.0%)	0	(0.0%)
	NAUSEA	12	(10.3%)	4	(3.1%)	0	(0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Digestive System	TOOTH DISORDER	1 (0.9%)	1 (0.8%)	2 (1.7%)
	VOMITING	0 (0.0%)	0 (0.0%)	1 (0.8%)
Endocrine System	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	OVARY DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	2 (1.5%)	0 (0.0%)
	ANEMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	LYMPHADENOPATHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
Metabolic and Nutritional Disorders	TOTAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Musculoskeletal System	TOTAL	1 (0.9%)	3 (2.3%)	5 (4.2%)
	ARTHRALGIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
	MYALGIA	1 (0.9%)	2 (1.5%)	2 (1.7%)
	TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	20 (17.2%)	24 (18.5%)	8 (6.7%)
	ABNORMAL DREAMS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	AMNESIA	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ANXIETY	2 (1.7%)	0 (0.0%)	1 (0.8%)
	CONCENTRATION IMPAIRED	1 (0.9%)	1 (0.8%)	0 (0.0%)
	DEPRESSION	0 (0.0%)	2 (1.5%)	1 (0.8%)
	DIZZINESS	3 (2.6%)	4 (3.1%)	1 (0.8%)
	HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	2 (1.7%)	10 (7.7%)	0 (0.0%)
	LACK OF EMOTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	LIBIDO DECREASED	6 (5.2%)	4 (3.1%)	2 (1.7%)
	NERVOUSNESS	0 (0.0%)	3 (2.3%)	1 (0.8%)
	SOMNOLENCE	3 (2.6%)	2 (1.5%)	1 (0.8%)
	THINKING ABNORMAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	TREMOR	2 (1.7%)	1 (0.8%)	0 (0.0%)
	VERTIGO	1 (0.9%)	1 (0.8%)	1 (0.8%)
Respiratory System	TOTAL	7 (6.0%)	14 (10.8%)	10 (8.3%)
	ASTHMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BRONCHITIS	0 (0.0%)	2 (1.5%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Respiratory System	COUGH INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
	PHARYNGITIS	3 (2.6%)	0 (0.0%)	3 (2.5%)
	PNEUMONIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	3 (2.6%)	7 (5.4%)	5 (4.2%)
	SINUSITIS	1 (0.9%)	5 (3.8%)	2 (1.7%)
Skin and Appendages	TOTAL	5 (4.3%)	6 (4.6%)	3 (2.5%)
	ACNE	0 (0.0%)	1 (0.8%)	0 (0.0%)
	ECZEMA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	HERPES SIMPLEX	0 (0.0%)	1 (0.8%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PRURITUS	0 (0.0%)	1 (0.8%)	2 (1.7%)
	PUSTULAR RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SWEATING	4 (3.4%)	2 (1.5%)	0 (0.0%)
Special Senses	TOTAL	2 (1.7%)	2 (1.5%)	2 (1.7%)
	ABNORMAL VISION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	EAR PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	OTITIS MEDIA	0 (0.0%)	1 (0.8%)	2 (1.7%)
Urogenital System	TOTAL	7 (6.0%)	6 (4.6%)	8 (6.7%)
	CYSTITIS	2 (1.7%)	1 (0.8%)	2 (1.7%)
	DYSMENORRHEA	3 (2.6%)	3 (2.3%)	4 (3.3%)
	FEMALE GENITAL DISORDERS	1 (0.9%)	1 (0.8%)	0 (0.0%)
	MENORRHAGIA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VAGINAL MONILIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VAGINITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Severe

Body System	Preferred Term	Paroxetine CR 25 mg (N=116)		Treatment Group Paroxetine CR 12.5 mg (N=130)		Placebo (N=120)	
TOTAL	TOTAL	29	(25.0%)	26	(20.0%)	17	(14.2%)
Body as a Whole	TOTAL	11	(9.5%)	11	(8.5%)	11	(9.2%)
	ABDOMINAL PAIN	1	(0.9%)	1	(0.8%)	0	(0.0%)
	ANAPHYLACTOID REACTION	1	(0.9%)	0	(0.0%)	0	(0.0%)
	ASTHENIA	4	(3.4%)	4	(3.1%)	0	(0.0%)
	BACK PAIN	1	(0.9%)	1	(0.8%)	1	(0.8%)
	HEADACHE	3	(2.6%)	3	(2.3%)	4	(3.3%)
	INFECTION	2	(1.7%)	1	(0.8%)	3	(2.5%)
	PAIN	0	(0.0%)	1	(0.8%)	0	(0.0%)
	TRAUMA	0	(0.0%)	0	(0.0%)	3	(2.5%)
Cardiovascular System	TOTAL	0	(0.0%)	1	(0.8%)	3	(2.5%)
	MIGRAINE	0	(0.0%)	0	(0.0%)	3	(2.5%)
	VASCULAR DISORDER	0	(0.0%)	1	(0.8%)	0	(0.0%)
Digestive System	TOTAL	8	(6.9%)	5	(3.8%)	0	(0.0%)
	DIARRHEA	1	(0.9%)	0	(0.0%)	0	(0.0%)
	DRY MOUTH	2	(1.7%)	0	(0.0%)	0	(0.0%)
	DYSPHAGIA	0	(0.0%)	1	(0.8%)	0	(0.0%)
	NAUSEA	5	(4.3%)	3	(2.3%)	0	(0.0%)
	VOMITING	1	(0.9%)	1	(0.8%)	0	(0.0%)
Metabolic and Nutritional Disorders	TOTAL	1	(0.9%)	1	(0.8%)	0	(0.0%)
	EDEMA	0	(0.0%)	1	(0.8%)	0	(0.0%)
	GENERALIZED EDEMA	1	(0.9%)	0	(0.0%)	0	(0.0%)
Musculoskeletal System	TOTAL	0	(0.0%)	0	(0.0%)	1	(0.8%)
	MYALGIA	0	(0.0%)	0	(0.0%)	1	(0.8%)
Nervous System	TOTAL	13	(11.2%)	12	(9.2%)	2	(1.7%)
	ALCOHOL ABUSE	1	(0.9%)	0	(0.0%)	0	(0.0%)
	ANXIETY	0	(0.0%)	2	(1.5%)	1	(0.8%)
	DEPRESSION	2	(1.7%)	1	(0.8%)	0	(0.0%)
	DIZZINESS	2	(1.7%)	0	(0.0%)	0	(0.0%)
	EMOTIONAL LABILITY	0	(0.0%)	1	(0.8%)	0	(0.0%)
	INSOMNIA	0	(0.0%)	2	(1.5%)	0	(0.0%)
	LIBIDO DECREASED	6	(5.2%)	3	(2.3%)	1	(0.8%)
	MYOCLONUS	0	(0.0%)	1	(0.8%)	0	(0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.22

Number (%) of Subjects with Emergent Adverse Events During the Treatment Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population

Severity : Severe

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
Nervous System	SOMNOLENCE	2 (1.7%)	1 (0.8%)	0 (0.0%)
	THINKING ABNORMAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TREMOR	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VERTIGO	0 (0.0%)	1 (0.8%)	0 (0.0%)
Respiratory System	TOTAL	3 (2.6%)	0 (0.0%)	2 (1.7%)
	BRONCHITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	PHARYNGITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	RESPIRATORY DISORDER	0 (0.0%)	0 (0.0%)	2 (1.7%)
	SINUSITIS	2 (1.7%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	TOTAL	6 (5.2%)	1 (0.8%)	2 (1.7%)
	RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)
	SWEATING	5 (4.3%)	1 (0.8%)	1 (0.8%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Senses	TOTAL	3 (2.6%)	0 (0.0%)	0 (0.0%)
	ABNORMAL VISION	2 (1.7%)	0 (0.0%)	0 (0.0%)
	ABNORMALITY OF ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	3 (2.6%)	3 (2.3%)	1 (0.8%)
	CYSTITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSMENORRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FEMALE GENITAL DISORDERS	2 (1.7%)	1 (0.8%)	0 (0.0%)
	MENSTRUAL DISORDER	1 (0.9%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 366
Total Number of Subjects with AEs 245

Table 15.23

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Mild

Body System	Preferred Term	Treatment Group		Placebo (N=120)
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	
TOTAL	TOTAL	8 (6.9%)	6 (4.7%)	6 (5.0%)
Body as a Whole	TOTAL	4 (3.4%)	3 (2.3%)	1 (0.8%)
	ABDOMINAL PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	BACK PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FEVER	0 (0.0%)	1 (0.8%)	0 (0.0%)
	FLU SYNDROME	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	1 (0.9%)	0 (0.0%)	1 (0.8%)
	INFECTION	1 (0.9%)	1 (0.8%)	0 (0.0%)
	NEOPLASM	1 (0.9%)	0 (0.0%)	0 (0.0%)
Cardiovascular System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MIGRAINE	1 (0.9%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	TOTAL	0 (0.0%)	0 (0.0%)	3 (2.5%)
	ANEMIA	0 (0.0%)	0 (0.0%)	3 (2.5%)
	LEUKOPENIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Metabolic and Nutritional Disorders	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	LIPODYSTROPHY	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SGPT INCREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)
Respiratory System	TOTAL	2 (1.7%)	0 (0.0%)	1 (0.8%)
	EPISTAXIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
	RESPIRATORY DISORDER	1 (0.9%)	0 (0.0%)	1 (0.8%)
Skin and Appendages	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)
	URTICARIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Senses	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ABNORMAL VISION	1 (0.9%)	0 (0.0%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)
	BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)
	CREATININE CLEARANCE DECREASED	1 (0.9%)	0 (0.0%)	0 (0.0%)
	VAGINAL MONILIASIS	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.23

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	TOTAL	9 (7.8%)	18 (14.0%)	7 (5.8%)
Body as a Whole	TOTAL	2 (1.7%)	8 (6.2%)	3 (2.5%)
	ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)
	ASTHENIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	BACK PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)
	HEADACHE	0 (0.0%)	5 (3.9%)	1 (0.8%)
	INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)
	MALAISE	0 (0.0%)	1 (0.8%)	0 (0.0%)
	TRAUMA	0 (0.0%)	2 (1.6%)	0 (0.0%)
Cardiovascular System	TOTAL	1 (0.9%)	3 (2.3%)	0 (0.0%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PALPITATION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
Digestive System	TOTAL	2 (1.7%)	3 (2.3%)	2 (1.7%)
	DIARRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	DYSPEPSIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	GASTROENTERITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)
	LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	0 (0.0%)	1 (0.8%)
	NAUSEA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	VOMITING	0 (0.0%)	1 (0.8%)	1 (0.8%)
Hemic and Lymphatic System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ANEMIA	1 (0.9%)	0 (0.0%)	0 (0.0%)
Musculoskeletal System	TOTAL	1 (0.9%)	0 (0.0%)	0 (0.0%)
	ARTHRITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)
Nervous System	TOTAL	3 (2.6%)	4 (3.1%)	2 (1.7%)
	DEPRESSION	1 (0.9%)	1 (0.8%)	1 (0.8%)
	INSOMNIA	1 (0.9%)	2 (1.6%)	0 (0.0%)
	LIBIDO DECREASED	0 (0.0%)	1 (0.8%)	0 (0.0%)
	PARESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.8%)
	VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)
Respiratory System	TOTAL	0 (0.0%)	2 (1.6%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.23

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Moderate

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
Respiratory System	RESPIRATORY DISORDER	0 (0.0%)	2 (1.6%)	0 (0.0%)
Skin and Appendages	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	SKIN DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)
Special Senses	TOTAL	0 (0.0%)	1 (0.8%)	0 (0.0%)
	ABNORMAL VISION	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	1 (0.8%)	1 (0.8%)
	BREAST PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	DYSMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	0 (0.0%)	1 (0.8%)	0 (0.0%)
	URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	1 (0.8%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.23

Number (%) of Subjects with Emergent Adverse Events During the Follow-up Phase by Maximum Severity
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-up)

Severity : Severe

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=129)	Placebo (N=120)
TOTAL	TOTAL	6 (5.2%)	7 (5.4%)	3 (2.5%)
Body as a Whole	TOTAL	5 (4.3%)	2 (1.6%)	2 (1.7%)
	ALLERGIC REACTION	1 (0.9%)	0 (0.0%)	1 (0.8%)
	ASTHENIA	1 (0.9%)	1 (0.8%)	0 (0.0%)
	HEADACHE	1 (0.9%)	0 (0.0%)	0 (0.0%)
	INFECTION	2 (1.7%)	1 (0.8%)	1 (0.8%)
Cardiovascular System	TOTAL	0 (0.0%)	1 (0.8%)	1 (0.8%)
	HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MIGRAINE	0 (0.0%)	0 (0.0%)	1 (0.8%)
Nervous System	TOTAL	0 (0.0%)	2 (1.6%)	0 (0.0%)
	DEPRESSION	0 (0.0%)	2 (1.6%)	0 (0.0%)
	EMOTIONAL LABILITY	0 (0.0%)	1 (0.8%)	0 (0.0%)
Urogenital System	TOTAL	1 (0.9%)	2 (1.6%)	0 (0.0%)
	ABORTION	1 (0.9%)	0 (0.0%)	0 (0.0%)
	BREAST PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)
	MENSTRUAL DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)

Total Number of Subjects 365
Total Number of Subjects with AEs 63

Table 15.24

Summary Statistics For Baseline and Change from Baseline for Vital Signs by Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 25 mg (N=116)

Vital Signs Parameter	Visit	N	Mean	Median	Std. Dev.	Minimum	Maximum
Diastolic Blood Pressure (MMHG)	Baseline	116	75.8	76.0	9.47	54	105
	Treatment Cycle 1	97	-0.7	0.0	7.18	-22	21
	Treatment Cycle 2	92	-1.3	0.0	8.22	-25	20
	Treatment Cycle 3	3	4.7	0.0	9.87	-2	16
	Follow Up	102	-1.1	0.0	9.12	-35	24
	Endpoint	112	-1.1	0.0	9.11	-35	24
Pulse (BPM)	Baseline	116	70.7	70.5	9.22	48	106
	Treatment Cycle 1	97	-1.3	-1.0	7.94	-26	16
	Treatment Cycle 2	92	-1.1	0.0	8.32	-23	16
	Treatment Cycle 3	3	7.0	9.0	14.11	-8	20
	Follow Up	102	0.1	0.0	8.96	-24	25
	Endpoint	112	0.5	0.0	8.82	-24	25
Systolic Blood Pressure (MMHG)	Baseline	116	118.0	115.0	13.83	90	160
	Treatment Cycle 1	97	-0.9	0.0	10.69	-36	22
	Treatment Cycle 2	92	-1.9	0.0	12.47	-60	25
	Treatment Cycle 3	3	3.7	3.0	6.03	-2	10
	Follow Up	102	-2.3	0.0	12.29	-50	24
	Endpoint	112	-2.3	0.0	12.30	-50	24

Baseline is the last measurement prior to start of Randomised Study Medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.24

Summary Statistics For Baseline and Change from Baseline for Vital Signs by Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 12.5 mg (N=130)

Vital Signs Parameter	Visit	N	Mean	Median	Std. Dev.	Minimum	Maximum
Diastolic Blood Pressure (MMHG)	Baseline	130	74.2	74.5	9.90	50	105
	Treatment Cycle 1	118	0.0	0.0	7.10	-15	20
	Treatment Cycle 2	105	-1.5	-2.0	7.91	-27	20
	Treatment Cycle 3	3	-1.7	0.0	7.64	-10	5
	Follow Up	112	-0.2	0.0	8.15	-20	23
	Endpoint	124	-0.3	0.0	8.29	-20	23
Pulse (BPM)	Baseline	130	70.4	70.0	8.93	42	104
	Treatment Cycle 1	118	-0.3	0.0	7.80	-22	20
	Treatment Cycle 2	105	-0.6	0.0	7.38	-24	23
	Treatment Cycle 3	3	-2.3	-3.0	2.08	-4	0
	Follow Up	112	-0.1	0.0	9.08	-33	28
	Endpoint	124	-0.2	0.0	8.82	-33	28
Systolic Blood Pressure (MMHG)	Baseline	130	116.4	112.0	13.37	85	165
	Treatment Cycle 1	118	0.0	0.0	10.43	-30	27
	Treatment Cycle 2	105	-1.2	0.0	13.12	-58	33
	Treatment Cycle 3	3	-6.3	-5.0	7.09	-14	0
	Follow Up	112	1.4	0.0	10.78	-23	33
	Endpoint	124	0.5	0.0	10.99	-25	33

Baseline is the last measurement prior to start of Randomised Study Medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.24

Summary Statistics For Baseline and Change from Baseline for Vital Signs by Visit
Intention-to-Treat Population

Treatment Group:Placebo (N=120)

Vital Signs Parameter	Visit	N	Mean	Median	Std. Dev.	Minimum	Maximum
Diastolic Blood Pressure (MMHG)	Baseline	120	74.0	73.0	9.17	50	95
	Treatment Cycle 1	115	0.5	0.0	8.26	-30	29
	Treatment Cycle 2	98	1.3	0.0	8.78	-20	27
	Treatment Cycle 3	5	0.4	-4.0	8.96	-5	16
	Follow Up	109	-0.2	0.0	9.57	-37	30
	Endpoint	118	0.2	0.0	9.52	-37	30
Pulse (BPM)	Baseline	120	69.0	68.0	8.88	52	92
	Treatment Cycle 1	115	1.7	1.0	8.86	-20	42
	Treatment Cycle 2	98	0.7	0.0	7.75	-23	21
	Treatment Cycle 3	5	-1.2	0.0	9.55	-16	8
	Follow Up	109	1.4	0.0	8.48	-20	34
	Endpoint	118	1.0	0.0	8.52	-20	34
Systolic Blood Pressure (MMHG)	Baseline	120	117.3	115.0	11.60	90	148
	Treatment Cycle 1	115	-0.2	0.0	9.59	-30	28
	Treatment Cycle 2	98	-0.8	0.0	9.92	-25	26
	Treatment Cycle 3	5	-0.6	-7.0	13.18	-10	22
	Follow Up	109	-1.7	0.0	10.05	-34	20
	Endpoint	118	-1.1	0.0	10.24	-34	22

Baseline is the last measurement prior to start of Randomised Study Medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.25

Number (%) of Subjects with Vital Signs of Potential Clinical Concern During the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Sitting Systolic BP (mmHg)

Flag	Treatment Group		
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	Placebo
Low and Significant Decrease	0 (0.0%)	1 (0.8%)	1 (0.8%)
Number of Subjects with Baseline and Post Baseline Assessment	112 (100.0%)	124 (100.0%)	118 (100.0%)

Sitting Systolic BP, Sitting Diastolic BP and Sitting Pulse Rate Flags only shown
if both Significant Increase/Decrease from Baseline and outside Normal Range
Note: if no clinical concern results exist only the number of Subjects assessed will be presented in this table

Table 15.25

Number (%) of Subjects with Vital Signs of Potential Clinical Concern During the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Sitting Diastolic BP (mmHg)

Flag	Treatment Group		
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	Placebo
Low and Significant Decrease	0 (0.0%)	0 (0.0%)	1 (0.8%)
Number of Subjects with Baseline and Post Baseline Assessment	112 (100.0%)	124 (100.0%)	118 (100.0%)

Sitting Systolic BP, Sitting Diastolic BP and Sitting Pulse Rate Flags only shown
if both Significant Increase/Decrease from Baseline and outside Normal Range
Note: if no clinical concern results exist only the number of Subjects assessed will be presented in this table

Table 15.25

Number (%) of Subjects with Vital Signs of Potential Clinical Concern During the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Sitting Pulse Rate (bpm)

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Baseline and Post Baseline Assessment	112 (100.0%)	124 (100.0%)	118 (100.0%)

Sitting Systolic BP, Sitting Diastolic BP and Sitting Pulse Rate Flags only shown
if both Significant Increase/Decrease from Baseline and outside Normal Range
Note: if no clinical concern results exist only the number of Subjects assessed will be presented in this table

Table 15.25

Number (%) of Subjects with Vital Signs of Potential Clinical Concern During the Treatment or Follow-up Phase
Intention-to-Treat Population

Flag	Parameter:Weight (Kg)		
	Paroxetine CR 25 mg	Treatment Group Paroxetine CR 12.5 mg	Placebo
Number of Subjects with Baseline and Post Baseline Assessment	99 (100.0%)	112 (100.0%)	108 (100.0%)

Sitting Systolic BP, Sitting Diastolic BP and Sitting Pulse Rate Flags only shown
if both Significant Increase/Decrease from Baseline and outside Normal Range
Note: if no clinical concern results exist only the number of Subjects assessed will be presented in this table

Table 15.26

Number (%) of Subjects with Vital Sign Transitions from Baseline to Endpoint and/or Follow-up
Intention-to-Treat Population

----- Treatment Group=Paroxetine CR 25 mg -----							
Parameter	Baseline	Endpoint					
		L	%	I	%	H	%
Diastolic Blood Pressure	I			112	100.00		
Pulse	L	1	100.00				
Pulse	I	1	0.90	110	99.10		
Systolic Blood Pressure	I			112	100.00		

H : Above Clinical Concern, I : In Range, L : Below Clinical Concern
U: Unflaggable N: Clinical Concern Flags not requested
Baseline is the last measurement prior to start of Randomised Study Medication
Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.26

Number (%) of Subjects with Vital Sign Transitions from Baseline to Endpoint and/or Follow-up
Intention-to-Treat Population

----- Treatment Group=Paroxetine CR 12.5 mg -----							
Parameter	Baseline	Endpoint					
		L	%	I	%	H	%
Diastolic Blood Pressure	I			123	99.19	1	0.81
Pulse	L			3	100.00		
Pulse	I			121	100.00		
Systolic Blood Pressure	L			1	100.00		
Systolic Blood Pressure	I	1	0.81	121	98.37	1	0.81

H : Above Clinical Concern, I : In Range, L : Below Clinical Concern
U: Unflaggable N: Clinical Concern Flags not requested
Baseline is the last measurement prior to start of Randomised Study Medication
Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.26

Number (%) of Subjects with Vital Sign Transitions from Baseline to Endpoint and/or Follow-up
Intention-to-Treat Population

----- Treatment Group=Placebo -----							
Parameter	Baseline	Endpoint					
		L	%	I	%	H	%
Diastolic Blood Pressure	I	1	0.85	117	99.15		
Pulse	I			118	100.00		
Systolic Blood Pressure	I	1	0.85	117	99.15		

H : Above Clinical Concern, I : In Range, L : Below Clinical Concern
U: Unflaggable N: Clinical Concern Flags not requested
Baseline is the last measurement prior to start of Randomised Study Medication
Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Hemoglobin, Unit: G/L

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Hematocrit, Unit: %

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Low (Extended)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Red Blood Cell Count, Unit: $10^{12}/L$

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: White Blood Cell Count, Unit: $10^9/L$

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Low (Extended)	0 (0.0%)	2 (2.0%)	0 (0.0%)
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Segmented Neutrophils, Unit: Percentage

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Lymphocytes, Unit: Percentage

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Monocytes, Unit: Percentage

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Eosinophils, Unit: Percentage

Flag	Treatment Group		
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	Placebo
High (Extended)	1 (1.1%)	2 (2.0%)	1 (1.0%)
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Basophils, Unit: Percentage

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	92 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Platelets, Unit: $10^9/L$

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	90 (100.0%)	100 (100.0%)	98 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Blood Urea Nitrogen, Unit: MMOL/L

Flag	Paroxetine CR 25 mg		Treatment Group Paroxetine CR 12.5 mg		Placebo	
Number of Subjects with Assessment	93	(100.0%)	102	(100.0%)	102	(100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Creatinine, Unit: UMOL/L

Flag	Paroxetine CR 25 mg		Treatment Group Paroxetine CR 12.5 mg		Placebo	
Number of Subjects with Assessment	93	(100.0%)	102	(100.0%)	103	(100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Alkaline Phosphatase, Unit: IU/L

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	93 (100.0%)	102 (100.0%)	103 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Aspartate Aminotransferase, Unit: IU/L

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	93 (100.0%)	102 (100.0%)	103 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Alanine Aminotransferase, Unit: IU/L

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
High (Extended)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Number of Subjects with Assessment	93 (100.0%)	102 (100.0%)	103 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Total Bilirubin, Unit: UMOL/L

Flag	Paroxetine CR 25 mg		Treatment Group Paroxetine CR 12.5 mg		Placebo	
Number of Subjects with Assessment	93	(100.0%)	102	(100.0%)	103	(100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Thyroid Stimulating Hormone, Unit: MU/L

Flag	Treatment Group		Placebo
	Paroxetine CR 25 mg	Paroxetine CR 12.5 mg	
Number of Subjects with Assessment	1 (100.0%)	2 (100.0%)	4 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Free T3, Unit: PMOL/L

Flag	Treatment Group	
	Paroxetine CR 12.5 mg	Placebo
Number of Subjects with Assessment	2 (100.0%)	4 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.27

Number (%) of Subjects with Laboratory Values Flagged as of Clinical Concern during the Treatment or Follow-up Phase
Intention-to-Treat Population

Parameter: Total Free Thyroxine, Unit: PMOL/L

Flag	Treatment Group	
	Paroxetine CR 12.5 mg	Placebo
Number of Subjects with Assessment	2 (100.0%)	4 (100.0%)

Note: if no clinical concern records exist only the number of subjects assessed will be presented in this table

Table 15.29

Criteria for Clinical Concern Flagging of Laboratory Parameters

Parameter	Clinical Concern Low Value	Clinical Concern High Value	Unit
Hemoglobin	95.00		G/L
Hematocrit	32.00		%
Red Blood Cell Count		10.00	10 ¹² /L
White Blood Cell Count	2.80	16.00	10 ⁹ /L
Neutrophil Bands		10.00	Percentage
Segmented Neutrophils	15.00		Percentage
Lymphocytes		75.00	Percentage
Monocytes		15.00	Percentage
Eosinophils		10.00	Percentage
Basophils		10.00	Percentage
Platelets	75.00	700.00	10 ⁹ /L
Blood Urea Nitrogen		10.71	MMOL/L
Creatinine		176.80	UMOL/L
Alkaline Phosphatase		390.00	IU/L
Aspartate Aminotransferase		150.00	IU/L
Alanine Aminotransferase		165.00	IU/L
Total Bilirubin		34.20	UMOL/L
Thyroid Stimulating Hormone		10.00	MU/L
Free T3	1.75	13.00	PMOL/L
Total Free Thyroxine	5.15	46.40	PMOL/L

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Hemoglobin, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	76	8	0	84
L	N	0	0	3	5	0	8
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	90	10	0	100
L	%	0	0	38	63	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Hemoglobin, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	85	5	0	90
L	N	0	0	7	3	0	10
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	94	6	0	100
L	%	0	0	70	30	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Hemoglobin, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	81	6	0	87
L	N	0	0	5	6	0	11
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	93	7	0	100
L	%	0	0	45	55	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Hematocrit, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	85	2	0	87
L	N	0	0	4	1	0	5
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	98	2	0	100
L	%	0	0	80	20	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Hematocrit, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	94	3	0	97
L	N	0	0	2	1	0	3
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	97	3	0	100
L	%	0	0	67	33	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Hematocrit, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	91	2	0	93
L	N	0	0	1	3	1	5
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	98	2	0	100
L	%	0	0	20	60	20	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
By Laboratory Parameter
Intention-to-Treat Population
Parameter: Red Blood Cell Count, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	79	6	0	85
L	N	0	0	3	4	0	7
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	93	7	0	100
L	%	0	0	43	57	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
Baseline is last measurement prior to the start of randomised study medication
Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Red Blood Cell Count, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	1	0	0	0	1
I	N	0	0	89	4	0	93
L	N	0	0	3	3	0	6
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	100	0	0	0	100
I	%	0	0	96	4	0	100
L	%	0	0	50	50	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Red Blood Cell Count, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	89	4	0	93
L	N	0	0	1	4	0	5
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	96	4	0	100
L	%	0	0	20	80	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: White Blood Cell Count, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	1	0	0	0	1
I	N	0	2	87	1	0	90
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	100	0	0	0	100
I	%	0	2	97	1	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: White Blood Cell Count, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	2	90	2	1	95
L	N	0	0	4	0	0	4
-	N	0	0	0	0	1	1
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	2	95	2	1	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	100	100

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:White Blood Cell Count, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	1	2	0	0	3
I	N	0	2	89	4	0	95
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	33	67	0	0	100
I	%	0	2	94	4	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Segmented Neutrophils, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	3	87	1	0	91
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	3	96	1	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Segmented Neutrophils, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	4	0	0	4
I	N	0	3	91	1	0	95
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	3	96	1	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Segmented Neutrophils, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	5	0	0	5
I	N	0	5	85	1	0	91
L	N	0	0	0	1	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	5	93	1	0	100
L	%	0	0	0	100	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Lymphocytes, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	5	83	1	0	89
L	N	0	0	2	0	0	2
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	6	93	1	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Lymphocytes, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	3	92	2	0	97
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	3	95	2	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Lymphocytes, Treatment Group:Placebo

		=====					
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	1	0	0	0	1
I	N	0	4	88	3	0	95
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	100	0	0	0	100
I	%	0	4	93	3	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Monocytes, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	1	90	0	0	91
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	1	99	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Monocytes, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	0	2	0	0	2
I	N	0	1	96	0	0	97
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	1	99	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Monocytes, Treatment Group: Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	97	0	0	97
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Eosinophils, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	2	0	0	2
I	N	1	2	87	0	0	90
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	1	2	97	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Eosinophils, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	1	0	0	1
H	N	1	0	0	0	0	1
I	N	1	2	94	0	0	97
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	100	0	0	100
H	%	100	0	0	0	0	100
I	%	1	2	97	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Eosinophils, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	1	0	0	0	1
H	N	0	1	1	0	0	2
I	N	1	2	91	0	0	94
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	100	0	0	0	100
H	%	0	50	50	0	0	100
I	%	1	2	97	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Basophils, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	92	0	0	92
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Basophils, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	99	0	0	99
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Basophils, Treatment Group: Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	97	0	0	97
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Platelets, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	1	0	0	0	1
I	N	0	2	87	0	0	89
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	100	0	0	0	100
I	%	0	2	98	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Platelets, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	1	1	0	0	2
I	N	0	3	94	1	0	98
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	50	50	0	0	100
I	%	0	3	96	1	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Platelets, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	3	0	0	0	3
I	N	0	0	95	0	0	95
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	100	0	0	0	100
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Blood Urea Nitrogen, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	93	0	0	93
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Blood Urea Nitrogen, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	98	2	0	100
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	98	2	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Blood Urea Nitrogen, Treatment Group: Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	99	0	0	99
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Creatinine, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	88	1	0	89
L	N	0	0	0	2	0	2
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	99	1	0	100
L	%	0	0	0	100	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Creatinine, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	1	99	1	0	101
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	1	98	1	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Creatinine, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	0	95	3	0	98
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	0	97	3	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Alkaline Phosphatase, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	91	0	0	91
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Alkaline Phosphatase, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	101	0	0	101
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Alkaline Phosphatase, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	1	99	0	0	100
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	1	99	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Aspartate Aminotransferase, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	0	91	0	0	91
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Aspartate Aminotransferase, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	1	1	0	0	2
I	N	0	1	98	0	0	99
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	50	50	0	0	100
I	%	0	1	99	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Aspartate Aminotransferase, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	3	97	0	0	100
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	3	97	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Alanine Aminotransferase, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	92	0	0	92
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Alanine Aminotransferase, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	2	0	0	2
I	N	0	2	97	0	0	99
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	2	98	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Alanine Aminotransferase, Treatment Group: Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	1	0	0	0	1
I	N	1	1	97	0	0	99
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	100	0	0	0	100
I	%	1	1	98	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Total Bilirubin, Treatment Group: Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	3	89	0	0	92
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	3	97	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Total Bilirubin, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	101	0	0	101
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Total Bilirubin, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	2	2	0	0	4
I	N	0	0	96	0	0	96
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	50	50	0	0	100
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Thyroid Stimulating Hormone, Treatment Group:Paroxetine CR 25 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	1	0	0	1
I	N	0	0	0	0	0	0
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	100	0	0	100
I	%	0	0	0	0	0	0
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Thyroid Stimulating Hormone, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	1	0	0	1
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Thyroid Stimulating Hormone, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	1	0	0	1
L	N	0	0	1	0	0	1
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	100	0	0	100
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Free T3, Treatment Group:Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	1	0	0	1
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter:Free T3, Treatment Group:Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	2	0	0	2
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Total Free Thyroxine, Treatment Group: Paroxetine CR 12.5 mg

=====							
BASELINE				Endpoint			
		+	H	I	L	-	T

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	0	1	0	1
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	0	100	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.30

Number (%) of Subjects with Transitions from Baseline to Endpoint
 By Laboratory Parameter
 Intention-to-Treat Population
 Parameter: Total Free Thyroxine, Treatment Group: Placebo

=====							
BASELINE		+	H	Endpoint		-	T
				I	L		

+	N	0	0	0	0	0	0
H	N	0	0	0	0	0	0
I	N	0	0	2	0	0	2
L	N	0	0	0	0	0	0
-	N	0	0	0	0	0	0
+	%	0	0	0	0	0	0
H	%	0	0	0	0	0	0
I	%	0	0	100	0	0	100
L	%	0	0	0	0	0	0
-	%	0	0	0	0	0	0

+ : Above Clinical Concern High, H : Above Normal Range High, I : In Range
 L : Below Normal Range Low, - : Below Clinical Concern Low, T: Total
 Baseline is last measurement prior to the start of randomised study medication
 Endpoint is the last available value on treatment or within 14 days of the last study dose

Table 15.31

Number (%) of Subjects with Positive Serum Pregnancy Test Results During the Treatment or Follow-up Phase
Intention-to-Treat Population

NO DATA AVAILABLE FOR THIS REPORT

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 25 mg

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Hemoglobin	Grams per Litre	Baseline	112	131.46	8.7938	131.16	106.35	153.88
		On Treatment	2	132.53	6.2665	132.53	128.10	136.96
		Endpoint	92	129.60	8.1369	129.31	111.18	153.07
		Endpoint Change	92	-1.643	6.2986	-1.208	-19.34	16.113
Hematocrit	Percentage	Baseline	112	39.333	2.9116	39.000	32.000	52.000
		On Treatment	2	38.500	2.1213	38.500	37.000	40.000
		Endpoint	92	38.429	2.4400	38.000	32.000	46.000
		Endpoint Change	92	-0.671	1.9169	-0.950	-7.000	4.000
Red Blood Cell Count	10 ¹² per Litre	Baseline	112	4.287	0.3295	4.300	3.600	6.000
		On Treatment	2	4.200	0.2828	4.200	4.000	4.400
		Endpoint	92	4.205	0.2884	4.200	3.300	4.800
		Endpoint Change	92	-0.060	0.1973	-0.100	-0.700	0.500
White Blood Cell Count	10 ⁹ per Litre	Baseline	112	6.842	1.7324	6.500	3.300	11.400
		On Treatment	2	6.550	1.9092	6.550	5.200	7.900
		Endpoint	92	6.415	1.8720	6.000	3.600	12.700
		Endpoint Change	92	-0.375	1.5921	-0.500	-5.300	4.100
Segmented Neutrophils	10 ⁹ per Litre	Baseline	112	4.378	1.3695	4.192	1.942	8.456
		On Treatment	2	3.661	1.1690	3.661	2.834	4.487
		Endpoint	92	3.875	1.4615	3.650	1.404	8.303
		Endpoint Change	92	-0.467	1.3679	-0.498	-4.808	3.956
Platelets	10 ⁹ per Litre	Baseline	111	277.45	57.813	273.00	153.00	424.00
		On Treatment	2	249.50	64.347	249.50	204.00	295.00
		Endpoint	90	263.44	56.864	261.50	162.00	414.00
		Endpoint Change	90	-8.611	30.502	-6.500	-101.0	65.000
Blood Urea Nitrogen	Millimoles per Litre	Baseline	115	4.556	1.1141	4.500	2.500	7.497
		On Treatment	2	3.300	0.0000	3.300	3.300	3.300
		Endpoint	93	4.620	0.9905	4.641	2.499	7.497
		Endpoint Change	93	0.033	0.8348	0.000	-2.300	1.800
Creatinine	Micromoles per Litre	Baseline	113	63.119	10.742	62.000	41.000	103.00
		On Treatment	2	55.500	6.3640	55.500	51.000	60.000
		Endpoint	93	62.166	10.458	61.880	36.000	94.000
		Endpoint Change	91	-1.566	9.6763	0.000	-46.00	18.000
Alkaline Phosphatase	International Units	Baseline	113	60.018	16.681	57.000	26.000	118.00
		On Treatment	2	46.500	2.1213	46.500	45.000	48.000
		Endpoint	93	59.978	16.162	57.000	25.000	103.00

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 25 mg

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Alkaline Phosphatase	International Units	Endpoint Change	91	-0.549	7.9656	0.000	-28.00	22.000
Aspartate Aminotransferase	International Units	Baseline	114	17.658	4.6102	17.000	10.000	46.000
		On Treatment	2	16.500	4.9497	16.500	13.000	20.000
		Endpoint	93	18.462	4.7194	17.000	10.000	40.000
		Endpoint Change	92	0.935	3.7234	1.000	-9.000	15.000
Alanine Aminotransferase	International Units	Baseline	114	14.105	6.1333	13.000	3.000	36.000
		On Treatment	2	9.500	3.5355	9.500	7.000	12.000
		Endpoint	93	14.505	6.0029	13.000	4.000	35.000
		Endpoint Change	92	0.391	5.0687	0.000	-13.00	14.000
Total Bilirubin	Micromoles per Litre	Baseline	114	9.022	3.6474	9.000	3.000	21.000
		On Treatment	2	11.000	4.2426	11.000	8.000	14.000
		Endpoint	93	9.774	5.1856	8.550	3.000	30.000
		Endpoint Change	92	0.456	3.8663	0.000	-6.000	18.000
Total Protein	Grams per Litre	Baseline	115	71.183	3.9859	71.000	64.000	89.000
		On Treatment	2	69.500	0.7071	69.500	69.000	70.000
		Endpoint	93	69.849	3.3361	70.000	61.000	76.000
		Endpoint Change	93	-0.978	3.2770	-1.000	-11.00	7.000
Albumin	Grams per Litre	Baseline	114	44.140	2.0776	44.000	38.000	50.000
		On Treatment	2	45.000	0.0000	45.000	45.000	45.000
		Endpoint	93	43.656	1.8910	44.000	36.000	48.000
		Endpoint Change	92	-0.380	1.9603	0.000	-6.000	5.000
Globulin	Grams per Litre	Baseline	114	27.026	3.1608	27.000	18.000	41.000
		On Treatment	2	24.500	0.7071	24.500	24.000	25.000
		Endpoint	93	26.194	2.7436	26.000	18.000	32.000
		Endpoint Change	92	-0.554	2.1553	0.000	-7.000	4.000
Thyroid Stimulating Hormone	MU/L	Baseline	114	1.547	0.8649	1.450	0.200	6.600
		Endpoint	1	4.300		4.300	4.300	4.300
		Endpoint Change	1	-2.300		-2.300	-2.300	-2.300
Basophils Absolute	10 ⁹ per Litre	Baseline	112	0.019	0.0138	0.020	0.000	0.060
		On Treatment	2	0.025	0.0071	0.025	0.020	0.030
		Endpoint	92	0.018	0.0126	0.015	0.000	0.070
		Endpoint Change	92	-0.000	0.0166	0.000	-0.050	0.040
Eosinophils Absolute	10 ⁹ per Litre	Baseline	112	0.161	0.1146	0.130	0.010	0.520
		On Treatment	2	0.170	0.0566	0.170	0.130	0.210

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 25 mg

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Eosinophils Absolute	10 ⁹ per Litre	Endpoint	92	0.171	0.1147	0.150	0.010	0.550
		Endpoint Change	92	0.009	0.0901	0.010	-0.360	0.230
Free T3	Picomoles per Litre	Baseline	114	4.442	0.4395	4.400	3.300	5.529
Lymphocytes Absolute	10 ⁹ per Litre	Baseline	112	1.914	0.5853	1.790	0.850	4.020
		On Treatment	2	2.225	0.7142	2.225	1.720	2.730
		Endpoint	92	1.989	0.6201	1.960	0.590	4.600
		Endpoint Change	92	0.087	0.4879	0.120	-1.560	1.740
Monocytes Absolute	10 ⁹ per Litre	Baseline	112	0.370	0.1457	0.345	0.070	1.030
		On Treatment	2	0.480	0.0990	0.480	0.410	0.550
		Endpoint	92	0.362	0.1599	0.330	0.080	0.950
		Endpoint Change	92	-0.004	0.1494	-0.005	-0.430	0.600
Neutrophils Absolute	10 ⁹ per Litre	Baseline	112	4.378	1.3699	4.195	1.940	8.460
		On Treatment	2	3.660	1.1738	3.660	2.830	4.490
		Endpoint	92	3.875	1.4621	3.650	1.400	8.300
		Endpoint Change	92	-0.467	1.3685	-0.505	-4.810	3.950
Total Free Thyroxine	Picomoles per Litre	Baseline	114	14.441	1.9861	14.190	10.320	20.100

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 12.5 mg

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Hemoglobin	Grams per Litre	Baseline	127	130.41	8.2495	130.00	106.00	149.05
		On Treatment	5	128.32	8.1804	128.10	116.01	136.15
		Endpoint	100	128.87	7.6591	128.50	107.96	145.82
		Endpoint Change	100	-1.596	6.5129	-0.903	-27.39	12.085
Hematocrit	Percentage	Baseline	127	38.996	2.3984	39.000	32.800	45.000
		On Treatment	5	38.100	1.8841	37.000	36.500	41.000
		Endpoint	100	38.479	2.3149	38.000	32.000	44.300
		Endpoint Change	100	-0.499	2.0029	-0.650	-7.000	4.300
Red Blood Cell Count	10 ¹² per Litre	Baseline	127	4.285	0.3117	4.300	3.600	5.400
		On Treatment	5	4.500	0.6124	4.300	3.900	5.500
		Endpoint	100	4.225	0.2879	4.200	3.500	5.500
		Endpoint Change	100	-0.068	0.2127	0.000	-0.900	0.400
White Blood Cell Count	10 ⁹ per Litre	Baseline	127	6.319	1.7082	6.100	2.500	12.200
		On Treatment	5	7.140	1.5469	6.900	4.900	9.000
		Endpoint	100	6.239	1.7535	6.050	2.400	13.200
		Endpoint Change	100	-0.085	1.5435	0.050	-5.700	3.300
Segmented Neutrophils	10 ⁹ per Litre	Baseline	126	3.925	1.3684	3.677	1.173	8.808
		On Treatment	5	4.331	1.4882	4.332	2.293	5.949
		Endpoint	100	3.820	1.4106	3.643	0.934	10.969
		Endpoint Change	99	-0.114	1.3915	0.079	-4.828	4.179
Platelets	10 ⁹ per Litre	Baseline	126	286.22	61.502	283.00	158.00	517.00
		On Treatment	5	304.20	25.577	297.00	276.00	342.00
		Endpoint	100	276.44	59.821	277.00	116.00	462.00
		Endpoint Change	100	-6.050	41.992	-9.000	-96.00	173.00
Blood Urea Nitrogen	Millimoles per Litre	Baseline	129	4.326	1.0458	4.200	1.800	7.200
		On Treatment	7	4.849	0.4688	4.700	4.300	5.600
		Endpoint	102	4.319	0.8934	4.300	2.142	6.500
		Endpoint Change	101	-0.022	1.1591	0.000	-3.500	2.500
Creatinine	Micromoles per Litre	Baseline	129	61.797	10.019	61.880	44.000	100.00
		On Treatment	7	60.674	8.9604	60.000	44.000	70.720
		Endpoint	102	63.850	12.659	61.880	42.000	140.00
		Endpoint Change	101	1.868	11.686	0.000	-32.00	61.000
Alkaline Phosphatase	International Units	Baseline	129	60.062	16.504	58.000	34.000	114.00
		On Treatment	7	51.143	3.6253	53.000	47.000	55.000
		Endpoint	102	59.588	15.668	54.500	34.000	108.00

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 12.5 mg

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Alkaline Phosphatase	International Units	Endpoint Change	101	-0.347	7.3436	0.000	-35.00	15.000
Aspartate Aminotransferase	International Units	Baseline	129	18.938	8.9344	17.000	9.000	91.000
		On Treatment	7	14.857	3.1320	15.000	11.000	19.000
		Endpoint	102	19.745	13.834	17.000	10.000	144.00
		Endpoint Change	101	0.465	7.7647	0.000	-30.00	53.000
Alanine Aminotransferase	International Units	Baseline	129	15.357	8.9152	13.000	5.000	62.000
		On Treatment	7	13.714	4.6445	12.000	9.000	23.000
		Endpoint	102	16.216	11.382	13.000	7.000	95.000
		Endpoint Change	101	0.475	9.3398	0.000	-43.00	48.000
Total Bilirubin	Micromoles per Litre	Baseline	129	8.875	4.1699	8.000	2.000	32.490
		On Treatment	7	7.120	1.9547	6.840	5.000	11.000
		Endpoint	102	9.305	3.2953	9.000	2.000	22.000
		Endpoint Change	101	0.639	3.7112	1.000	-9.000	8.000
Total Protein	Grams per Litre	Baseline	129	71.326	3.7169	71.000	65.000	83.000
		On Treatment	7	70.143	4.0999	70.000	65.000	78.000
		Endpoint	102	70.324	3.7022	70.000	63.000	81.000
		Endpoint Change	101	-1.287	3.4766	-1.000	-17.00	8.000
Albumin	Grams per Litre	Baseline	129	44.333	2.0207	44.000	40.000	51.000
		On Treatment	7	44.286	2.8115	44.000	41.000	49.000
		Endpoint	102	43.971	2.0121	44.000	39.000	49.000
		Endpoint Change	101	-0.505	1.9628	-1.000	-5.000	4.000
Globulin	Grams per Litre	Baseline	129	26.992	3.0246	27.000	21.000	38.000
		On Treatment	7	25.857	2.7343	27.000	21.000	29.000
		Endpoint	102	26.353	2.8792	26.000	21.000	35.000
		Endpoint Change	101	-0.782	2.1982	-1.000	-12.00	5.000
Thyroid Stimulating Hormone	MU/L	Baseline	129	1.650	1.1511	1.400	0.300	10.700
		On Treatment	1	1.600		1.600	1.600	1.600
		Endpoint	2	1.300	0.4243	1.300	1.000	1.600
		Endpoint Change	1	-0.100		-0.100	-0.100	-0.100
Basophils Absolute	10 ⁹ per Litre	Baseline	126	0.017	0.0099	0.020	0.000	0.050
		On Treatment	5	0.016	0.0114	0.020	0.000	0.030
		Endpoint	100	0.018	0.0106	0.020	0.000	0.050
		Endpoint Change	99	-0.000	0.0132	0.000	-0.040	0.030
Eosinophils Absolute	10 ⁹ per Litre	Baseline	126	0.161	0.1233	0.140	0.010	0.720

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Paroxetine CR 12.5 mg

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Eosinophils Absolute	10 ⁹ per Litre	On Treatment	5	0.186	0.0838	0.220	0.050	0.270
		Endpoint	100	0.171	0.1414	0.135	0.010	1.050
		Endpoint Change	99	0.010	0.1098	0.000	-0.350	0.350
Free T3	Picomoles per Litre	Baseline	129	4.499	0.4236	4.500	3.200	6.145
		On Treatment	1	4.800		4.800	4.800	4.800
		Endpoint	2	4.500	0.4243	4.500	4.200	4.800
		Endpoint Change	1	-0.100		-0.100	-0.100	-0.100
Lymphocytes Absolute	10 ⁹ per Litre	Baseline	126	1.861	0.5379	1.820	0.720	3.370
		On Treatment	5	2.214	0.4067	1.990	1.880	2.710
		Endpoint	100	1.906	0.6110	1.830	0.460	3.340
		Endpoint Change	99	0.050	0.4879	0.050	-1.400	1.570
Monocytes Absolute	10 ⁹ per Litre	Baseline	126	0.348	0.1267	0.340	0.070	0.760
		On Treatment	5	0.394	0.1893	0.450	0.070	0.560
		Endpoint	100	0.325	0.1290	0.310	0.060	0.640
		Endpoint Change	99	-0.031	0.1325	-0.020	-0.500	0.250
Neutrophils Absolute	10 ⁹ per Litre	Baseline	126	3.925	1.3682	3.680	1.170	8.810
		On Treatment	5	4.330	1.4895	4.330	2.290	5.950
		Endpoint	100	3.821	1.4106	3.645	0.930	10.970
		Endpoint Change	99	-0.114	1.3912	0.080	-4.830	4.180
Total Free Thyroxine	Picomoles per Litre	Baseline	129	14.248	1.7865	14.190	10.500	21.900
		On Treatment	1	15.400		15.400	15.400	15.400
		Endpoint	2	12.600	3.9598	12.600	9.800	15.400
		Endpoint Change	1	-1.600		-1.600	-1.600	-1.600

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Placebo

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Hemoglobin	Grams per Litre	Baseline	116	129.70	8.5398	128.95	103.93	151.00
		On Treatment	5	133.37	8.7547	135.00	120.04	141.79
		Endpoint	98	130.10	8.9647	132.13	98.289	148.24
		Endpoint Change	98	0.754	6.4303	0.806	-19.34	21.753
Hematocrit	Percentage	Baseline	116	38.914	2.3751	39.000	33.000	44.700
		On Treatment	5	40.500	2.6239	40.300	37.000	43.900
		Endpoint	98	38.615	2.5843	39.000	30.000	44.600
		Endpoint Change	98	-0.202	1.9298	0.000	-5.000	5.300
Red Blood Cell Count	10 ¹² per Litre	Baseline	116	4.294	0.2863	4.300	3.600	5.200
		On Treatment	5	4.300	0.3317	4.400	3.800	4.700
		Endpoint	98	4.270	0.2908	4.300	3.500	5.000
		Endpoint Change	98	-0.010	0.1987	0.000	-0.600	0.500
White Blood Cell Count	10 ⁹ per Litre	Baseline	116	6.505	1.8611	6.200	3.400	14.700
		On Treatment	5	7.380	1.0592	7.400	6.200	8.900
		Endpoint	98	6.476	1.8363	6.200	3.200	13.200
		Endpoint Change	98	0.085	1.6529	0.150	-4.800	6.400
Segmented Neutrophils	10 ⁹ per Litre	Baseline	115	4.075	1.5832	3.803	1.352	10.731
		On Treatment	5	4.589	1.0807	4.958	2.827	5.447
		Endpoint	98	3.997	1.5415	3.758	1.034	9.240
		Endpoint Change	97	-0.013	1.4801	0.082	-4.925	5.832
Platelets	10 ⁹ per Litre	Baseline	116	281.53	59.198	280.00	153.00	490.00
		On Treatment	5	323.80	111.57	334.00	193.00	477.00
		Endpoint	98	278.30	63.675	281.00	154.00	477.00
		Endpoint Change	98	-2.112	35.740	-4.500	-80.00	97.000
Blood Urea Nitrogen	Millimoles per Litre	Baseline	118	4.468	1.0394	4.300	2.200	7.700
		On Treatment	7	3.744	1.0872	3.600	2.800	5.712
		Endpoint	102	4.358	0.9073	4.284	2.500	6.600
		Endpoint Change	100	-0.056	0.8727	0.000	-2.400	2.000
Creatinine	Micromoles per Litre	Baseline	117	63.493	12.502	61.880	42.000	146.00
		On Treatment	7	68.474	16.630	60.000	53.040	100.00
		Endpoint	103	62.783	9.8054	63.000	39.000	100.00
		Endpoint Change	100	-0.610	11.975	0.000	-74.00	26.000
Alkaline Phosphatase	International Units	Baseline	117	59.744	16.138	58.000	29.000	111.00
		On Treatment	7	66.714	19.172	65.000	45.000	98.000
		Endpoint	103	60.883	20.589	58.000	28.000	167.00

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Placebo

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Alkaline Phosphatase	International Units	Endpoint Change	100	1.110	13.787	0.000	-15.00	119.00
Aspartate Aminotransferase	International Units	Baseline	117	16.932	4.9336	16.000	8.000	40.000
		On Treatment	7	17.429	3.9521	19.000	12.000	23.000
		Endpoint	103	19.311	11.698	17.000	9.000	114.00
		Endpoint Change	100	2.150	10.736	1.000	-9.000	96.000
Alanine Aminotransferase	International Units	Baseline	117	13.769	7.4236	12.000	6.000	66.000
		On Treatment	7	12.857	4.0999	12.000	8.000	19.000
		Endpoint	103	17.049	22.279	12.000	6.000	217.00
		Endpoint Change	100	3.070	21.159	1.000	-34.00	199.00
Total Bilirubin	Micromoles per Litre	Baseline	117	8.941	4.7338	8.000	1.000	30.000
		On Treatment	7	11.010	6.6743	10.260	3.000	20.000
		Endpoint	103	9.971	4.8882	9.000	3.000	31.000
		Endpoint Change	100	0.848	3.0202	1.000	-10.00	8.000
Total Protein	Grams per Litre	Baseline	118	70.568	3.3626	71.000	61.000	80.000
		On Treatment	7	70.714	5.4380	71.000	65.000	81.000
		Endpoint	103	70.515	3.7308	70.000	61.000	81.000
		Endpoint Change	101	-0.089	3.0037	0.000	-11.00	8.000
Albumin	Grams per Litre	Baseline	118	44.153	1.8748	44.000	40.000	51.000
		On Treatment	7	44.571	2.7603	45.000	41.000	48.000
		Endpoint	103	44.078	1.8508	44.000	40.000	49.000
		Endpoint Change	101	-0.158	1.9428	0.000	-7.000	6.000
Globulin	Grams per Litre	Baseline	118	26.415	2.7960	26.000	20.000	34.000
		On Treatment	7	26.143	3.5790	26.000	22.000	33.000
		Endpoint	103	26.437	3.1829	26.000	20.000	36.000
		Endpoint Change	101	0.069	2.0162	0.000	-5.000	8.000
Thyroid Stimulating Hormone	MU/L	Baseline	117	1.726	2.0827	1.400	0.100	21.700
		On Treatment	2	1.700	1.5556	1.700	0.600	2.800
		Endpoint	4	1.325	0.9979	0.950	0.600	2.800
		Endpoint Change	2	0.450	0.4950	0.450	0.100	0.800
Basophils Absolute	10 ⁹ per Litre	Baseline	115	0.018	0.0160	0.020	0.000	0.140
		On Treatment	5	0.016	0.0055	0.020	0.010	0.020
		Endpoint	98	0.021	0.0123	0.020	0.000	0.080
		Endpoint Change	97	0.002	0.0199	0.000	-0.120	0.050
Eosinophils Absolute	10 ⁹ per Litre	Baseline	115	0.163	0.1144	0.130	0.010	0.600

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.33

Summary Statistics for Visit and Change from Baseline for Laboratory Parameters
By Treatment Group and Visit
Intention-to-Treat Population

Treatment Group: Placebo

Parameter	Units	Visit	N	Mean	Std Dev	Median	Min	Max
Eosinophils Absolute	10 ⁹ per Litre	On Treatment	5	0.136	0.0550	0.110	0.080	0.220
		Endpoint	98	0.182	0.1300	0.145	0.000	0.760
		Endpoint Change	97	0.017	0.1146	0.010	-0.310	0.560
Free T3	Picomoles per Litre	Baseline	118	4.470	0.6340	4.400	2.900	9.394
		On Treatment	2	5.050	0.4950	5.050	4.700	5.400
		Endpoint	4	4.775	0.4349	4.650	4.400	5.400
		Endpoint Change	2	-0.050	0.0707	-0.050	-0.100	0.000
Lymphocytes Absolute	10 ⁹ per Litre	Baseline	115	1.904	0.5032	1.880	1.010	3.320
		On Treatment	5	2.268	0.5037	1.980	1.810	2.850
		Endpoint	98	1.924	0.5347	1.890	0.790	3.820
		Endpoint Change	97	0.064	0.4821	0.030	-0.990	2.520
Monocytes Absolute	10 ⁹ per Litre	Baseline	115	0.366	0.1332	0.350	0.020	0.910
		On Treatment	5	0.370	0.0935	0.370	0.230	0.460
		Endpoint	98	0.353	0.1485	0.340	0.080	0.870
		Endpoint Change	97	-0.004	0.1417	-0.010	-0.510	0.420
Neutrophils Absolute	10 ⁹ per Litre	Baseline	115	4.075	1.5833	3.800	1.350	10.730
		On Treatment	5	4.590	1.0800	4.960	2.830	5.450
		Endpoint	98	3.997	1.5411	3.755	1.030	9.240
		Endpoint Change	97	-0.013	1.4794	0.080	-4.920	5.830
Total Free Thyroxine	Picomoles per Litre	Baseline	118	14.710	2.1298	14.400	8.700	21.400
		On Treatment	2	14.750	1.9092	14.750	13.400	16.100
		Endpoint	4	14.400	1.6104	14.400	12.700	16.100
		Endpoint Change	2	-0.900	1.4142	-0.900	-1.900	0.100

Baseline is the last measurement prior to the start of randomised study medication
Endpoint is last on measurement on treatment or in the 14 day follow-up

Table 15.34

Number (%) of Subjects Exposed to Study Medication
By Treatment Group and Time Intervals
Intention-to-Treat Population

Days	Treatment Group			
	Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)	Total (N=366)
1-7 Days	7 (6.0%)	5 (3.8%)	1 (0.8%)	13 (3.6%)
8-14 Days	9 (7.8%)	4 (3.1%)	1 (0.8%)	14 (3.8%)
15-21 Days	3 (2.6%)	8 (6.2%)	3 (2.5%)	14 (3.8%)
22-28 Days	2 (1.7%)	5 (3.8%)	6 (5.0%)	13 (3.6%)
29-44 Days	62 (53.4%)	69 (53.1%)	73 (60.8%)	204 (55.7%)
45-60 Days	33 (28.4%)	37 (28.5%)	34 (28.3%)	104 (28.4%)
>=61 Days	116 (100.0%)	130 (100.0%)	120 (100.0%)	366 (100.0%)
Total Years	11.6	13.8	13.4	38.7
Overall Mean	36.5	38.6	40.8	38.7
Std Dev	12.83	12.85	8.82	11.77
Median	41.0	41.0	42.0	41.0
Min	4	1	7	1
Max	53	88	65	88

Table 15.35 Narrative Locator Table

Subject Number	Non-fatal SAE	Withdrawn for AE	Lab Value of Concern
This section contained data from each individual patient, rather than in aggregate. They have been excluded to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the Sponsor Clinical Study Register.			

*This section contained patient narratives which are textual descriptions of medical history, treatment and outcome for individual patients who experienced a clinically important adverse event including serious adverse events during the trial. They have been excluded to protect patient privacy. This data may be made available subject to an approved research proposal and a determination of the ability to provide information from the specific narratives whilst protecting the patient's privacy. For further information please see the Patient Level Data section of the **GSK Clinical Study Register**.*

Supplementary Table 15.1

Number (%) of Subjects with Treatment Emergent Adverse Events Occurring in 5% or More of the Paroxetine CR Subjects
and at Least Twice the Incidence of Placebo*
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	Treatment Group		
		Paroxetine CR 25 mg (N=116)	Paroxetine CR 12.5 mg (N=130)	Placebo (N=120)
TOTAL	TOTAL	60 (51.7%)	51 (39.2%)	20 (16.7%)
Body as a Whole	TOTAL	22 (19.0%)	16 (12.3%)	5 (4.2%)
	ASTHENIA	22 (19.0%)	16 (12.3%)	5 (4.2%)
Digestive System	TOTAL	32 (27.6%)	22 (16.9%)	2 (1.7%)
	DIARRHEA	8 (6.9%)	7 (5.4%)	0 (0.0%)
	NAUSEA	27 (23.3%)	16 (12.3%)	2 (1.7%)
Nervous System	TOTAL	25 (21.6%)	26 (20.0%)	13 (10.8%)
	DIZZINESS	8 (6.9%)	7 (5.4%)	3 (2.5%)
	INSOMNIA	4 (3.4%)	13 (10.0%)	3 (2.5%)
	LIBIDO DECREASED	15 (12.9%)	7 (5.4%)	7 (5.8%)
	TREMOR	7 (6.0%)	4 (3.1%)	0 (0.0%)
Respiratory System	TOTAL	3 (2.6%)	7 (5.4%)	2 (1.7%)
	SINUSITIS	3 (2.6%)	7 (5.4%)	2 (1.7%)
Skin and Appendages	TOTAL	10 (8.6%)	4 (3.1%)	1 (0.8%)
	SWEATING	10 (8.6%)	4 (3.1%)	1 (0.8%)

* In comparison with either Parox CR 25mg or Parox CR 12.5mg
Total Number of Subjects 366
Total Number of Subjects with AEs 245

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: ACETYLSALICYLIC ACID

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=3)	No (N=113)	Yes (N=10)	No (N=120)	Yes (N=9)	No (N=111)
TOTAL	2 (66.7%)	87 (77.0%)	7 (70.0%)	81 (67.5%)	8 (88.9%)	60 (54.1%)
Body as a Whole	0 (0.0%)	50 (44.2%)	3 (30.0%)	39 (32.5%)	5 (55.6%)	32 (28.8%)
ABDOMINAL PAIN	0 (0.0%)	4 (3.5%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (0.9%)	2 (20.0%)	0 (0.0%)	0 (0.0%)	3 (2.7%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	0 (0.0%)	22 (19.5%)	0 (0.0%)	16 (13.3%)	0 (0.0%)	5 (4.5%)
BACK PAIN	0 (0.0%)	2 (1.8%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	5 (4.5%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHILLS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FLU SYNDROME	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HEADACHE	0 (0.0%)	18 (15.9%)	3 (30.0%)	13 (10.8%)	4 (44.4%)	13 (11.7%)
INFECTION	0 (0.0%)	10 (8.8%)	0 (0.0%)	5 (4.2%)	2 (22.2%)	6 (5.4%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	2 (1.8%)	0 (0.0%)	2 (1.7%)	1 (11.1%)	1 (0.9%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.8%)	1 (10.0%)	2 (1.7%)	0 (0.0%)	4 (3.6%)
Cardiovascular System	1 (33.3%)	2 (1.8%)	2 (20.0%)	5 (4.2%)	1 (11.1%)	3 (2.7%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	1 (11.1%)	2 (1.8%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	2 (66.7%)	41 (36.3%)	4 (40.0%)	29 (24.2%)	0 (0.0%)	11 (9.9%)
COLITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (2.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
DECREASED APPETITE	0 (0.0%)	4 (3.5%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DIARRHEA	0 (0.0%)	8 (7.1%)	0 (0.0%)	7 (5.8%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	0 (0.0%)	3 (2.7%)	1 (10.0%)	2 (1.7%)	0 (0.0%)	1 (0.9%)
DYSPEPSIA	1 (33.3%)	2 (1.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.8%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: ACETYSALICYLIC ACID

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=3)	No (N=113)	Yes (N=10)	No (N=120)	Yes (N=9)	No (N=111)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
GASTROENTERITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
NAUSEA	0 (0.0%)	27 (23.9%)	2 (20.0%)	14 (11.7%)	0 (0.0%)	2 (1.8%)
TOOTH DISORDER	1 (33.3%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
VOMITING	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	0 (0.0%)	4 (3.5%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	3 (2.7%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.9%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Musculoskeletal System	1 (33.3%)	1 (0.9%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	7 (6.3%)
ARTHRALGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
MYALGIA	1 (33.3%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.7%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
Nervous System	1 (33.3%)	36 (31.9%)	3 (30.0%)	35 (29.2%)	2 (22.2%)	15 (13.5%)
ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (1.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.7%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.5%)	1 (11.1%)	0 (0.0%)
DIZZINESS	0 (0.0%)	8 (7.1%)	1 (10.0%)	6 (5.0%)	0 (0.0%)	3 (2.7%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: ACETYLSALICYLIC ACID

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=3)	No (N=113)	Yes (N=10)	No (N=120)	Yes (N=9)	No (N=111)
INCOORDINATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	4 (3.5%)	2 (20.0%)	11 (9.2%)	0 (0.0%)	3 (2.7%)
LACK OF EMOTION	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	1 (33.3%)	14 (12.4%)	0 (0.0%)	7 (5.8%)	1 (11.1%)	6 (5.4%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (0.9%)	1 (10.0%)	5 (4.2%)	0 (0.0%)	2 (1.8%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	0 (0.0%)	5 (4.4%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	1 (0.9%)
THINKING ABNORMAL	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TREMOR	0 (0.0%)	7 (6.2%)	2 (20.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	1 (0.9%)
Respiratory System	0 (0.0%)	13 (11.5%)	2 (20.0%)	18 (15.0%)	4 (44.4%)	14 (12.6%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
EPISTAXIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (4.5%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
RESPIRATORY DISORDER	0 (0.0%)	5 (4.4%)	2 (20.0%)	7 (5.8%)	4 (44.4%)	9 (8.1%)
SINUSITIS	0 (0.0%)	3 (2.7%)	0 (0.0%)	7 (5.8%)	0 (0.0%)	2 (1.8%)
YAWN	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	0 (0.0%)	12 (10.6%)	1 (10.0%)	9 (7.5%)	0 (0.0%)	9 (8.1%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.9%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HERPES SIMPLEX	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
PUSTULAR RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SWEATING	0 (0.0%)	10 (8.8%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	1 (0.9%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: ACETYSALICYLIC ACID

Body System Preferred Term	---Paroxetine CR 25 mg---		--Paroxetine CR 12.5 mg--		-----Placebo-----	
	Yes (N=3)	No (N=113)	Yes (N=10)	No (N=120)	Yes (N=9)	No (N=111)
Special Senses	0 (0.0%)	4 (3.5%)	1 (10.0%)	4 (3.3%)	1 (11.1%)	1 (0.9%)
ABNORMAL VISION	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (11.1%)	1 (0.9%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Urogenital System	2 (66.7%)	14 (12.4%)	0 (0.0%)	13 (10.8%)	3 (33.3%)	10 (9.0%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.7%)
DYSMENORRHEA	1 (33.3%)	3 (2.7%)	0 (0.0%)	4 (3.3%)	2 (22.2%)	2 (1.8%)
FEMALE GENITAL DISORDERS	0 (0.0%)	3 (2.7%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)
LEUKORRHEA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MENSTRUAL DISORDER	1 (33.3%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
VAGINAL MONILIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins

The Top 5 Medications are Presented in Alphabetical Order

Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: CAFFEINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=2)	No (N=114)	Yes (N=5)	No (N=125)	Yes (N=5)	No (N=115)
TOTAL	2 (100.0%)	87 (76.3%)	2 (40.0%)	86 (68.8%)	5 (100.0%)	63 (54.8%)
Body as a Whole	0 (0.0%)	50 (43.9%)	1 (20.0%)	41 (32.8%)	3 (60.0%)	34 (29.6%)
ABDOMINAL PAIN	0 (0.0%)	4 (3.5%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (0.9%)	1 (20.0%)	1 (0.8%)	0 (0.0%)	3 (2.6%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	0 (0.0%)	22 (19.3%)	0 (0.0%)	16 (12.8%)	0 (0.0%)	5 (4.3%)
BACK PAIN	0 (0.0%)	2 (1.8%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	5 (4.3%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHILLS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FLU SYNDROME	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HEADACHE	0 (0.0%)	18 (15.8%)	1 (20.0%)	15 (12.0%)	2 (40.0%)	15 (13.0%)
INFECTION	0 (0.0%)	10 (8.8%)	0 (0.0%)	5 (4.0%)	0 (0.0%)	8 (7.0%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	2 (1.8%)	0 (0.0%)	2 (1.6%)	1 (20.0%)	1 (0.9%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	1 (20.0%)	3 (2.6%)
Cardiovascular System	0 (0.0%)	3 (2.6%)	1 (20.0%)	6 (4.8%)	0 (0.0%)	4 (3.5%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	3 (2.6%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	2 (100.0%)	41 (36.0%)	2 (40.0%)	31 (24.8%)	0 (0.0%)	11 (9.6%)
COLITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (2.6%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
DECREASED APPETITE	0 (0.0%)	4 (3.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
DIARRHEA	0 (0.0%)	8 (7.0%)	0 (0.0%)	7 (5.6%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	0 (0.0%)	3 (2.6%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
DYSPEPSIA	0 (0.0%)	3 (2.6%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (1.7%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: CAFFEINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=2)	No (N=114)	Yes (N=5)	No (N=125)	Yes (N=5)	No (N=115)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
GASTROENTERITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
NAUSEA	1 (50.0%)	26 (22.8%)	2 (40.0%)	14 (11.2%)	0 (0.0%)	2 (1.7%)
TOOTH DISORDER	1 (50.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
VOMITING	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	0 (0.0%)	4 (3.5%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	3 (2.6%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.9%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Musculoskeletal System	1 (50.0%)	1 (0.9%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	7 (6.1%)
ARTHRALGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
MYALGIA	1 (50.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	3 (2.6%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
Nervous System	1 (50.0%)	36 (31.6%)	1 (20.0%)	37 (29.6%)	1 (20.0%)	16 (13.9%)
ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (1.8%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	3 (2.6%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
DIZZINESS	0 (0.0%)	8 (7.0%)	1 (20.0%)	6 (4.8%)	0 (0.0%)	3 (2.6%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: CAFFEINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=2)	No (N=114)	Yes (N=5)	No (N=125)	Yes (N=5)	No (N=115)
INCOORDINATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	4 (3.5%)	0 (0.0%)	13 (10.4%)	0 (0.0%)	3 (2.6%)
LACK OF EMOTION	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	1 (50.0%)	14 (12.3%)	0 (0.0%)	7 (5.6%)	1 (20.0%)	6 (5.2%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (0.9%)	0 (0.0%)	6 (4.8%)	0 (0.0%)	2 (1.7%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	0 (0.0%)	5 (4.4%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
THINKING ABNORMAL	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TREMOR	0 (0.0%)	7 (6.1%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
Respiratory System	0 (0.0%)	13 (11.4%)	0 (0.0%)	20 (16.0%)	2 (40.0%)	16 (13.9%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
EPISTAXIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	0 (0.0%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (4.3%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
RESPIRATORY DISORDER	0 (0.0%)	5 (4.4%)	0 (0.0%)	9 (7.2%)	2 (40.0%)	11 (9.6%)
SINUSITIS	0 (0.0%)	3 (2.6%)	0 (0.0%)	7 (5.6%)	0 (0.0%)	2 (1.7%)
YAWN	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	0 (0.0%)	12 (10.5%)	0 (0.0%)	10 (8.0%)	0 (0.0%)	9 (7.8%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.9%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HERPES SIMPLEX	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
PUSTULAR RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SWEATING	0 (0.0%)	10 (8.8%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	1 (0.9%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: CAFFEINE

Body System Preferred Term	---Paroxetine CR 25 mg---		--Paroxetine CR 12.5 mg--		-----Placebo-----	
	Yes (N=2)	No (N=114)	Yes (N=5)	No (N=125)	Yes (N=5)	No (N=115)
Special Senses	0 (0.0%)	4 (3.5%)	0 (0.0%)	5 (4.0%)	0 (0.0%)	2 (1.7%)
ABNORMAL VISION	0 (0.0%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Urogenital System	1 (50.0%)	15 (13.2%)	0 (0.0%)	13 (10.4%)	4 (80.0%)	9 (7.8%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	1 (20.0%)	2 (1.7%)
DYSMENORRHEA	1 (50.0%)	3 (2.6%)	0 (0.0%)	4 (3.2%)	2 (40.0%)	2 (1.7%)
FEMALE GENITAL DISORDERS	0 (0.0%)	3 (2.6%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)
LEUKORRHEA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MENSTRUAL DISORDER	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
VAGINAL MONILIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins

The Top 5 Medications are Presented in Alphabetical Order

Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: IBUPROFEN

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=26)	No (N=90)	Yes (N=33)	No (N=97)	Yes (N=24)	No (N=96)
TOTAL	26 (100.0%)	63 (70.0%)	29 (87.9%)	59 (60.8%)	22 (91.7%)	46 (47.9%)
Body as a Whole	17 (65.4%)	33 (36.7%)	18 (54.5%)	24 (24.7%)	11 (45.8%)	26 (27.1%)
ABDOMINAL PAIN	0 (0.0%)	4 (4.4%)	3 (9.1%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	1 (3.8%)	0 (0.0%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	3 (3.1%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	9 (34.6%)	13 (14.4%)	7 (21.2%)	9 (9.3%)	0 (0.0%)	5 (5.2%)
BACK PAIN	1 (3.8%)	1 (1.1%)	1 (3.0%)	3 (3.1%)	1 (4.2%)	4 (4.2%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
CHILLS	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FEVER	1 (3.8%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)
FLU SYNDROME	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	9 (34.6%)	9 (10.0%)	6 (18.2%)	10 (10.3%)	7 (29.2%)	10 (10.4%)
INFECTION	3 (11.5%)	7 (7.8%)	2 (6.1%)	3 (3.1%)	4 (16.7%)	4 (4.2%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (1.1%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	1 (3.8%)	1 (1.1%)	1 (3.0%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
SHOCK	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (2.2%)	2 (6.1%)	1 (1.0%)	0 (0.0%)	4 (4.2%)
Cardiovascular System	0 (0.0%)	3 (3.3%)	3 (9.1%)	4 (4.1%)	3 (12.5%)	1 (1.0%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	2 (8.3%)	1 (1.0%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	14 (53.8%)	29 (32.2%)	8 (24.2%)	25 (25.8%)	4 (16.7%)	7 (7.3%)
COLITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	2 (7.7%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)
DECREASED APPETITE	1 (3.8%)	3 (3.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DIARRHEA	4 (15.4%)	4 (4.4%)	0 (0.0%)	7 (7.2%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	1 (3.8%)	2 (2.2%)	2 (6.1%)	1 (1.0%)	1 (4.2%)	0 (0.0%)
DYSPEPSIA	0 (0.0%)	3 (3.3%)	1 (3.0%)	1 (1.0%)	1 (4.2%)	1 (1.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: IBUPROFEN

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=26)	No (N=90)	Yes (N=33)	No (N=97)	Yes (N=24)	No (N=96)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.1%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
GASTROENTERITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	2 (2.2%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)
NAUSEA	7 (26.9%)	20 (22.2%)	5 (15.2%)	11 (11.3%)	0 (0.0%)	2 (2.1%)
TOOTH DISORDER	1 (3.8%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	2 (8.3%)	0 (0.0%)
VOMITING	0 (0.0%)	1 (1.1%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.1%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	1 (3.8%)	3 (3.3%)	0 (0.0%)	3 (3.1%)	2 (8.3%)	1 (1.0%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	1 (3.8%)	0 (0.0%)	0 (0.0%)	2 (2.1%)	1 (4.2%)	0 (0.0%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
WEIGHT GAIN	0 (0.0%)	3 (3.3%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)
Musculoskeletal System	2 (7.7%)	0 (0.0%)	3 (9.1%)	0 (0.0%)	3 (12.5%)	4 (4.2%)
ARTHRALGIA	1 (3.8%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	1 (4.2%)	1 (1.0%)
MYALGIA	1 (3.8%)	0 (0.0%)	2 (6.1%)	0 (0.0%)	2 (8.3%)	1 (1.0%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.1%)
Nervous System	11 (42.3%)	26 (28.9%)	12 (36.4%)	26 (26.8%)	5 (20.8%)	12 (12.5%)
ABNORMAL DREAMS	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (2.2%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	3 (3.1%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (2.1%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
DEPRESSION	1 (3.8%)	1 (1.1%)	1 (3.0%)	2 (2.1%)	1 (4.2%)	0 (0.0%)
DIZZINESS	2 (7.7%)	6 (6.7%)	3 (9.1%)	4 (4.1%)	1 (4.2%)	2 (2.1%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (3.8%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: IBUPROFEN

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=26)	No (N=90)	Yes (N=33)	No (N=97)	Yes (N=24)	No (N=96)
INCOORDINATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	2 (7.7%)	2 (2.2%)	4 (12.1%)	9 (9.3%)	0 (0.0%)	3 (3.1%)
LACK OF EMOTION	0 (0.0%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	4 (15.4%)	11 (12.2%)	3 (9.1%)	4 (4.1%)	2 (8.3%)	5 (5.2%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	1 (3.8%)	0 (0.0%)	0 (0.0%)	6 (6.2%)	0 (0.0%)	2 (2.1%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
SOMNOLENCE	2 (7.7%)	3 (3.3%)	0 (0.0%)	3 (3.1%)	0 (0.0%)	1 (1.0%)
THINKING ABNORMAL	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TREMOR	2 (7.7%)	5 (5.6%)	0 (0.0%)	4 (4.1%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (2.2%)	0 (0.0%)	3 (3.1%)	1 (4.2%)	0 (0.0%)
Respiratory System	5 (19.2%)	8 (8.9%)	6 (18.2%)	14 (14.4%)	6 (25.0%)	12 (12.5%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	1 (3.8%)	0 (0.0%)	1 (3.0%)	2 (2.1%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (1.0%)
EPISTAXIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	3 (11.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	4 (4.2%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
RESPIRATORY DISORDER	0 (0.0%)	5 (5.6%)	3 (9.1%)	6 (6.2%)	5 (20.8%)	8 (8.3%)
SINUSITIS	1 (3.8%)	2 (2.2%)	2 (6.1%)	5 (5.2%)	1 (4.2%)	1 (1.0%)
YAWN	0 (0.0%)	0 (0.0%)	1 (3.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	2 (7.7%)	10 (11.1%)	3 (9.1%)	7 (7.2%)	3 (12.5%)	6 (6.3%)
ACNE	0 (0.0%)	0 (0.0%)	2 (6.1%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
HERPES SIMPLEX	0 (0.0%)	1 (1.1%)	1 (3.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	1 (4.2%)	1 (1.0%)
PUSTULAR RASH	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
SWEATING	2 (7.7%)	8 (8.9%)	0 (0.0%)	4 (4.1%)	1 (4.2%)	0 (0.0%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: IBUPROFEN

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=26)	No (N=90)	Yes (N=33)	No (N=97)	Yes (N=24)	No (N=96)
Special Senses	0 (0.0%)	4 (4.4%)	2 (6.1%)	3 (3.1%)	0 (0.0%)	2 (2.1%)
ABNORMAL VISION	0 (0.0%)	3 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Urogenital System	6 (23.1%)	10 (11.1%)	4 (12.1%)	9 (9.3%)	3 (12.5%)	10 (10.4%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (4.2%)	0 (0.0%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	2 (7.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	3 (3.1%)
DYSMENORRHEA	3 (11.5%)	1 (1.1%)	3 (9.1%)	1 (1.0%)	2 (8.3%)	2 (2.1%)
FEMALE GENITAL DISORDERS	0 (0.0%)	3 (3.3%)	1 (3.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
LEUKORRHEA	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)
MENSTRUAL DISORDER	0 (0.0%)	2 (2.2%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
METrorrhagia	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
VAGINAL MONILIASIS	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins

The Top 5 Medications are Presented in Alphabetical Order

Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: LORATADINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=6)	No (N=110)	Yes (N=3)	No (N=127)	Yes (N=1)	No (N=119)
TOTAL	5 (83.3%)	84 (76.4%)	3 (100.0%)	85 (66.9%)	1 (100.0%)	67 (56.3%)
Body as a Whole	5 (83.3%)	45 (40.9%)	1 (33.3%)	41 (32.3%)	0 (0.0%)	37 (31.1%)
ABDOMINAL PAIN	0 (0.0%)	4 (3.6%)	0 (0.0%)	4 (3.1%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (0.9%)	1 (33.3%)	1 (0.8%)	0 (0.0%)	3 (2.5%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	4 (66.7%)	18 (16.4%)	0 (0.0%)	16 (12.6%)	0 (0.0%)	5 (4.2%)
BACK PAIN	0 (0.0%)	2 (1.8%)	0 (0.0%)	4 (3.1%)	0 (0.0%)	5 (4.2%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
CHILLS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEVER	1 (16.7%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
FLU SYNDROME	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HEADACHE	1 (16.7%)	17 (15.5%)	1 (33.3%)	15 (11.8%)	0 (0.0%)	17 (14.3%)
INFECTION	1 (16.7%)	9 (8.2%)	0 (0.0%)	5 (3.9%)	0 (0.0%)	8 (6.7%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PAIN	1 (16.7%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (1.7%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.8%)	1 (33.3%)	2 (1.6%)	0 (0.0%)	4 (3.4%)
Cardiovascular System	0 (0.0%)	3 (2.7%)	0 (0.0%)	7 (5.5%)	0 (0.0%)	4 (3.4%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.5%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	4 (66.7%)	39 (35.5%)	1 (33.3%)	32 (25.2%)	1 (100.0%)	10 (8.4%)
COLITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (2.7%)	0 (0.0%)	1 (0.8%)	1 (100.0%)	0 (0.0%)
DECREASED APPETITE	1 (16.7%)	3 (2.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
DIARRHEA	2 (33.3%)	6 (5.5%)	1 (33.3%)	6 (4.7%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	0 (0.0%)	3 (2.7%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.8%)
DYSPEPSIA	0 (0.0%)	3 (2.7%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (1.7%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: LORATADINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=6)	No (N=110)	Yes (N=3)	No (N=127)	Yes (N=1)	No (N=119)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
GASTROENTERITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
NAUSEA	3 (50.0%)	24 (21.8%)	0 (0.0%)	16 (12.6%)	0 (0.0%)	2 (1.7%)
TOOTH DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
VOMITING	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	0 (0.0%)	4 (3.6%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	3 (2.5%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.8%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
WEIGHT GAIN	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
Musculoskeletal System	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	7 (5.9%)
ARTHRALGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
MYALGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	3 (2.5%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
Nervous System	2 (33.3%)	35 (31.8%)	0 (0.0%)	38 (29.9%)	0 (0.0%)	17 (14.3%)
ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (1.8%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	3 (2.5%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
DEPRESSION	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.8%)
DIZZINESS	0 (0.0%)	8 (7.3%)	0 (0.0%)	7 (5.5%)	0 (0.0%)	3 (2.5%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (16.7%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: LORATADINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=6)	No (N=110)	Yes (N=3)	No (N=127)	Yes (N=1)	No (N=119)
INCOORDINATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	4 (3.6%)	0 (0.0%)	13 (10.2%)	0 (0.0%)	3 (2.5%)
LACK OF EMOTION	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	1 (16.7%)	14 (12.7%)	0 (0.0%)	7 (5.5%)	0 (0.0%)	7 (5.9%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (0.9%)	0 (0.0%)	6 (4.7%)	0 (0.0%)	2 (1.7%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
SOMNOLENCE	0 (0.0%)	5 (4.5%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.8%)
THINKING ABNORMAL	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TREMOR	2 (33.3%)	5 (4.5%)	0 (0.0%)	4 (3.1%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.8%)
Respiratory System	4 (66.7%)	9 (8.2%)	2 (66.7%)	18 (14.2%)	0 (0.0%)	18 (15.1%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	1 (16.7%)	0 (0.0%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
EPISTAXIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	2 (33.3%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (4.2%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
RESPIRATORY DISORDER	1 (16.7%)	4 (3.6%)	0 (0.0%)	9 (7.1%)	0 (0.0%)	13 (10.9%)
SINUSITIS	0 (0.0%)	3 (2.7%)	2 (66.7%)	5 (3.9%)	0 (0.0%)	2 (1.7%)
YAWN	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	1 (16.7%)	11 (10.0%)	0 (0.0%)	10 (7.9%)	1 (100.0%)	8 (6.7%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.8%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
HERPES SIMPLEX	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
PUSTULAR RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SWEATING	1 (16.7%)	9 (8.2%)	0 (0.0%)	4 (3.1%)	0 (0.0%)	1 (0.8%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: LORATADINE

Body System Preferred Term	---Paroxetine CR 25 mg---		--Paroxetine CR 12.5 mg--		-----Placebo-----	
	Yes (N=6)	No (N=110)	Yes (N=3)	No (N=127)	Yes (N=1)	No (N=119)
Special Senses	0 (0.0%)	4 (3.6%)	2 (66.7%)	3 (2.4%)	0 (0.0%)	2 (1.7%)
ABNORMAL VISION	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Urogenital System	1 (16.7%)	15 (13.6%)	0 (0.0%)	13 (10.2%)	0 (0.0%)	13 (10.9%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.5%)
DYSMENORRHEA	0 (0.0%)	4 (3.6%)	0 (0.0%)	4 (3.1%)	0 (0.0%)	4 (3.4%)
FEMALE GENITAL DISORDERS	1 (16.7%)	2 (1.8%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
LEUKORRHEA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
MENSTRUAL DISORDER	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
VAGINAL MONILIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins

The Top 5 Medications are Presented in Alphabetical Order

Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: PARACETAMOL

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=30)	No (N=86)	Yes (N=26)	No (N=104)	Yes (N=40)	No (N=80)
TOTAL	28 (93.3%)	61 (70.9%)	24 (92.3%)	64 (61.5%)	30 (75.0%)	38 (47.5%)
Body as a Whole	19 (63.3%)	31 (36.0%)	14 (53.8%)	28 (26.9%)	22 (55.0%)	15 (18.8%)
ABDOMINAL PAIN	1 (3.3%)	3 (3.5%)	1 (3.8%)	3 (2.9%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (1.2%)	2 (7.7%)	0 (0.0%)	3 (7.5%)	0 (0.0%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	9 (30.0%)	13 (15.1%)	5 (19.2%)	11 (10.6%)	1 (2.5%)	4 (5.0%)
BACK PAIN	1 (3.3%)	1 (1.2%)	1 (3.8%)	3 (2.9%)	3 (7.5%)	2 (2.5%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
CHILLS	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FEVER	1 (3.3%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
FLU SYNDROME	1 (3.3%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	9 (30.0%)	9 (10.5%)	7 (26.9%)	9 (8.7%)	13 (32.5%)	4 (5.0%)
INFECTION	5 (16.7%)	5 (5.8%)	2 (7.7%)	3 (2.9%)	5 (12.5%)	3 (3.8%)
MONILIASIS	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NEOPLASM	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PAIN	2 (6.7%)	0 (0.0%)	1 (3.8%)	1 (1.0%)	2 (5.0%)	0 (0.0%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	1 (3.3%)	1 (1.2%)	2 (7.7%)	1 (1.0%)	2 (5.0%)	2 (2.5%)
Cardiovascular System	1 (3.3%)	2 (2.3%)	3 (11.5%)	4 (3.8%)	2 (5.0%)	2 (2.5%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	2 (5.0%)	1 (1.3%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
VASODILATATION	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	17 (56.7%)	26 (30.2%)	15 (57.7%)	18 (17.3%)	6 (15.0%)	5 (6.3%)
COLITIS	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	1 (3.3%)	2 (2.3%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
DECREASED APPETITE	1 (3.3%)	3 (3.5%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DIARRHEA	5 (16.7%)	3 (3.5%)	3 (11.5%)	4 (3.8%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	1 (3.3%)	2 (2.3%)	1 (3.8%)	2 (1.9%)	0 (0.0%)	1 (1.3%)
DYSPEPSIA	1 (3.3%)	2 (2.3%)	2 (7.7%)	0 (0.0%)	2 (5.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: PARACETAMOL

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=30)	No (N=86)	Yes (N=26)	No (N=104)	Yes (N=40)	No (N=80)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
GASTROENTERITIS	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	1 (3.3%)	1 (1.2%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
NAUSEA	11 (36.7%)	16 (18.6%)	8 (30.8%)	8 (7.7%)	1 (2.5%)	1 (1.3%)
TOOTH DISORDER	1 (3.3%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	2 (5.0%)	0 (0.0%)
VOMITING	0 (0.0%)	1 (1.2%)	1 (3.8%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	2 (6.7%)	2 (2.3%)	0 (0.0%)	3 (2.9%)	2 (5.0%)	1 (1.3%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (1.2%)	0 (0.0%)	2 (1.9%)	1 (2.5%)	0 (0.0%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
WEIGHT GAIN	2 (6.7%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
Musculoskeletal System	2 (6.7%)	0 (0.0%)	0 (0.0%)	3 (2.9%)	2 (5.0%)	5 (6.3%)
ARTHRALGIA	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.5%)
MYALGIA	1 (3.3%)	0 (0.0%)	0 (0.0%)	2 (1.9%)	1 (2.5%)	2 (2.5%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (1.3%)
Nervous System	11 (36.7%)	26 (30.2%)	6 (23.1%)	32 (30.8%)	11 (27.5%)	6 (7.5%)
ABNORMAL DREAMS	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	1 (3.3%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (2.3%)	0 (0.0%)	2 (1.9%)	2 (5.0%)	1 (1.3%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (1.2%)	1 (3.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
DEPRESSION	0 (0.0%)	2 (2.3%)	0 (0.0%)	3 (2.9%)	0 (0.0%)	1 (1.3%)
DIZZINESS	2 (6.7%)	6 (7.0%)	3 (11.5%)	4 (3.8%)	2 (5.0%)	1 (1.3%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: PARACETAMOL

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=30)	No (N=86)	Yes (N=26)	No (N=104)	Yes (N=40)	No (N=80)
INCOORDINATION	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	2 (6.7%)	2 (2.3%)	1 (3.8%)	12 (11.5%)	3 (7.5%)	0 (0.0%)
LACK OF EMOTION	1 (3.3%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	7 (23.3%)	8 (9.3%)	1 (3.8%)	6 (5.8%)	4 (10.0%)	3 (3.8%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (1.2%)	0 (0.0%)	6 (5.8%)	2 (5.0%)	0 (0.0%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
SOMNOLENCE	1 (3.3%)	4 (4.7%)	1 (3.8%)	2 (1.9%)	0 (0.0%)	1 (1.3%)
THINKING ABNORMAL	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TREMOR	3 (10.0%)	4 (4.7%)	1 (3.8%)	3 (2.9%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (2.3%)	1 (3.8%)	2 (1.9%)	1 (2.5%)	0 (0.0%)
Respiratory System	5 (16.7%)	8 (9.3%)	5 (19.2%)	15 (14.4%)	7 (17.5%)	11 (13.8%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	1 (3.3%)	0 (0.0%)	0 (0.0%)	3 (2.9%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (1.3%)
EPISTAXIS	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	2 (6.7%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	4 (10.0%)	1 (1.3%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
RESPIRATORY DISORDER	1 (3.3%)	4 (4.7%)	2 (7.7%)	7 (6.7%)	4 (10.0%)	9 (11.3%)
SINUSITIS	1 (3.3%)	2 (2.3%)	2 (7.7%)	5 (4.8%)	2 (5.0%)	0 (0.0%)
YAWN	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	4 (13.3%)	8 (9.3%)	3 (11.5%)	7 (6.7%)	4 (10.0%)	5 (6.3%)
ACNE	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (1.0%)	0 (0.0%)	1 (1.3%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
HERPES SIMPLEX	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.3%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (2.5%)	1 (1.3%)
PUSTULAR RASH	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SWEATING	4 (13.3%)	6 (7.0%)	1 (3.8%)	3 (2.9%)	1 (2.5%)	0 (0.0%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins
The Top 5 Medications are Presented in Alphabetical Order
Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.2

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Concomitant Medications
Intention-to-Treat Population

Concomitant Medication: PARACETAMOL

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=30)	No (N=86)	Yes (N=26)	No (N=104)	Yes (N=40)	No (N=80)
Special Senses	0 (0.0%)	4 (4.7%)	2 (7.7%)	3 (2.9%)	1 (2.5%)	1 (1.3%)
ABNORMAL VISION	0 (0.0%)	3 (3.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (2.5%)	1 (1.3%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Urogenital System	7 (23.3%)	9 (10.5%)	6 (23.1%)	7 (6.7%)	6 (15.0%)	7 (8.8%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.3%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	1 (3.3%)	1 (1.2%)	0 (0.0%)	1 (1.0%)	3 (7.5%)	0 (0.0%)
DYSMENORRHEA	4 (13.3%)	0 (0.0%)	2 (7.7%)	2 (1.9%)	2 (5.0%)	2 (2.5%)
FEMALE GENITAL DISORDERS	2 (6.7%)	1 (1.2%)	1 (3.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
LEUKORRHEA	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (1.2%)	1 (3.8%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
MENSTRUAL DISORDER	0 (0.0%)	2 (2.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (1.2%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	2 (2.5%)
VAGINAL MONILIASIS	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)

*The Top 5 Concomitant Medications Taken by the Paroxetine CR Population During the Treatment Phase, excluding Vitamins

The Top 5 Medications are Presented in Alphabetical Order

Yes = Subject took Selected Medication; No = Subject did not take Selected Medication

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: ALLERGY, NEC

Body System Preferred Term	---Paroxetine CR 25 mg---		--Paroxetine CR 12.5 mg--		-----Placebo-----	
	Yes (N=4)	No (N=112)	Yes (N=6)	No (N=124)	Yes (N=5)	No (N=115)
TOTAL	2 (50.0%)	87 (77.7%)	6 (100.0%)	82 (66.1%)	2 (40.0%)	66 (57.4%)
Body as a Whole	1 (25.0%)	49 (43.8%)	3 (50.0%)	39 (31.5%)	1 (20.0%)	36 (31.3%)
ABDOMINAL PAIN	0 (0.0%)	4 (3.6%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	1 (20.0%)	2 (1.7%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	0 (0.0%)	22 (19.6%)	1 (16.7%)	15 (12.1%)	0 (0.0%)	5 (4.3%)
BACK PAIN	0 (0.0%)	2 (1.8%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	5 (4.3%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHILLS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FLU SYNDROME	0 (0.0%)	1 (0.9%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	1 (25.0%)	17 (15.2%)	2 (33.3%)	14 (11.3%)	0 (0.0%)	17 (14.8%)
INFECTION	0 (0.0%)	10 (8.9%)	0 (0.0%)	5 (4.0%)	0 (0.0%)	8 (7.0%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (0.9%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	2 (1.8%)	1 (16.7%)	1 (0.8%)	1 (20.0%)	1 (0.9%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	4 (3.5%)
Cardiovascular System	0 (0.0%)	3 (2.7%)	1 (16.7%)	6 (4.8%)	0 (0.0%)	4 (3.5%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.6%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	1 (25.0%)	42 (37.5%)	3 (50.0%)	30 (24.2%)	0 (0.0%)	11 (9.6%)
COLITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (2.7%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DECREASED APPETITE	0 (0.0%)	4 (3.6%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
DIARRHEA	1 (25.0%)	7 (6.3%)	0 (0.0%)	7 (5.6%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	0 (0.0%)	3 (2.7%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: ALLERGY, NEC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=4)	No (N=112)	Yes (N=6)	No (N=124)	Yes (N=5)	No (N=115)
DYSPEPSIA	0 (0.0%)	3 (2.7%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (1.7%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
GASTROENTERITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
NAUSEA	0 (0.0%)	27 (24.1%)	1 (16.7%)	15 (12.1%)	0 (0.0%)	2 (1.7%)
TOOTH DISORDER	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
VOMITING	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	0 (0.0%)	4 (3.6%)	1 (16.7%)	2 (1.6%)	0 (0.0%)	3 (2.6%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (0.9%)	1 (16.7%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Musculoskeletal System	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	1 (20.0%)	6 (5.2%)
ARTHRALGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
MYALGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	1 (20.0%)	2 (1.7%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
Nervous System	1 (25.0%)	36 (32.1%)	1 (16.7%)	37 (29.8%)	0 (0.0%)	17 (14.8%)
ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (1.8%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	3 (2.6%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
DIZZINESS	0 (0.0%)	8 (7.1%)	1 (16.7%)	6 (4.8%)	0 (0.0%)	3 (2.6%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: ALLERGY, NEC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=4)	No (N=112)	Yes (N=6)	No (N=124)	Yes (N=5)	No (N=115)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	4 (3.6%)	0 (0.0%)	13 (10.5%)	0 (0.0%)	3 (2.6%)
LACK OF EMOTION	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	0 (0.0%)	15 (13.4%)	0 (0.0%)	7 (5.6%)	0 (0.0%)	7 (6.1%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (0.9%)	0 (0.0%)	6 (4.8%)	0 (0.0%)	2 (1.7%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	1 (25.0%)	4 (3.6%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
THINKING ABNORMAL	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TREMOR	0 (0.0%)	7 (6.3%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (1.8%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
Respiratory System	0 (0.0%)	13 (11.6%)	2 (33.3%)	18 (14.5%)	0 (0.0%)	18 (15.7%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
EPISTAXIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (4.3%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
RESPIRATORY DISORDER	0 (0.0%)	5 (4.5%)	2 (33.3%)	7 (5.6%)	0 (0.0%)	13 (11.3%)
SINUSITIS	0 (0.0%)	3 (2.7%)	0 (0.0%)	7 (5.6%)	0 (0.0%)	2 (1.7%)
YAWN	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	0 (0.0%)	12 (10.7%)	1 (16.7%)	9 (7.3%)	0 (0.0%)	9 (7.8%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.9%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HERPES SIMPLEX	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
PUSTULAR RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SWEATING	0 (0.0%)	10 (8.9%)	1 (16.7%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase
Excluding the Medical History Condition: Management, Contraceptive
The Top 5 Medical History Conditions are Presented in Alphabetical Order
Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: ALLERGY, NEC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=4)	No (N=112)	Yes (N=6)	No (N=124)	Yes (N=5)	No (N=115)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Special Senses	0 (0.0%)	4 (3.6%)	1 (16.7%)	4 (3.2%)	0 (0.0%)	2 (1.7%)
ABNORMAL VISION	0 (0.0%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Urogenital System	0 (0.0%)	16 (14.3%)	0 (0.0%)	13 (10.5%)	0 (0.0%)	13 (11.3%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.6%)
DYSMENORRHEA	0 (0.0%)	4 (3.6%)	0 (0.0%)	4 (3.2%)	0 (0.0%)	4 (3.5%)
FEMALE GENITAL DISORDERS	0 (0.0%)	3 (2.7%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LEUKORRHEA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MENSTRUAL DISORDER	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
METRRORRHAGIA	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)
VAGINAL MONILIASIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: GENITAL FEMALE DISORD, OTHER

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=28)	No (N=88)	Yes (N=34)	No (N=96)	Yes (N=25)	No (N=95)
TOTAL	23 (82.1%)	66 (75.0%)	28 (82.4%)	60 (62.5%)	18 (72.0%)	50 (52.6%)
Body as a Whole	15 (53.6%)	35 (39.8%)	17 (50.0%)	25 (26.0%)	7 (28.0%)	30 (31.6%)
ABDOMINAL PAIN	1 (3.6%)	3 (3.4%)	0 (0.0%)	4 (4.2%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (1.1%)	1 (2.9%)	1 (1.0%)	0 (0.0%)	3 (3.2%)
ANAPHYLACTOID REACTION	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	8 (28.6%)	14 (15.9%)	7 (20.6%)	9 (9.4%)	0 (0.0%)	5 (5.3%)
BACK PAIN	2 (7.1%)	0 (0.0%)	1 (2.9%)	3 (3.1%)	1 (4.0%)	4 (4.2%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
CHILLS	0 (0.0%)	1 (1.1%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEVER	1 (3.6%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
FLU SYNDROME	0 (0.0%)	1 (1.1%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	5 (17.9%)	13 (14.8%)	7 (20.6%)	9 (9.4%)	3 (12.0%)	14 (14.7%)
INFECTION	3 (10.7%)	7 (8.0%)	2 (5.9%)	3 (3.1%)	3 (12.0%)	5 (5.3%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
NEOPLASM	1 (3.6%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	1 (3.6%)	1 (1.1%)	1 (2.9%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (2.3%)	1 (2.9%)	2 (2.1%)	1 (4.0%)	3 (3.2%)
Cardiovascular System	1 (3.6%)	2 (2.3%)	0 (0.0%)	7 (7.3%)	1 (4.0%)	3 (3.2%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (4.0%)	2 (2.1%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
VASODILATATION	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	15 (53.6%)	28 (31.8%)	10 (29.4%)	23 (24.0%)	3 (12.0%)	8 (8.4%)
COLITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (3.4%)	0 (0.0%)	1 (1.0%)	1 (4.0%)	0 (0.0%)
DECREASED APPETITE	1 (3.6%)	3 (3.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DIARRHEA	4 (14.3%)	4 (4.5%)	2 (5.9%)	5 (5.2%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	1 (3.6%)	2 (2.3%)	2 (5.9%)	1 (1.0%)	0 (0.0%)	1 (1.1%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: GENITAL FEMALE DISORD, OTHER

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=28)	No (N=88)	Yes (N=34)	No (N=96)	Yes (N=25)	No (N=95)
DYSPEPSIA	0 (0.0%)	3 (3.4%)	0 (0.0%)	2 (2.1%)	1 (4.0%)	1 (1.1%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	1 (2.9%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
GASTROENTERITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	1 (3.6%)	1 (1.1%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)
NAUSEA	11 (39.3%)	16 (18.2%)	4 (11.8%)	12 (12.5%)	0 (0.0%)	2 (2.1%)
TOOTH DISORDER	0 (0.0%)	1 (1.1%)	1 (2.9%)	0 (0.0%)	1 (4.0%)	1 (1.1%)
VOMITING	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
Endocrine System	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.1%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	1 (3.6%)	3 (3.4%)	0 (0.0%)	3 (3.1%)	2 (8.0%)	1 (1.1%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (2.1%)	1 (4.0%)	0 (0.0%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
WEIGHT GAIN	1 (3.6%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)
Musculoskeletal System	0 (0.0%)	2 (2.3%)	0 (0.0%)	3 (3.1%)	2 (8.0%)	5 (5.3%)
ARTHRALGIA	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
MYALGIA	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (2.1%)	2 (8.0%)	1 (1.1%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.1%)
Nervous System	11 (39.3%)	26 (29.5%)	11 (32.4%)	27 (28.1%)	7 (28.0%)	10 (10.5%)
ABNORMAL DREAMS	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (2.3%)	2 (5.9%)	0 (0.0%)	2 (8.0%)	1 (1.1%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (1.1%)	1 (2.9%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
DEPRESSION	1 (3.6%)	1 (1.1%)	1 (2.9%)	2 (2.1%)	0 (0.0%)	1 (1.1%)
DIZZINESS	3 (10.7%)	5 (5.7%)	2 (5.9%)	5 (5.2%)	3 (12.0%)	0 (0.0%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: GENITAL FEMALE DISORD, OTHER

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=28)	No (N=88)	Yes (N=34)	No (N=96)	Yes (N=25)	No (N=95)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (3.6%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	2 (7.1%)	2 (2.3%)	2 (5.9%)	11 (11.5%)	1 (4.0%)	2 (2.1%)
LACK OF EMOTION	0 (0.0%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	5 (17.9%)	10 (11.4%)	2 (5.9%)	5 (5.2%)	3 (12.0%)	4 (4.2%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (1.1%)	1 (2.9%)	5 (5.2%)	0 (0.0%)	2 (2.1%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)
SOMNOLENCE	2 (7.1%)	3 (3.4%)	2 (5.9%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
THINKING ABNORMAL	1 (3.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
TREMOR	3 (10.7%)	4 (4.5%)	1 (2.9%)	3 (3.1%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (2.3%)	0 (0.0%)	3 (3.1%)	0 (0.0%)	1 (1.1%)
Respiratory System	3 (10.7%)	10 (11.4%)	6 (17.6%)	14 (14.6%)	4 (16.0%)	14 (14.7%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	3 (3.1%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (1.1%)
EPISTAXIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	2 (7.1%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	2 (8.0%)	3 (3.2%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
RESPIRATORY DISORDER	1 (3.6%)	4 (4.5%)	3 (8.8%)	6 (6.3%)	2 (8.0%)	11 (11.6%)
SINUSITIS	0 (0.0%)	3 (3.4%)	2 (5.9%)	5 (5.2%)	1 (4.0%)	1 (1.1%)
YAWN	0 (0.0%)	0 (0.0%)	2 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	3 (10.7%)	9 (10.2%)	0 (0.0%)	10 (10.4%)	1 (4.0%)	8 (8.4%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.1%)	0 (0.0%)	1 (1.1%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
HERPES SIMPLEX	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
PUSTULAR RASH	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
SWEATING	3 (10.7%)	7 (8.0%)	0 (0.0%)	4 (4.2%)	0 (0.0%)	1 (1.1%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: GENITAL FEMALE DISORD, OTHER

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=28)	No (N=88)	Yes (N=34)	No (N=96)	Yes (N=25)	No (N=95)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Special Senses	1 (3.6%)	3 (3.4%)	3 (8.8%)	2 (2.1%)	0 (0.0%)	2 (2.1%)
ABNORMAL VISION	1 (3.6%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.1%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Urogenital System	3 (10.7%)	13 (14.8%)	5 (14.7%)	8 (8.3%)	5 (20.0%)	8 (8.4%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (4.0%)	0 (0.0%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	1 (3.6%)	1 (1.1%)	0 (0.0%)	1 (1.0%)	2 (8.0%)	1 (1.1%)
DYSMENORRHEA	1 (3.6%)	3 (3.4%)	2 (5.9%)	2 (2.1%)	1 (4.0%)	3 (3.2%)
FEMALE GENITAL DISORDERS	2 (7.1%)	1 (1.1%)	1 (2.9%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
LEUKORRHEA	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (1.1%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
MENSTRUAL DISORDER	0 (0.0%)	2 (2.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
METrorrhagia	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (1.1%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	2 (2.1%)
VAGINAL MONILIASIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: HEADACHE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=40)	No (N=76)	Yes (N=39)	No (N=91)	Yes (N=36)	No (N=84)
TOTAL	34 (85.0%)	55 (72.4%)	27 (69.2%)	61 (67.0%)	25 (69.4%)	43 (51.2%)
Body as a Whole	19 (47.5%)	31 (40.8%)	13 (33.3%)	29 (31.9%)	10 (27.8%)	27 (32.1%)
ABDOMINAL PAIN	1 (2.5%)	3 (3.9%)	0 (0.0%)	4 (4.4%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (1.3%)	1 (2.6%)	1 (1.1%)	1 (2.8%)	2 (2.4%)
ANAPHYLACTOID REACTION	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	10 (25.0%)	12 (15.8%)	3 (7.7%)	13 (14.3%)	1 (2.8%)	4 (4.8%)
BACK PAIN	1 (2.5%)	1 (1.3%)	1 (2.6%)	3 (3.3%)	3 (8.3%)	2 (2.4%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
CHILLS	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
FEVER	1 (2.5%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
FLU SYNDROME	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
HEADACHE	6 (15.0%)	12 (15.8%)	4 (10.3%)	12 (13.2%)	2 (5.6%)	15 (17.9%)
INFECTION	1 (2.5%)	9 (11.8%)	4 (10.3%)	1 (1.1%)	1 (2.8%)	7 (8.3%)
MONILIASIS	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NEOPLASM	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
PAIN	2 (5.0%)	0 (0.0%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	2 (2.4%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
TRAUMA	1 (2.5%)	1 (1.3%)	1 (2.6%)	2 (2.2%)	2 (5.6%)	2 (2.4%)
Cardiovascular System	1 (2.5%)	2 (2.6%)	1 (2.6%)	6 (6.6%)	2 (5.6%)	2 (2.4%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	2 (5.6%)	1 (1.2%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	19 (47.5%)	24 (31.6%)	12 (30.8%)	21 (23.1%)	2 (5.6%)	9 (10.7%)
COLITIS	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	3 (7.5%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.2%)
DECREASED APPETITE	3 (7.5%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
DIARRHEA	5 (12.5%)	3 (3.9%)	3 (7.7%)	4 (4.4%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	1 (2.5%)	2 (2.6%)	1 (2.6%)	2 (2.2%)	1 (2.8%)	0 (0.0%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: HEADACHE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=40)	No (N=76)	Yes (N=39)	No (N=91)	Yes (N=36)	No (N=84)
DYSPEPSIA	2 (5.0%)	1 (1.3%)	1 (2.6%)	1 (1.1%)	1 (2.8%)	1 (1.2%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	2 (5.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
GASTROENTERITIS	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	1 (2.5%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)
NAUSEA	11 (27.5%)	16 (21.1%)	6 (15.4%)	10 (11.0%)	0 (0.0%)	2 (2.4%)
TOOTH DISORDER	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (2.4%)
VOMITING	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.2%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	2 (5.0%)	2 (2.6%)	2 (5.1%)	1 (1.1%)	1 (2.8%)	2 (2.4%)
EDEMA	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (1.3%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	1 (1.2%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
WEIGHT GAIN	2 (5.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)
Musculoskeletal System	1 (2.5%)	1 (1.3%)	0 (0.0%)	3 (3.3%)	3 (8.3%)	4 (4.8%)
ARTHRALGIA	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (2.4%)
MYALGIA	0 (0.0%)	1 (1.3%)	0 (0.0%)	2 (2.2%)	1 (2.8%)	2 (2.4%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.6%)	0 (0.0%)
Nervous System	16 (40.0%)	21 (27.6%)	10 (25.6%)	28 (30.8%)	7 (19.4%)	10 (11.9%)
ABNORMAL DREAMS	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	1 (2.5%)	2 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	1 (2.5%)	1 (1.3%)	2 (5.1%)	0 (0.0%)	1 (2.8%)	2 (2.4%)
CONCENTRATION IMPAIRED	1 (2.5%)	0 (0.0%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
DEPRESSION	0 (0.0%)	2 (2.6%)	0 (0.0%)	3 (3.3%)	1 (2.8%)	0 (0.0%)
DIZZINESS	3 (7.5%)	5 (6.6%)	4 (10.3%)	3 (3.3%)	3 (8.3%)	0 (0.0%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: HEADACHE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=40)	No (N=76)	Yes (N=39)	No (N=91)	Yes (N=36)	No (N=84)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (2.5%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	2 (5.0%)	2 (2.6%)	2 (5.1%)	11 (12.1%)	1 (2.8%)	2 (2.4%)
LACK OF EMOTION	0 (0.0%)	2 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	5 (12.5%)	10 (13.2%)	1 (2.6%)	6 (6.6%)	2 (5.6%)	5 (6.0%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	1 (2.5%)	0 (0.0%)	1 (2.6%)	5 (5.5%)	0 (0.0%)	2 (2.4%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)
SOMNOLENCE	2 (5.0%)	3 (3.9%)	2 (5.1%)	1 (1.1%)	0 (0.0%)	1 (1.2%)
THINKING ABNORMAL	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
TREMOR	5 (12.5%)	2 (2.6%)	1 (2.6%)	3 (3.3%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (2.6%)	0 (0.0%)	3 (3.3%)	0 (0.0%)	1 (1.2%)
Respiratory System	6 (15.0%)	7 (9.2%)	7 (17.9%)	13 (14.3%)	9 (25.0%)	9 (10.7%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	1 (2.5%)	0 (0.0%)	2 (5.1%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (1.2%)
EPISTAXIS	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	3 (7.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.6%)	3 (3.6%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
RESPIRATORY DISORDER	2 (5.0%)	3 (3.9%)	2 (5.1%)	7 (7.7%)	7 (19.4%)	6 (7.1%)
SINUSITIS	0 (0.0%)	3 (3.9%)	3 (7.7%)	4 (4.4%)	1 (2.8%)	1 (1.2%)
YAWN	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	2 (5.0%)	10 (13.2%)	2 (5.1%)	8 (8.8%)	3 (8.3%)	6 (7.1%)
ACNE	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	1 (1.2%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
HERPES SIMPLEX	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	1 (2.8%)	0 (0.0%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (2.8%)	1 (1.2%)
PUSTULAR RASH	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
SWEATING	2 (5.0%)	8 (10.5%)	1 (2.6%)	3 (3.3%)	0 (0.0%)	1 (1.2%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase
Excluding the Medical History Condition: Management, Contraceptive
The Top 5 Medical History Conditions are Presented in Alphabetical Order
Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: HEADACHE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=40)	No (N=76)	Yes (N=39)	No (N=91)	Yes (N=36)	No (N=84)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Special Senses	3 (7.5%)	1 (1.3%)	2 (5.1%)	3 (3.3%)	2 (5.6%)	0 (0.0%)
ABNORMAL VISION	3 (7.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	2 (5.6%)	0 (0.0%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Urogenital System	6 (15.0%)	10 (13.2%)	4 (10.3%)	9 (9.9%)	4 (11.1%)	9 (10.7%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (1.2%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	1 (2.5%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	2 (5.6%)	1 (1.2%)
DYSMENORRHEA	0 (0.0%)	4 (5.3%)	0 (0.0%)	4 (4.4%)	1 (2.8%)	3 (3.6%)
FEMALE GENITAL DISORDERS	2 (5.0%)	1 (1.3%)	1 (2.6%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
LEUKORRHEA	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (1.3%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
MENSTRUAL DISORDER	1 (2.5%)	1 (1.3%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
METRRORRHAGIA	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (1.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (2.4%)
VAGINAL MONILIASIS	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: MIGRAINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=12)	No (N=104)	Yes (N=9)	No (N=121)	Yes (N=10)	No (N=110)
TOTAL	9 (75.0%)	80 (76.9%)	5 (55.6%)	83 (68.6%)	5 (50.0%)	63 (57.3%)
Body as a Whole	2 (16.7%)	48 (46.2%)	3 (33.3%)	39 (32.2%)	2 (20.0%)	35 (31.8%)
ABDOMINAL PAIN	0 (0.0%)	4 (3.8%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	1 (1.0%)	1 (11.1%)	1 (0.8%)	0 (0.0%)	3 (2.7%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	1 (8.3%)	21 (20.2%)	1 (11.1%)	15 (12.4%)	0 (0.0%)	5 (4.5%)
BACK PAIN	1 (8.3%)	1 (1.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	5 (4.5%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHILLS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
FLU SYNDROME	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HEADACHE	0 (0.0%)	18 (17.3%)	2 (22.2%)	14 (11.6%)	2 (20.0%)	15 (13.6%)
INFECTION	0 (0.0%)	10 (9.6%)	0 (0.0%)	5 (4.1%)	0 (0.0%)	8 (7.3%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	2 (1.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.8%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (1.9%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	4 (3.6%)
Cardiovascular System	0 (0.0%)	3 (2.9%)	1 (11.1%)	6 (5.0%)	1 (10.0%)	3 (2.7%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	1 (10.0%)	2 (1.8%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	9 (75.0%)	34 (32.7%)	2 (22.2%)	31 (25.6%)	2 (20.0%)	9 (8.2%)
COLITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (2.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
DECREASED APPETITE	1 (8.3%)	3 (2.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
DIARRHEA	1 (8.3%)	7 (6.7%)	0 (0.0%)	7 (5.8%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	2 (16.7%)	1 (1.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: MIGRAINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=12)	No (N=104)	Yes (N=9)	No (N=121)	Yes (N=10)	No (N=110)
DYSPEPSIA	0 (0.0%)	3 (2.9%)	0 (0.0%)	2 (1.7%)	1 (10.0%)	1 (0.9%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	1 (11.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
GASTROENTERITIS	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	1 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	1 (8.3%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
NAUSEA	5 (41.7%)	22 (21.2%)	1 (11.1%)	15 (12.4%)	0 (0.0%)	2 (1.8%)
TOOTH DISORDER	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	1 (10.0%)	1 (0.9%)
VOMITING	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	0 (0.0%)	4 (3.8%)	0 (0.0%)	3 (2.5%)	1 (10.0%)	2 (1.8%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.9%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
Musculoskeletal System	0 (0.0%)	2 (1.9%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	7 (6.4%)
ARTHRALGIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
MYALGIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.7%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
Nervous System	3 (25.0%)	34 (32.7%)	4 (44.4%)	34 (28.1%)	4 (40.0%)	13 (11.8%)
ABNORMAL DREAMS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (1.9%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	3 (2.7%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (1.0%)	1 (11.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	2 (1.9%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	1 (0.9%)
DIZZINESS	1 (8.3%)	7 (6.7%)	2 (22.2%)	5 (4.1%)	1 (10.0%)	2 (1.8%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: MIGRAINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=12)	No (N=104)	Yes (N=9)	No (N=121)	Yes (N=10)	No (N=110)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	0 (0.0%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	4 (3.8%)	1 (11.1%)	12 (9.9%)	0 (0.0%)	3 (2.7%)
LACK OF EMOTION	0 (0.0%)	2 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	1 (8.3%)	14 (13.5%)	0 (0.0%)	7 (5.8%)	2 (20.0%)	5 (4.5%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (1.0%)	0 (0.0%)	6 (5.0%)	0 (0.0%)	2 (1.8%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	1 (8.3%)	4 (3.8%)	1 (11.1%)	2 (1.7%)	0 (0.0%)	1 (0.9%)
THINKING ABNORMAL	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TREMOR	0 (0.0%)	7 (6.7%)	1 (11.1%)	3 (2.5%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (1.9%)	0 (0.0%)	3 (2.5%)	1 (10.0%)	0 (0.0%)
Respiratory System	0 (0.0%)	13 (12.5%)	0 (0.0%)	20 (16.5%)	1 (10.0%)	17 (15.5%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	1 (0.9%)
EPISTAXIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	0 (0.0%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	4 (3.6%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
RESPIRATORY DISORDER	0 (0.0%)	5 (4.8%)	0 (0.0%)	9 (7.4%)	0 (0.0%)	13 (11.8%)
SINUSITIS	0 (0.0%)	3 (2.9%)	0 (0.0%)	7 (5.8%)	1 (10.0%)	1 (0.9%)
YAWN	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	1 (8.3%)	11 (10.6%)	0 (0.0%)	10 (8.3%)	1 (10.0%)	8 (7.3%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.9%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HERPES SIMPLEX	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
PUSTULAR RASH	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SWEATING	1 (8.3%)	9 (8.7%)	0 (0.0%)	4 (3.3%)	1 (10.0%)	0 (0.0%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase
Excluding the Medical History Condition: Management, Contraceptive
The Top 5 Medical History Conditions are Presented in Alphabetical Order
Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: MIGRAINE

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=12)	No (N=104)	Yes (N=9)	No (N=121)	Yes (N=10)	No (N=110)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Special Senses	0 (0.0%)	4 (3.8%)	0 (0.0%)	5 (4.1%)	0 (0.0%)	2 (1.8%)
ABNORMAL VISION	0 (0.0%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Urogenital System	1 (8.3%)	15 (14.4%)	2 (22.2%)	11 (9.1%)	0 (0.0%)	13 (11.8%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	2 (1.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.7%)
DYSMENORRHEA	0 (0.0%)	4 (3.8%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	4 (3.6%)
FEMALE GENITAL DISORDERS	0 (0.0%)	3 (2.9%)	1 (11.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LEUKORRHEA	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MENSTRUAL DISORDER	0 (0.0%)	2 (1.9%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
METrorrhagia	1 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
VAGINAL MONILIASIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: RHINITIS, ALLERGIC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=16)	No (N=100)	Yes (N=7)	No (N=123)	Yes (N=9)	No (N=111)
TOTAL	13 (81.3%)	76 (76.0%)	4 (57.1%)	84 (68.3%)	8 (88.9%)	60 (54.1%)
Body as a Whole	9 (56.3%)	41 (41.0%)	1 (14.3%)	41 (33.3%)	4 (44.4%)	33 (29.7%)
ABDOMINAL PAIN	0 (0.0%)	4 (4.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	1 (6.3%)	0 (0.0%)	1 (14.3%)	1 (0.8%)	1 (11.1%)	2 (1.8%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	5 (31.3%)	17 (17.0%)	0 (0.0%)	16 (13.0%)	0 (0.0%)	5 (4.5%)
BACK PAIN	1 (6.3%)	1 (1.0%)	0 (0.0%)	4 (3.3%)	1 (11.1%)	4 (3.6%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHILLS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEVER	1 (6.3%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FLU SYNDROME	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HEADACHE	2 (12.5%)	16 (16.0%)	1 (14.3%)	15 (12.2%)	2 (22.2%)	15 (13.5%)
INFECTION	2 (12.5%)	8 (8.0%)	0 (0.0%)	5 (4.1%)	0 (0.0%)	8 (7.2%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PAIN	1 (6.3%)	1 (1.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (1.8%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	2 (2.0%)	1 (14.3%)	2 (1.6%)	1 (11.1%)	3 (2.7%)
Cardiovascular System	0 (0.0%)	3 (3.0%)	0 (0.0%)	7 (5.7%)	1 (11.1%)	3 (2.7%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (11.1%)	2 (1.8%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Digestive System	9 (56.3%)	34 (34.0%)	2 (28.6%)	31 (25.2%)	3 (33.3%)	8 (7.2%)
COLITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	3 (3.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
DECREASED APPETITE	2 (12.5%)	2 (2.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
DIARRHEA	1 (6.3%)	7 (7.0%)	2 (28.6%)	5 (4.1%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	1 (6.3%)	2 (2.0%)	0 (0.0%)	3 (2.4%)	1 (11.1%)	0 (0.0%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: RHINITIS, ALLERGIC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=16)	No (N=100)	Yes (N=7)	No (N=123)	Yes (N=9)	No (N=111)
DYSPEPSIA	1 (6.3%)	2 (2.0%)	0 (0.0%)	2 (1.6%)	1 (11.1%)	1 (0.9%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (11.1%)	0 (0.0%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
GASTROENTERITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	1 (6.3%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)
NAUSEA	7 (43.8%)	20 (20.0%)	0 (0.0%)	16 (13.0%)	0 (0.0%)	2 (1.8%)
TOOTH DISORDER	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
VOMITING	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	1 (6.3%)	3 (3.0%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	3 (2.7%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	1 (6.3%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.9%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	3 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Musculoskeletal System	0 (0.0%)	2 (2.0%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	7 (6.3%)
ARTHRALGIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
MYALGIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	3 (2.7%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
Nervous System	4 (25.0%)	33 (33.0%)	2 (28.6%)	36 (29.3%)	3 (33.3%)	14 (12.6%)
ABNORMAL DREAMS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	3 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	2 (2.0%)	0 (0.0%)	2 (1.6%)	1 (11.1%)	2 (1.8%)
CONCENTRATION IMPAIRED	0 (0.0%)	1 (1.0%)	1 (14.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	2 (2.0%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
DIZZINESS	0 (0.0%)	8 (8.0%)	0 (0.0%)	7 (5.7%)	1 (11.1%)	2 (1.8%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: RHINITIS, ALLERGIC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=16)	No (N=100)	Yes (N=7)	No (N=123)	Yes (N=9)	No (N=111)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (6.3%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	4 (4.0%)	0 (0.0%)	13 (10.6%)	1 (11.1%)	2 (1.8%)
LACK OF EMOTION	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	3 (18.8%)	12 (12.0%)	2 (28.6%)	5 (4.1%)	1 (11.1%)	6 (5.4%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	1 (1.0%)	0 (0.0%)	6 (4.9%)	0 (0.0%)	2 (1.8%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	0 (0.0%)	5 (5.0%)	1 (14.3%)	2 (1.6%)	0 (0.0%)	1 (0.9%)
THINKING ABNORMAL	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TREMOR	2 (12.5%)	5 (5.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	2 (2.0%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	1 (0.9%)
Respiratory System	3 (18.8%)	10 (10.0%)	2 (28.6%)	18 (14.6%)	3 (33.3%)	15 (13.5%)
ASTHMA	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	1 (6.3%)	0 (0.0%)	0 (0.0%)	3 (2.4%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	1 (0.9%)
EPISTAXIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	1 (6.3%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (22.2%)	3 (2.7%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
RESPIRATORY DISORDER	1 (6.3%)	4 (4.0%)	0 (0.0%)	9 (7.3%)	1 (11.1%)	12 (10.8%)
SINUSITIS	0 (0.0%)	3 (3.0%)	0 (0.0%)	7 (5.7%)	1 (11.1%)	1 (0.9%)
YAWN	0 (0.0%)	0 (0.0%)	1 (14.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Skin and Appendages	2 (12.5%)	10 (10.0%)	1 (14.3%)	9 (7.3%)	0 (0.0%)	9 (8.1%)
ACNE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (0.9%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ECZEMA	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HERPES SIMPLEX	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
PUSTULAR RASH	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SWEATING	1 (6.3%)	9 (9.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	1 (0.9%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.3

Number (%) of Subjects with Treatment Emergent Adverse Events by Selected* Active Conditions
Intention-to-Treat Population

Concurrent Medical Condition: RHINITIS, ALLERGIC

Body System Preferred Term	---Paroxetine CR 25 mg---		---Paroxetine CR 12.5 mg---		-----Placebo-----	
	Yes (N=16)	No (N=100)	Yes (N=7)	No (N=123)	Yes (N=9)	No (N=111)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Special Senses	0 (0.0%)	4 (4.0%)	1 (14.3%)	4 (3.3%)	0 (0.0%)	2 (1.8%)
ABNORMAL VISION	0 (0.0%)	3 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Urogenital System	2 (12.5%)	14 (14.0%)	1 (14.3%)	12 (9.8%)	0 (0.0%)	13 (11.7%)
AMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	2 (2.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	3 (2.7%)
DYSMENORRHEA	0 (0.0%)	4 (4.0%)	0 (0.0%)	4 (3.3%)	0 (0.0%)	4 (3.6%)
FEMALE GENITAL DISORDERS	1 (6.3%)	2 (2.0%)	1 (14.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LEUKORRHEA	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	1 (6.3%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MENSTRUAL DISORDER	0 (0.0%)	2 (2.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
VAGINAL MONILIASIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

*The Top 5 Medical History Conditions of the Total Paroxetine CR Population During the Treatment Phase

Excluding the Medical History Condition: Management, Contraceptive

The Top 5 Medical History Conditions are Presented in Alphabetical Order

Yes = Subject had Medical History Condition; No = Subject did not have Medical History Condition

Supplementary Table 15.4

Comparative Summary of Treatment Emergent Adverse Events between North America and Europe
By Body System and Preferred Term
Intention-to-Treat Population

Body System Preferred Term	-----North America-----			-----Europe-----		
	Paroxetine CR 25 mg (N=26)	Paroxetine CR 12.5 mg (N=30)	Placebo (N=24)	Paroxetine CR 25 mg (N=91)	Paroxetine CR 12.5 mg (N=87)	Placebo (N=108)
TOTAL	18 (69.2%)	26 (86.7%)	16 (66.7%)	59 (64.8%)	61 (70.1%)	64 (59.3%)
Body as a Whole	7 (26.9%)	11 (36.7%)	9 (37.5%)	34 (37.4%)	34 (39.1%)	33 (30.6%)
ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (1.1%)	5 (5.7%)	1 (0.9%)
ALLERGIC REACTION	0 (0.0%)	1 (3.3%)	0 (0.0%)	3 (3.3%)	2 (2.3%)	0 (0.0%)
ANAPHYLACTOID REACTION	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	2 (7.7%)	4 (13.3%)	3 (12.5%)	11 (12.1%)	14 (16.1%)	9 (8.3%)
BACK PAIN	1 (3.8%)	1 (3.3%)	0 (0.0%)	2 (2.2%)	3 (3.4%)	4 (3.7%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
CHILLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.3%)	0 (0.0%)
FEVER	0 (0.0%)	1 (3.3%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FLU SYNDROME	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
HEADACHE	2 (7.7%)	3 (10.0%)	4 (16.7%)	17 (18.7%)	12 (13.8%)	12 (11.1%)
INFECTION	2 (7.7%)	1 (3.3%)	1 (4.2%)	8 (8.8%)	5 (5.7%)	6 (5.6%)
MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
NEOPLASM	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
PAIN	1 (3.8%)	1 (3.3%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	1 (0.9%)
SHOCK	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
TRAUMA	1 (3.8%)	2 (6.7%)	0 (0.0%)	1 (1.1%)	2 (2.3%)	3 (2.8%)
Cardiovascular System	0 (0.0%)	0 (0.0%)	2 (8.3%)	4 (4.4%)	6 (6.9%)	2 (1.9%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	1 (4.2%)	3 (3.3%)	0 (0.0%)	0 (0.0%)
MYOCARDIAL INFARCT	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
PALPITATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TACHYCARDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
VASODILATATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
Digestive System	6 (23.1%)	12 (40.0%)	9 (37.5%)	21 (23.1%)	20 (23.0%)	19 (17.6%)
COLITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CONSTIPATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	2 (2.3%)	2 (1.9%)
DECREASED APPETITE	2 (7.7%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	2 (1.9%)
DIARRHEA	2 (7.7%)	4 (13.3%)	0 (0.0%)	3 (3.3%)	5 (5.7%)	1 (0.9%)
DRY MOUTH	2 (7.7%)	1 (3.3%)	0 (0.0%)	1 (1.1%)	2 (2.3%)	1 (0.9%)
DYSPEPSIA	1 (3.8%)	2 (6.7%)	1 (4.2%)	0 (0.0%)	1 (1.1%)	1 (0.9%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	0 (0.0%)
FLATULENCE	0 (0.0%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
GASTROENTERITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (0.9%)
GASTROINTESTINAL DISORDER	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

Supplementary Table 15.4

Comparative Summary of Treatment Emergent Adverse Events between North America and Europe
By Body System and Preferred Term
Intention-to-Treat Population

Body System Preferred Term	-----North America-----			-----Europe-----		
	Paroxetine CR 25 mg (N=26)	Paroxetine CR 12.5 mg (N=30)	Placebo (N=24)	Paroxetine CR 25 mg (N=91)	Paroxetine CR 12.5 mg (N=87)	Placebo (N=108)
GINGIVITIS	1 (3.8%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
INCREASED APPETITE	0 (0.0%)	1 (3.3%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	2 (7.7%)	5 (16.7%)	6 (25.0%)	14 (15.4%)	9 (10.3%)	9 (8.3%)
TOOTH DISORDER	0 (0.0%)	0 (0.0%)	2 (8.3%)	0 (0.0%)	1 (1.1%)	1 (0.9%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)	1 (1.1%)	0 (0.0%)
Endocrine System	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Hemic and Lymphatic System	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	1 (3.8%)	0 (0.0%)	1 (4.2%)	2 (2.2%)	4 (4.6%)	2 (1.9%)
EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (1.1%)	2 (2.3%)	0 (0.0%)
THIRST	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	1 (0.9%)
Musculoskeletal System	2 (7.7%)	2 (6.7%)	0 (0.0%)	1 (1.1%)	3 (3.4%)	4 (3.7%)
ARTHRALGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	2 (2.3%)	1 (0.9%)
MYALGIA	2 (7.7%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.9%)
TENDINOUS DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (0.9%)
Nervous System	11 (42.3%)	7 (23.3%)	7 (29.2%)	25 (27.5%)	25 (28.7%)	17 (15.7%)
ABNORMAL DREAMS	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
ALCOHOL ABUSE	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	2 (2.3%)	0 (0.0%)
ANXIETY	2 (7.7%)	1 (3.3%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	1 (0.9%)
CONCENTRATION IMPAIRED	1 (3.8%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CONFUSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	0 (0.0%)	2 (8.3%)	1 (1.1%)	2 (2.3%)	0 (0.0%)
DIZZINESS	2 (7.7%)	2 (6.7%)	1 (4.2%)	6 (6.6%)	6 (6.9%)	1 (0.9%)
EMOTIONAL LABILITY	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
INSOMNIA	2 (7.7%)	0 (0.0%)	0 (0.0%)	5 (5.5%)	4 (4.6%)	9 (8.3%)
LACK OF EMOTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (0.9%)
LIBIDO DECREASED	2 (7.7%)	3 (10.0%)	3 (12.5%)	10 (11.0%)	6 (6.9%)	5 (4.6%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)	3 (3.4%)	4 (3.7%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
SOMNOLENCE	2 (7.7%)	2 (6.7%)	1 (4.2%)	0 (0.0%)	2 (2.3%)	1 (0.9%)
THINKING ABNORMAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.3%)	0 (0.0%)
TREMOR	1 (3.8%)	0 (0.0%)	2 (8.3%)	1 (1.1%)	3 (3.4%)	4 (3.7%)

Supplementary Table 15.4

Comparative Summary of Treatment Emergent Adverse Events between North America and Europe
By Body System and Preferred Term
Intention-to-Treat Population

Body System Preferred Term	-----North America-----			-----Europe-----		
	Paroxetine CR 25 mg (N=26)	Paroxetine CR 12.5 mg (N=30)	Placebo (N=24)	Paroxetine CR 25 mg (N=91)	Paroxetine CR 12.5 mg (N=87)	Placebo (N=108)
VERTIGO	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (1.1%)	2 (2.3%)	2 (1.9%)
WITHDRAWAL SYNDROME	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	0 (0.0%)
Respiratory System	3 (11.5%)	12 (40.0%)	3 (12.5%)	12 (13.2%)	11 (12.6%)	10 (9.3%)
ASTHMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	1 (3.8%)	0 (0.0%)	1 (4.2%)	2 (2.2%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
EPISTAXIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
PHARYNGITIS	1 (3.8%)	2 (6.7%)	2 (8.3%)	2 (2.2%)	0 (0.0%)	1 (0.9%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
RESPIRATORY DISORDER	1 (3.8%)	6 (20.0%)	0 (0.0%)	4 (4.4%)	7 (8.0%)	9 (8.3%)
SINUSITIS	2 (7.7%)	3 (10.0%)	2 (8.3%)	2 (2.2%)	1 (1.1%)	2 (1.9%)
YAWN	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
Skin and Appendages	1 (3.8%)	3 (10.0%)	2 (8.3%)	9 (9.9%)	6 (6.9%)	10 (9.3%)
ACNE	0 (0.0%)	1 (3.3%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (0.9%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ECZEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	0 (0.0%)	1 (3.3%)	0 (0.0%)	2 (2.2%)	0 (0.0%)	0 (0.0%)
PUSTULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
RASH	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SWEATING	1 (3.8%)	1 (3.3%)	1 (4.2%)	4 (4.4%)	5 (5.7%)	3 (2.8%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
Special Searches	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Special Senses	1 (3.8%)	3 (10.0%)	1 (4.2%)	2 (2.2%)	1 (1.1%)	3 (2.8%)
ABNORMAL VISION	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.9%)
ABNORMALITY OF ACCOMMODATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	1 (3.3%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	0 (0.0%)
TASTE PERVERSION	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
Urogenital System	3 (11.5%)	3 (10.0%)	1 (4.2%)	8 (8.8%)	7 (8.0%)	21 (19.4%)
AMENORRHEA	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)

Supplementary Table 15.4

Comparative Summary of Treatment Emergent Adverse Events between North America and Europe
By Body System and Preferred Term
Intention-to-Treat Population

Body System Preferred Term	-----North America-----			-----Europe-----		
	Paroxetine CR 25 mg (N=26)	Paroxetine CR 12.5 mg (N=30)	Placebo (N=24)	Paroxetine CR 25 mg (N=91)	Paroxetine CR 12.5 mg (N=87)	Placebo (N=108)
BREAST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
CYSTITIS	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	4 (3.7%)
DYSMENORRHEA	0 (0.0%)	1 (3.3%)	0 (0.0%)	3 (3.3%)	2 (2.3%)	7 (6.5%)
FEMALE GENITAL DISORDERS	1 (3.8%)	2 (6.7%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LEUKORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
MENORRHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	1 (0.9%)
MENSTRUAL DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)	1 (0.9%)
METORRHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (3.7%)
VAGINAL MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.9%)

Supplementary Table 15.5

Comparative Summary of Treatment Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=246)	Placebo (N=120)	Paroxetine CR (N=681)	Placebo (N=349)
TOTAL	TOTAL	177 (72.0%)	68 (56.7%)	518 (76.1%)	215 (61.6%)
Body as a Whole	ABDOMINAL PAIN	8 (3.3%)	0 (0.0%)	12 (1.8%)	7 (2.0%)
	ABSCCESS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	ALLERGIC REACTION	3 (1.2%)	3 (2.5%)	5 (0.7%)	5 (1.4%)
	ANAPHYLACTOID REACTION	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	ASTHENIA	38 (15.4%)	5 (4.2%)	118 (17.3%)	20 (5.7%)
	BACK PAIN	6 (2.4%)	5 (4.2%)	15 (2.2%)	11 (3.2%)
	CELLULITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.6%)
	CHEST PAIN	0 (0.0%)	1 (0.8%)	4 (0.6%)	2 (0.6%)
	CHILLS	2 (0.8%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	FACE EDEMA	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	FEVER	2 (0.8%)	1 (0.8%)	3 (0.4%)	2 (0.6%)
	FLU SYNDROME	2 (0.8%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	HEADACHE	34 (13.8%)	17 (14.2%)	103 (15.1%)	42 (12.0%)
	HYPOTHERMIA	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	INFECTION	15 (6.1%)	8 (6.7%)	42 (6.2%)	15 (4.3%)
	MALAISE	0 (0.0%)	0 (0.0%)	5 (0.7%)	0 (0.0%)
	MONILIASIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NEOPLASM	2 (0.8%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	PAIN	4 (1.6%)	2 (1.7%)	7 (1.0%)	5 (1.4%)
	SHOCK	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	TRAUMA	5 (2.0%)	4 (3.3%)	22 (3.2%)	11 (3.2%)
Cardiovascular System	ANGINA PECTORIS	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	ARRHYTHMIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	HAEMATOMA	1 (0.4%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	HYPERTENSION	1 (0.4%)	0 (0.0%)	3 (0.4%)	2 (0.6%)
	HYPOTENSION	0 (0.0%)	0 (0.0%)	1 (0.1%)	2 (0.6%)
	MIGRAINE	1 (0.4%)	3 (2.5%)	9 (1.3%)	3 (0.9%)
	MYOCARDIAL INFARCT	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	PALPITATION	1 (0.4%)	0 (0.0%)	6 (0.9%)	2 (0.6%)
	PERIPHERAL VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	POSTURAL HYPOTENSION	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PULMONARY EMBOLUS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SUPRAVENTRICULAR TACHYCARDIA	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	TACHYCARDIA	1 (0.4%)	0 (0.0%)	6 (0.9%)	0 (0.0%)
	VASCULAR DISORDER	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	VASODILATATION	1 (0.4%)	0 (0.0%)	3 (0.4%)	3 (0.9%)
Digestive System	BRUXISM	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	COLITIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	CONSTIPATION	4 (1.6%)	1 (0.8%)	32 (4.7%)	4 (1.1%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.5

Comparative Summary of Treatment Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=246)	Placebo (N=120)	Paroxetine CR (N=681)	Placebo (N=349)
Digestive System	DECREASED APPETITE	5 (2.0%)	0 (0.0%)	15 (2.2%)	2 (0.6%)
	DIARRHEA	15 (6.1%)	0 (0.0%)	38 (5.6%)	7 (2.0%)
	DRY MOUTH	6 (2.4%)	1 (0.8%)	27 (4.0%)	7 (2.0%)
	DYSPEPSIA	5 (2.0%)	2 (1.7%)	15 (2.2%)	5 (1.4%)
	DYSPHAGIA	2 (0.8%)	0 (0.0%)	2 (0.3%)	1 (0.3%)
	FLATULENCE	1 (0.4%)	1 (0.8%)	6 (0.9%)	3 (0.9%)
	GASTRITIS	0 (0.0%)	1 (0.8%)	2 (0.3%)	2 (0.6%)
	GASTROENTERITIS	2 (0.8%)	0 (0.0%)	5 (0.7%)	2 (0.6%)
	GASTROINTESTINAL DISORDER	1 (0.4%)	0 (0.0%)	2 (0.3%)	1 (0.3%)
	GINGIVITIS	3 (1.2%)	0 (0.0%)	6 (0.9%)	2 (0.6%)
	INCREASED APPETITE	1 (0.4%)	1 (0.8%)	17 (2.5%)	3 (0.9%)
	LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	MELENA	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	NAUSEA	43 (17.5%)	2 (1.7%)	118 (17.3%)	23 (6.6%)
	OROPHARYNX DISORDER	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	RECTAL DISORDER	0 (0.0%)	0 (0.0%)	3 (0.4%)	0 (0.0%)
	RECTAL HEMORRHAGE	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	TOOTH CARIES	0 (0.0%)	0 (0.0%)	1 (0.1%)	1 (0.3%)
	TOOTH DISORDER	2 (0.8%)	2 (1.7%)	6 (0.9%)	4 (1.1%)
	ULCERATIVE STOMATITIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	VOMITING	2 (0.8%)	1 (0.8%)	10 (1.5%)	8 (2.3%)
Endocrine System	DIABETES MELLITUS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	FERTILITY DECREASED FEMALE	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	GOITER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	OVARY DISORDER	1 (0.4%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	THYROID DISORDER	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
Hemic and Lymphatic System	ANEMIA	1 (0.4%)	0 (0.0%)	2 (0.3%)	2 (0.6%)
	HYPOCHROMIC ANEMIA	0 (0.0%)	0 (0.0%)	3 (0.4%)	1 (0.3%)
	LEUKOCYTOSIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	LEUKOPENIA	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	LYMPHADENOPATHY	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	PURPURA	0 (0.0%)	0 (0.0%)	5 (0.7%)	1 (0.3%)
Metabolic and Nutritional Disorders	EDEMA	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	GENERALIZED EDEMA	3 (1.2%)	1 (0.8%)	1 (0.1%)	1 (0.3%)
	OBESITY	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	PERIPHERAL EDEMA	0 (0.0%)	0 (0.0%)	3 (0.4%)	1 (0.3%)
	THIRST	0 (0.0%)	1 (0.8%)	2 (0.3%)	1 (0.3%)
	WEIGHT GAIN	3 (1.2%)	1 (0.8%)	16 (2.3%)	8 (2.3%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.5

Comparative Summary of Treatment Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=246)	Placebo (N=120)	Paroxetine CR (N=681)	Placebo (N=349)
Metabolic and Nutritional Disorders	WEIGHT LOSS	0 (0.0%)	0 (0.0%)	1 (0.1%)	2 (0.6%)
Musculoskeletal System	ARTHRALGIA	2 (0.8%)	2 (1.7%)	11 (1.6%)	5 (1.4%)
	ARTHRITIS	0 (0.0%)	0 (0.0%)	4 (0.6%)	0 (0.0%)
	ARTHROSIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	BURSITIS	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	MYALGIA	3 (1.2%)	3 (2.5%)	15 (2.2%)	7 (2.0%)
	MYOSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TENDINOUS DISORDER	0 (0.0%)	2 (1.7%)	1 (0.1%)	0 (0.0%)
Nervous System	ABNORMAL DREAMS	2 (0.8%)	0 (0.0%)	9 (1.3%)	1 (0.3%)
	AGITATION	0 (0.0%)	0 (0.0%)	1 (0.1%)	4 (1.1%)
	ALCOHOL ABUSE	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	AMNESIA	3 (1.2%)	0 (0.0%)	2 (0.3%)	2 (0.6%)
	ANXIETY	4 (1.6%)	3 (2.5%)	12 (1.8%)	4 (1.1%)
	ATAXIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.6%)
	CONCENTRATION IMPAIRED	3 (1.2%)	0 (0.0%)	20 (2.9%)	2 (0.6%)
	CONFUSION	0 (0.0%)	1 (0.8%)	3 (0.4%)	0 (0.0%)
	CONVULSION	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	DEPERSONALIZATION	0 (0.0%)	0 (0.0%)	2 (0.3%)	1 (0.3%)
	DEPRESSION	5 (2.0%)	1 (0.8%)	3 (0.4%)	4 (1.1%)
	DIZZINESS	15 (6.1%)	3 (2.5%)	46 (6.8%)	12 (3.4%)
	DYSTONIA	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	EMOTIONAL LABILITY	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	HALLUCINATIONS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	HYPERKINESIA	0 (0.0%)	0 (0.0%)	5 (0.7%)	0 (0.0%)
	HYPERTONIA	0 (0.0%)	0 (0.0%)	4 (0.6%)	2 (0.6%)
	HYPESTHESIA	2 (0.8%)	0 (0.0%)	3 (0.4%)	0 (0.0%)
	INCOORDINATION	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	INSOMNIA	17 (6.9%)	3 (2.5%)	54 (7.9%)	7 (2.0%)
	LACK OF EMOTION	2 (0.8%)	0 (0.0%)	10 (1.5%)	3 (0.9%)
	LIBIDO DECREASED	22 (8.9%)	7 (5.8%)	78 (11.5%)	17 (4.9%)
	LIBIDO INCREASED	0 (0.0%)	0 (0.0%)	4 (0.6%)	0 (0.0%)
	MYOCLONUS	1 (0.4%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	NERVOUSNESS	7 (2.8%)	2 (1.7%)	12 (1.8%)	2 (0.6%)
	NEURALGIA	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	NEUROPATHY	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	NEUROSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	NYSTAGMUS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	PARALYSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	PARESTHESIA	0 (0.0%)	1 (0.8%)	6 (0.9%)	1 (0.3%)
	SOMNOLENCE	8 (3.3%)	1 (0.8%)	62 (9.1%)	6 (1.7%)
	THINKING ABNORMAL	2 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	TORTICOLLIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.5

Comparative Summary of Treatment Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=246)	Placebo (N=120)	Paroxetine CR (N=681)	Placebo (N=349)
Nervous System	TREMOR	11 (4.5%)	0 (0.0%)	26 (3.8%)	1 (0.3%)
	VERTIGO	5 (2.0%)	1 (0.8%)	4 (0.6%)	2 (0.6%)
Respiratory System	ASTHMA	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	BRONCHITIS	4 (1.6%)	0 (0.0%)	6 (0.9%)	1 (0.3%)
	COUGH INCREASED	0 (0.0%)	2 (1.7%)	7 (1.0%)	2 (0.6%)
	DYSPNEA	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	EPISTAXIS	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	PHARYNGITIS	3 (1.2%)	5 (4.2%)	13 (1.9%)	6 (1.7%)
	PLEURA DISORDER	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	PNEUMONIA	0 (0.0%)	1 (0.8%)	4 (0.6%)	2 (0.6%)
	RESPIRATORY DISORDER	14 (5.7%)	13 (10.8%)	38 (5.6%)	28 (8.0%)
	RHINITIS	0 (0.0%)	0 (0.0%)	10 (1.5%)	6 (1.7%)
	SINUSITIS	10 (4.1%)	2 (1.7%)	19 (2.8%)	18 (5.2%)
	YAWN	2 (0.8%)	0 (0.0%)	14 (2.1%)	1 (0.3%)
Skin and Appendages	ACNE	2 (0.8%)	1 (0.8%)	5 (0.7%)	3 (0.9%)
	CONTACT DERMATITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.3%)
	DRY SKIN	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)
	ECZEMA	1 (0.4%)	0 (0.0%)	4 (0.6%)	0 (0.0%)
	FURUNCULOSIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	HERPES SIMPLEX	2 (0.8%)	1 (0.8%)	1 (0.1%)	2 (0.6%)
	HERPES ZOSTER	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	MACULOPAPULAR RASH	1 (0.4%)	0 (0.0%)	0 (0.0%)	2 (0.6%)
	NAIL DISORDER	0 (0.0%)	0 (0.0%)	1 (0.1%)	1 (0.3%)
	PRURITUS	1 (0.4%)	2 (1.7%)	8 (1.2%)	4 (1.1%)
	PUSTULAR RASH	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	RASH	1 (0.4%)	1 (0.8%)	2 (0.3%)	3 (0.9%)
	SEBORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SKIN BENIGN NEOPLASM	1 (0.4%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SKIN DISORDER	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	SWEAT GLAND DISORDER	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	SWEATING	14 (5.7%)	1 (0.8%)	45 (6.6%)	3 (0.9%)
	URTICARIA	0 (0.0%)	1 (0.8%)	1 (0.1%)	1 (0.3%)
Special Senses	ABNORMAL VISION	3 (1.2%)	0 (0.0%)	4 (0.6%)	0 (0.0%)
	ABNORMALITY OF ACCOMMODATION	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	BLEPHARITIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	CONJUNCTIVITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.6%)
	EAR DISORDER	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	EAR PAIN	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	EYE DISORDER	0 (0.0%)	0 (0.0%)	2 (0.3%)	1 (0.3%)
	EYE PAIN	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	KERATOCONJUNCTIVITIS	0 (0.0%)	0 (0.0%)	2 (0.3%)	0 (0.0%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.5

Comparative Summary of Treatment Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=246)	Placebo (N=120)	Paroxetine CR (N=681)	Placebo (N=349)
Special Senses	MYDRIASIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	OTITIS MEDIA	1 (0.4%)	2 (1.7%)	5 (0.7%)	0 (0.0%)
	PHOTOPHOBIA	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	TASTE PERVERSION	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	TINNITUS	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
Urogenital System	ABORTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	AMENORRHEA	1 (0.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	BREAST ATROPHY	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	BREAST NEOPLASM	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	BREAST PAIN	1 (0.4%)	0 (0.0%)	2 (0.3%)	1 (0.3%)
	CYSTITIS	3 (1.2%)	3 (2.5%)	3 (0.4%)	2 (0.6%)
	DYSMENORRHEA	8 (3.3%)	4 (3.3%)	22 (3.2%)	22 (6.3%)
	ENDOMETRIAL DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	FEMALE GENITAL DISORDERS	5 (2.0%)	0 (0.0%)	53 (7.8%)	4 (1.1%)
	FEMALE LACTATION	0 (0.0%)	1 (0.8%)	1 (0.1%)	0 (0.0%)
	KIDNEY CALCULUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	LEUKORRHEA	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	MENORRHAGIA	2 (0.8%)	1 (0.8%)	7 (1.0%)	3 (0.9%)
	MENSTRUAL DISORDER	3 (1.2%)	0 (0.0%)	7 (1.0%)	4 (1.1%)
	METORRHAGIA	1 (0.4%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	NEPHRITIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	1 (0.3%)
	PAPANICOLAU SMEAR	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
	SUSPICIOUS				
	SALPINGITIS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	UNINTENDED PREGNANCY	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	URINARY FREQUENCY	0 (0.0%)	0 (0.0%)	4 (0.6%)	0 (0.0%)
	URINARY RETENTION	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	URINARY TRACT INFECTION	2 (0.8%)	2 (1.7%)	9 (1.3%)	6 (1.7%)
	URINATION IMPAIRED	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	UTERINE FIBROIDS ENLARGED	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	UTERUS DISORDERS	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
	VAGINAL MONILIASIS	1 (0.4%)	0 (0.0%)	7 (1.0%)	2 (0.6%)
	VAGINITIS	1 (0.4%)	1 (0.8%)	5 (0.7%)	1 (0.3%)
Special Searches	PUNCTURE SITE REACTION	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.6

Comparative Summary of Follow-up Phase Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-Up)

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=245)	Placebo (N=120)	Paroxetine CR (N=289)	Placebo (N=168)
TOTAL	TOTAL	48 (19.6%)	15 (12.5%)	72 (24.9%)	21 (12.5%)
Body as a Whole	ABDOMINAL PAIN	1 (0.4%)	1 (0.8%)	2 (0.7%)	1 (0.6%)
	ALLERGIC REACTION	1 (0.4%)	1 (0.8%)	1 (0.3%)	1 (0.6%)
	ASTHENIA	3 (1.2%)	0 (0.0%)	5 (1.7%)	3 (1.8%)
	BACK PAIN	2 (0.8%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	FEVER	1 (0.4%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	FLU SYNDROME	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	HEADACHE	7 (2.9%)	2 (1.7%)	9 (3.1%)	5 (3.0%)
	INFECTION	5 (2.0%)	2 (1.7%)	5 (1.7%)	0 (0.0%)
	MALAISE	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	NEOPLASM	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	TRAUMA	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiovascular System	HYPERTENSION	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	HYPOTENSION	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	MIGRAINE	1 (0.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	PALPITATION	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SYNCOPE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)
	TACHYCARDIA	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	VASODILATATION	0 (0.0%)	0 (0.0%)	1 (0.3%)	2 (1.2%)
Digestive System	DIARRHEA	0 (0.0%)	1 (0.8%)	3 (1.0%)	0 (0.0%)
	DYSPEPSIA	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	DYSPHAGIA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	GASTROENTERITIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	NAUSEA	2 (0.8%)	0 (0.0%)	7 (2.4%)	1 (0.6%)
	VOMITING	1 (0.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Endocrine System	HYPOTHYROIDISM	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.2%)
Hemic and Lymphatic System	ANEMIA	1 (0.4%)	3 (2.5%)	1 (0.3%)	1 (0.6%)
	EOSINOPHILIA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	LEUKOPENIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
Metabolic and Nutritional Disorders	BILIRUBINEMIA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	HYPERGLYCEMIA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	LIPODYSTROPHY	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SGOT INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)
	SGPT INCREASED	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	THIRST	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.6

Comparative Summary of Follow-up Phase Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-Up)

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=245)	Placebo (N=120)	Paroxetine CR (N=289)	Placebo (N=168)
Musculoskeletal System	ARTHRITIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	ARTHROSIS	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	MYALGIA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
Nervous System	ABNORMAL DREAMS	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	AGITATION	0 (0.0%)	0 (0.0%)	2 (0.7%)	0 (0.0%)
	ANXIETY	0 (0.0%)	0 (0.0%)	5 (1.7%)	0 (0.0%)
	CONCENTRATION IMPAIRED	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.6%)
	CONFUSION	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	DEPRESSION	4 (1.6%)	1 (0.8%)	1 (0.3%)	0 (0.0%)
	DIZZINESS	0 (0.0%)	0 (0.0%)	23 (8.0%)	0 (0.0%)
	EMOTIONAL LABILITY	1 (0.4%)	0 (0.0%)	4 (1.4%)	0 (0.0%)
	HOSTILITY	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	HYPESTHESIA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	INCOORDINATION	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	INSOMNIA	3 (1.2%)	0 (0.0%)	2 (0.7%)	1 (0.6%)
	LIBIDO DECREASED	1 (0.4%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	LIBIDO INCREASED	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	MYOCLONUS	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	NERVOUSNESS	0 (0.0%)	0 (0.0%)	7 (2.4%)	0 (0.0%)
	PARESTHESIA	0 (0.0%)	1 (0.8%)	2 (0.7%)	0 (0.0%)
	SOMNOLENCE	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.6%)
	SPEECH DISORDER	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	VERTIGO	1 (0.4%)	0 (0.0%)	3 (1.0%)	0 (0.0%)
	WITHDRAWAL SYNDROME	0 (0.0%)	0 (0.0%)	2 (0.7%)	0 (0.0%)
Respiratory System	ASTHMA	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	EPISTAXIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	LARYNX DISORDER	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	PHARYNGITIS	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	RESPIRATORY DISORDER	3 (1.2%)	1 (0.8%)	2 (0.7%)	2 (1.2%)
Skin and Appendages	RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.2%)
	MACULOPAPULAR RASH	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SKIN DISORDER	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SWEATING	0 (0.0%)	0 (0.0%)	1 (0.3%)	1 (0.6%)
	URTICARIA	0 (0.0%)	1 (0.8%)	1 (0.3%)	0 (0.0%)
Special Senses	ABNORMAL VISION	2 (0.8%)	0 (0.0%)	2 (0.7%)	0 (0.0%)
	CONJUNCTIVITIS	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	EAR DISORDER	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	EAR PAIN	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
Urogenital System	ABORTION	1 (0.4%)	0 (0.0%)	1 (0.3%)	1 (0.6%)
	BREAST NEOPLASM	0 (0.0%)	1 (0.8%)	1 (0.3%)	0 (0.0%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

Supplementary Table 15.6

Comparative Summary of Follow-up Phase Emergent Adverse Events with PMDD CR Continuous Dosing
By Body System and Preferred Term
Intention-to-Treat Population (with Follow-Up)

Body System	Preferred Term	PMDD CR Intermittent Dosing		PMDD CR Continuous Dosing	
		Paroxetine CR (N=245)	Placebo (N=120)	Paroxetine CR (N=289)	Placebo (N=168)
Urogenital System	BREAST PAIN	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	CREATININE CLEARANCE DECREASED	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	DYSMENORRHEA	1 (0.4%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	FEMALE GENITAL DISORDERS	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	MENORRHAGIA	1 (0.4%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	MENSTRUAL DISORDER	1 (0.4%)	0 (0.0%)	5 (1.7%)	0 (0.0%)
	STILLBIRTH	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
	UNINTENDED PREGNANCY	0 (0.0%)	0 (0.0%)	3 (1.0%)	1 (0.6%)
	URINARY TRACT INFECTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
	VAGINAL MONILIASIS	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	VAGINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)

PMDD CR Continuous Dosing: Studies 677, 688 and 689

GSK 29060 - Protocol : 717

Supplementary Table 15.7

Summary of Paroxetine CR Treatment Emergent Adverse Events Unique to Intermittent PMDD
By Body System and Preferred Term
Intention-to-Treat Population

Body System	Preferred Term	PMDD CR Intermittent Dosing Paroxetine CR (N=246)
TOTAL	TOTAL	8 (3.3%)
Body as a Whole	MONILIASIS	1 (0.4%)
	SHOCK	1 (0.4%)
Cardiovascular System	MYOCARDIAL INFARCT	1 (0.4%)
	PULMONARY EMBOLUS	1 (0.4%)
Digestive System	COLITIS	1 (0.4%)
Skin and Appendages	MACULOPAPULAR RASH	1 (0.4%)
Urogenital System	BREAST ATROPHY	1 (0.4%)
	LEUKORRHEA	1 (0.4%)
Special Searches	PUNCTURE SITE REACTION	1 (0.4%)

For each study only ITT subjects randomised to Paroxetine CR are included
Panic Disorder: Studies 494, 495 and 497
Depression: Studies 448, 449 and 487
PMDD Continuous: Studies 677, 688 and 689

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 25 mg (N=116)
Severity: Mild

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
TOTAL	35 (30.2%)	10 (8.6%)	20 (20.0%)	10 (10.0%)	17 (18.3%)	7 (7.5%)
ABDOMINAL PAIN	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL VISION	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	3 (3.2%)	0 (0.0%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
ARTHRALGIA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	7 (6.0%)	1 (0.9%)	1 (1.0%)	1 (1.0%)	2 (2.2%)	0 (0.0%)
BACK PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CHILLS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
COLITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CREATININE CLEARANCE DECREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
CYSTITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DECREASED APPETITE	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DIARRHEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.1%)	0 (0.0%)
DIZZINESS	2 (1.7%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
DRY MOUTH	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
DYSMENORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DYSPEPSIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
EPISTAXIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
FLU SYNDROME	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	2 (1.7%)	3 (2.6%)	2 (2.0%)	1 (1.0%)	1 (1.1%)	2 (2.2%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
INSOMNIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
LACK OF EMOTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LEUKORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	1 (0.9%)	0 (0.0%)	3 (3.0%)	0 (0.0%)	3 (3.2%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 25 mg (N=116)
Severity: Mild

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
MENSTRUAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
NAUSEA	10 (8.6%)	0 (0.0%)	5 (5.0%)	0 (0.0%)	3 (3.2%)	0 (0.0%)
NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
NERVOUSNESS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
SINUSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
SOMNOLENCE	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
SWEATING	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TRAUMA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TREMOR	3 (2.6%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	3 (3.2%)	0 (0.0%)
URINARY TRACT INFECTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
VERTIGO	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
WEIGHT GAIN	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 25 mg (N=116)
Severity: Moderate

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
TOTAL	46 (39.7%)	11 (9.5%)	16 (16.0%)	11 (11.0%)	17 (18.3%)	10 (10.8%)
ABDOMINAL PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL VISION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMNESIA	2 (1.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ANXIETY	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ARTHRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ASTHENIA	10 (8.6%)	1 (0.9%)	5 (5.0%)	0 (0.0%)	5 (5.4%)	1 (1.1%)
BACK PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
CONCENTRATION IMPAIRED	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)
CYSTITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DECREASED APPETITE	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DEPRESSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
DIARRHEA	4 (3.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DIZZINESS	3 (2.6%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
DYSMENORRHEA	1 (0.9%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.2%)
DYSPEPSIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
FEMALE GENITAL DISORDERS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)
FLU SYNDROME	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROENTERITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
GINGIVITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	8 (6.9%)	1 (0.9%)	2 (2.0%)	3 (3.0%)	5 (5.4%)	0 (0.0%)
HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	1 (0.9%)	4 (3.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
LACK OF EMOTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	6 (5.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
MENORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYALGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
 By Severity
 Intention-to-Treat Population
 Treatment Group: Paroxetine CR 25 mg (N=116)
 Severity: Moderate

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
NAUSEA	9 (7.8%)	0 (0.0%)	2 (2.0%)	1 (1.0%)	2 (2.2%)	1 (1.1%)
NEOPLASM	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.1%)	0 (0.0%)
PUSTULAR RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	0 (0.0%)	0 (0.0%)	1 (1.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)
SINUSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
SOMNOLENCE	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
SWEATING	5 (4.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
THINKING ABNORMAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TOOTH DISORDER	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TREMOR	2 (1.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINAL MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
VASODILATATION	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
 Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 25 mg (N=116)
Severity: Severe

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
TOTAL	22 (19.0%)	4 (3.4%)	7 (7.0%)	2 (2.0%)	4 (4.3%)	5 (5.4%)
ABDOMINAL PAIN	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL VISION	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABORTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ALCOHOL ABUSE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	3 (2.6%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)
BACK PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DEPRESSION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
DIARRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DIZZINESS	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEMALE GENITAL DISORDERS	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	2 (1.7%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	2 (2.2%)	1 (1.1%)
INFECTION	1 (0.9%)	1 (0.9%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
LIBIDO DECREASED	5 (4.3%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
MENSTRUAL DISORDER	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	4 (3.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SINUSITIS	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
SOMNOLENCE	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SWEATING	2 (1.7%)	1 (0.9%)	2 (2.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TREMOR	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VOMITING	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Severity: Mild

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
TOTAL	27 (20.8%)	5 (3.8%)	17 (14.4%)	4 (3.4%)	14 (12.8%)	6 (5.5%)
ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ABNORMAL DREAMS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ACNE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ASTHENIA	5 (3.8%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	1 (0.9%)	0 (0.0%)
BACK PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
CONCENTRATION IMPAIRED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
DIARRHEA	4 (3.1%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
DIZZINESS	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSPEPSIA	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSPHAGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
FLATULENCE	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.9%)	1 (0.9%)
INSOMNIA	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
LIBIDO DECREASED	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIPODYSTROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
MACULOPAPULAR RASH	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MONILIASIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	8 (6.2%)	0 (0.0%)	3 (2.5%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
NERVOUSNESS	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
SINUSITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.

Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Severity: Mild

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
SWEATING	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TASTE PERVERSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TREMOR	4 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
VAGINAL MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
VERTIGO	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
YAWN	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Severity: Moderate

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
TOTAL	32 (24.6%)	17 (13.1%)	24 (20.3%)	15 (12.7%)	16 (14.7%)	13 (11.9%)
ABDOMINAL PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	1 (0.9%)	0 (0.0%)
ABNORMAL VISION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ACNE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ARTHRALGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	5 (3.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
ASTHMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BACK PAIN	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
BRONCHITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
CHILLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
CONCENTRATION IMPAIRED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DECREASED APPETITE	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DEPRESSION	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DIARRHEA	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DIZZINESS	2 (1.5%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSMENORRHEA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
DYSPHAGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ECZEMA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FEMALE GENITAL DISORDERS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FLATULENCE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FLU SYNDROME	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROENTERITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HEADACHE	5 (3.8%)	5 (3.8%)	6 (5.1%)	4 (3.4%)	4 (3.7%)	3 (2.8%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
INFECTION	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	6 (4.6%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	0 (0.0%)	2 (1.8%)
LIBIDO DECREASED	4 (3.1%)	0 (0.0%)	2 (1.7%)	1 (0.8%)	1 (0.9%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Severity: Moderate

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
MACULOPAPULAR RASH	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MALAISE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MYALGIA	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYOCARDIAL INFARCT	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	3 (2.3%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	4 (3.1%)	0 (0.0%)	1 (0.8%)	2 (1.7%)	1 (0.9%)	2 (1.8%)
SHOCK	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SINUSITIS	1 (0.8%)	2 (1.5%)	1 (0.8%)	1 (0.8%)	1 (0.9%)	0 (0.0%)
SKIN DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
SWEATING	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
TOOTH DISORDER	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
TREMOR	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Severity: Severe

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
TOTAL	13 (10.0%)	2 (1.5%)	10 (8.5%)	2 (1.7%)	11 (10.1%)	6 (5.5%)
ABDOMINAL PAIN	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANXIETY	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ASTHENIA	3 (2.3%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
BACK PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DEPRESSION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
DYSMENORRHEA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSPHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
EDEMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
FEMALE GENITAL DISORDERS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HEADACHE	2 (1.5%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.9%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
INFECTION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
INSOMNIA	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
LIBIDO DECREASED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
MENSTRUAL DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
RESPIRATORY DISORDER	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SOMNOLENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
SWEATING	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
THINKING ABNORMAL	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VOMITING	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.

Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Placebo (N=120)
Severity: Mild

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
TOTAL	13 (10.8%)	4 (3.3%)	15 (13.2%)	9 (7.9%)	10 (9.3%)	6 (5.6%)
ACNE	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AMENORRHEA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.8%)
ANXIETY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
ASTHENIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BACK PAIN	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONFUSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DIZZINESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)
DYSMENORRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
DYSPEPSIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
HEADACHE	0 (0.0%)	2 (1.7%)	3 (2.6%)	1 (0.9%)	2 (1.9%)	1 (0.9%)
INCREASED APPETITE	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INSOMNIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	2 (1.9%)	0 (0.0%)
LEUKOPENIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LIBIDO DECREASED	3 (2.5%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	1 (0.8%)	1 (0.8%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PARESTHESIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	1 (0.8%)	1 (0.8%)	1 (0.9%)	2 (1.8%)	1 (0.9%)	1 (0.9%)
SGPT INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
TENDINOUS DISORDER	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.

Percentages for each period are based on the number who progressed to the given interval

GSK 29060 - Protocol : 717

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Placebo (N=120)
Severity: Mild

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
THIRST	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Placebo (N=120)
Severity: Moderate

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
TOTAL	26 (21.7%)	8 (6.7%)	20 (17.5%)	6 (5.3%)	16 (15.0%)	7 (6.5%)
ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ALLERGIC REACTION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ANXIETY	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)
ARTHRALGIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ASTHENIA	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
BACK PAIN	1 (0.8%)	1 (0.8%)	1 (0.9%)	0 (0.0%)	2 (1.9%)	0 (0.0%)
CONSTIPATION	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
DEPRESSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DIZZINESS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSMENORRHEA	3 (2.5%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)
DYSPEPSIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FLATULENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTRITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HEADACHE	7 (5.8%)	2 (1.7%)	5 (4.4%)	2 (1.8%)	4 (3.7%)	1 (0.9%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.8%)	1 (0.9%)
LIBIDO DECREASED	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
MYALGIA	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
NERVOUSNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
PARESTHESIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
PHARYNGITIS	1 (0.8%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	1 (0.8%)	1 (0.8%)	2 (1.8%)	1 (0.9%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Placebo (N=120)
Severity: Moderate

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
SINUSITIS	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SOMNOLENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TENDINOUS DISORDER	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
TOOTH DISORDER	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
VAGINITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
 By Severity
 Intention-to-Treat Population
 Treatment Group: Placebo (N=120)
 Severity: Severe

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
TOTAL	6 (5.0%)	2 (1.7%)	5 (4.4%)	5 (4.4%)	6 (5.6%)	3 (2.8%)
ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ANXIETY	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BACK PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HEADACHE	2 (1.7%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	2 (1.9%)	1 (0.9%)
LIBIDO DECREASED	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	1 (0.9%)	1 (0.9%)
MYALGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
SWEATING	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
 Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 25 mg (N=116)
Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
TOTAL	71 (61.2%)	24 (20.7%)	31 (31.0%)	21 (21.0%)	33 (35.5%)	19 (20.4%)
ABDOMINAL PAIN	4 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL DREAMS	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL VISION	3 (2.6%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMALITY OF ACCOMMODATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABORTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ALCOHOL ABUSE	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
AMNESIA	2 (1.7%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	3 (3.2%)	0 (0.0%)
ANAPHYLACTOID REACTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ANXIETY	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
ARTHRALGIA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ARTHRITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
ASTHENIA	20 (17.2%)	2 (1.7%)	7 (7.0%)	1 (1.0%)	8 (8.6%)	2 (2.2%)
BACK PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
BREAST PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BRONCHITIS	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CHILLS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
COLITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
CONCENTRATION IMPAIRED	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	1 (0.9%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)
CREATININE CLEARANCE DECREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
CYSTITIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)
DECREASED APPETITE	4 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DEPRESSION	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
DIARRHEA	7 (6.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	1 (1.1%)	0 (0.0%)
DIZZINESS	6 (5.2%)	1 (0.9%)	2 (2.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)
DRY MOUTH	3 (2.6%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
DYSMENORRHEA	2 (1.7%)	3 (2.6%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.2%)
DYSPEPSIA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	1 (1.1%)
EPISTAXIS	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 25 mg (N=116)
Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
FEMALE GENITAL DISORDERS	2 (1.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)
FLU SYNDROME	1 (0.9%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROENTERITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
HEADACHE	12 (10.3%)	4 (3.4%)	5 (5.0%)	5 (5.0%)	8 (8.6%)	3 (3.2%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPERTENSION	1 (0.9%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HYPESTHESIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
INCOORDINATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
INCREASED APPETITE	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	3 (2.6%)	6 (5.2%)	1 (1.0%)	1 (1.0%)	0 (0.0%)	2 (2.2%)
INSOMNIA	3 (2.6%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
LACK OF EMOTION	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LEUKORRHEA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LIBIDO DECREASED	12 (10.3%)	0 (0.0%)	5 (5.0%)	0 (0.0%)	5 (5.4%)	0 (0.0%)
MENORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MENSTRUAL DISORDER	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
METORRHAGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
MYALGIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYDRIASIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	23 (19.8%)	0 (0.0%)	8 (8.0%)	1 (1.0%)	5 (5.4%)	1 (1.1%)
NEOPLASM	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
NERVOUSNESS	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
PALPITATION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PHARYNGITIS	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.1%)	0 (0.0%)
PUSTULAR RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	1 (0.9%)	1 (0.9%)	1 (1.0%)	2 (2.0%)	1 (1.1%)	0 (0.0%)
SINUSITIS	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	2 (2.2%)	0 (0.0%)
SOMNOLENCE	5 (4.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)
SWEATING	8 (6.9%)	1 (0.9%)	4 (4.0%)	0 (0.0%)	2 (2.2%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.

Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
 By Severity
 Intention-to-Treat Population
 Treatment Group: Paroxetine CR 25 mg (N=116)
 Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=116)	Off Medication following TC1 Medication (N=116)	On Medication during TC2 (N=100)	Off Medication following TC2 Medication (N=100)	On Medication during TC3 (N=93)	Off Medication following TC3 Medication (N=93)
TACHYCARDIA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
THINKING ABNORMAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TOOTH DISORDER	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
TREMOR	6 (5.2%)	0 (0.0%)	3 (3.0%)	0 (0.0%)	3 (3.2%)	0 (0.0%)
URINARY TRACT INFECTION	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VAGINAL MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
VAGINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)
VASODILATATION	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	1 (0.9%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.1%)
VOMITING	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
WEIGHT GAIN	3 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
 Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
TOTAL	57 (43.8%)	22 (16.9%)	41 (34.7%)	19 (16.1%)	32 (29.4%)	23 (21.1%)
ABDOMINAL PAIN	1 (0.8%)	1 (0.8%)	2 (1.7%)	1 (0.8%)	1 (0.9%)	1 (0.9%)
ABNORMAL DREAMS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ABNORMAL VISION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ACNE	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ALLERGIC REACTION	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ANXIETY	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ARTHRALGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ASTHENIA	13 (10.0%)	0 (0.0%)	6 (5.1%)	1 (0.8%)	4 (3.7%)	1 (0.9%)
ASTHMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BACK PAIN	2 (1.5%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	1 (0.9%)
BREAST ATROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BREAST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
BRONCHITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	1 (0.9%)	0 (0.0%)
CHILLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
CONCENTRATION IMPAIRED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
CONSTIPATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
CYSTITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DECREASED APPETITE	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DEPRESSION	1 (0.8%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.8%)
DIARRHEA	5 (3.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
DIZZINESS	5 (3.8%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
DRY MOUTH	2 (1.5%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSMENORRHEA	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
DYSPEPSIA	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSPHAGIA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
EAR DISORDER	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EAR PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ECZEMA	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
EDEMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EMOTIONAL LABILITY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
FEMALE GENITAL DISORDERS	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Paroxetine CR 12.5 mg (N=130)
Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
FLATULENCE	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FLU SYNDROME	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROENTERITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GINGIVITIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HAEMATOMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HEADACHE	9 (6.9%)	5 (3.8%)	8 (6.8%)	5 (4.2%)	5 (4.6%)	3 (2.8%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HYPERTENSION	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
INFECTION	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.9%)	2 (1.8%)
INSOMNIA	10 (7.7%)	0 (0.0%)	4 (3.4%)	1 (0.8%)	2 (1.8%)	3 (2.8%)
LIBIDO DECREASED	5 (3.8%)	0 (0.0%)	3 (2.5%)	1 (0.8%)	3 (2.8%)	0 (0.0%)
LIPODYSTROPHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LYMPHADENOPATHY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
MACULOPAPULAR RASH	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MALAISE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MENORRHAGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
MENSTRUAL DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
MIGRAINE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
MONILIASIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYALGIA	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYOCARDIAL INFARCT	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MYOCLONUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NAUSEA	14 (10.8%)	1 (0.8%)	4 (3.4%)	1 (0.8%)	2 (1.8%)	1 (0.9%)
NEOPLASM	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	5 (3.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)
OVARY DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
PALPITATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)
POSTURAL HYPOTENSION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PULMONARY EMBOLUS	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PUNCTURE SITE REACTION	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	5 (3.8%)	0 (0.0%)	2 (1.7%)	2 (1.7%)	3 (2.8%)	2 (1.8%)
SHOCK	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
 By Severity
 Intention-to-Treat Population
 Treatment Group: Paroxetine CR 12.5 mg (N=130)
 Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=130)	Off Medication following TC1 Medication (N=130)	On Medication during TC2 (N=118)	Off Medication following TC2 Medication (N=118)	On Medication during TC3 (N=109)	Off Medication following TC3 Medication (N=109)
SINUSITIS	1 (0.8%)	3 (2.3%)	1 (0.8%)	2 (1.7%)	1 (0.9%)	0 (0.0%)
SKIN BENIGN NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
SKIN DISORDER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SOMNOLENCE	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	0 (0.0%)
SWEATING	3 (2.3%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
TASTE PERVERSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
THINKING ABNORMAL	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TINNITUS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TOOTH DISORDER	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TRAUMA	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.8%)
TREMOR	4 (3.1%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
VAGINAL MONILIASIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
VASCULAR DISORDER	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	2 (1.5%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
VOMITING	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
YAWN	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
 Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Placebo (N=120)
Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
TOTAL	37 (30.8%)	13 (10.8%)	33 (28.9%)	18 (15.8%)	30 (28.0%)	15 (14.0%)
ABDOMINAL PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
ACNE	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ALLERGIC REACTION	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
AMENORRHEA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ANEMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.8%)
ANXIETY	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	1 (0.9%)	0 (0.0%)
ARRHYTHMIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
ARTHRALGIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
ASTHENIA	3 (2.5%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
BACK PAIN	2 (1.7%)	1 (0.8%)	2 (1.8%)	1 (0.9%)	2 (1.9%)	0 (0.0%)
BREAST NEOPLASM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONFUSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONSTIPATION	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONTACT DERMATITIS	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
COUGH INCREASED	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CYSTITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.9%)	0 (0.0%)
DEPRESSION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
DIZZINESS	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)
DRY MOUTH	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DYSMENORRHEA	3 (2.5%)	1 (0.8%)	0 (0.0%)	1 (0.9%)	2 (1.9%)	0 (0.0%)
DYSPEPSIA	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FEMALE LACTATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FEVER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
FLATULENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
FURUNCULOSIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
GASTRITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERALIZED EDEMA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
HEADACHE	9 (7.5%)	4 (3.3%)	10 (8.8%)	3 (2.6%)	6 (5.6%)	2 (1.9%)
HERPES SIMPLEX	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INCREASED APPETITE	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTION	2 (1.7%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	5 (4.7%)	2 (1.9%)
INSOMNIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	2 (1.9%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
Percentages for each period are based on the number who progressed to the given interval

Supplementary Table 15.8

Number (%) of Subjects with Adverse Events by Time of Occurrence Relating to Treatment Periods
By Severity
Intention-to-Treat Population
Treatment Group: Placebo (N=120)
Overall - All Severities Combined

Preferred Term	On Medication during TC1 (N=120)	Off Medication following TC1 Medication (N=120)	On Medication during TC2 (N=114)	Off Medication following TC2 Medication (N=114)	On Medication during TC3 (N=107)	Off Medication following TC3 Medication (N=107)
LEUKOPENIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
LIBIDO DECREASED	4 (3.3%)	0 (0.0%)	3 (2.6%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
LIVER FUNCTION TESTS ABNORMAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
MENORRHAGIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MIGRAINE	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.8%)	1 (0.9%)	1 (0.9%)
MYALGIA	2 (1.7%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
NAUSEA	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NERVOUSNESS	1 (0.8%)	1 (0.8%)	1 (0.9%)	0 (0.0%)	2 (1.9%)	0 (0.0%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
PARESTHESIA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
PHARYNGITIS	1 (0.8%)	0 (0.0%)	2 (1.8%)	1 (0.9%)	1 (0.9%)	0 (0.0%)
PNEUMONIA	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PRURITUS	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
RESPIRATORY DISORDER	2 (1.7%)	2 (1.7%)	5 (4.4%)	3 (2.6%)	2 (1.9%)	1 (0.9%)
SGPT INCREASED	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)
SINUSITIS	1 (0.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SOMNOLENCE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
SWEATING	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TENDINOUS DISORDER	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
THIRST	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
TOOTH DISORDER	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
TRAUMA	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.6%)	0 (0.0%)	0 (0.0%)
URINARY TRACT INFECTION	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
URTICARIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
VAGINITIS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VERTIGO	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.9%)
WEIGHT GAIN	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

For the three 'off medication' periods the denominator is the same as the number of subjects who progressed to the previous 'on medication' window and have a fixed duration of 14 days from the cycle last dose date, or up to the day prior to the start of medication of the next cycle if earlier.
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16. DATA SOURCE FIGURES: EFFICACY AND QUALITY OF LIFE

	Page
Figure 13.1 Adjusted Mean Change from Baseline (+/- 2 S.E.) In Mean Luteal Phase VAS-Mood Score By Treatment Group Intention-to-Treat Population	772
Figure 13.2 Treatment Difference (95% C.I.) for Change from Baseline In Mean Luteal Phase VAS-Mood Score Intention-to-Treat Population	773
Figure 13.3 Individual Subject Profile Plots of the Daily VAS - Mood Score (ITT).	774
Figure 13.4 Adjusted Mean Change from Baseline (+/- 2 S.E.) in Mean Luteal Phase VAS Physical Symptom Score By Treatment Group Intention-to-Treat Population.	813
Figure 13.5 Odds Ratio (95% C.I.) for Responders Defined by 50% Reduction in their Baseline Mean Luteal Phase VAS-Mood Score Intention-to-Treat Population.	814
Figure 13.6 Odds Ratio (95% C.I.) for Responders Defined by a Return to a Score Less Than or Equal to Baseline Mean Follicular Phase VAS-Mood Score Intention-to-Treat Population	815
Figure 13.7.1 Mean Change from Baseline (+/- 2 S.E.) In Mean Luteal Phase VAS Total Score by Treatment Group Intention-to-Treat Population	816
Figure 13.7.2.1 Mean Change from Baseline (+/- 2 S.E.) In the 11 Individual VAS Item Scores Depressed Mood Intention-to-Treat Population	817
Figure 13.7.2.2 Mean Change from Baseline (+/- 2 S.E.) In the 11 Individual VAS Item Scores Tension Intention-to-Treat Population	818
Figure 13.7.2.3 Mean Change from Baseline (+/- 2 S.E.) In the 11 Individual VAS Item Scores Affective Lability Intention-to-Treat Population	819
Figure 13.7.2.4 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Irritability Intention-to-Treat Population.	820
Figure 13.7.2.5 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Decreased Interest Intention-to-Treat Population.	821
Figure 13.7.2.6 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Difficulty Concentrating Intention-to-Treat Population .	822
Figure 13.7.2.7 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Scores Lack of Energy Intention-to-Treat Population	823
Figure 13.7.2.8 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Change in Appetite Intention-to-Treat Population	824
Figure 13.7.2.9 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Change in Sleep Pattern Intention-to-Treat Population	825
Figure 13.7.2.10 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Feeling out of Control Intention-to-Treat Population	826
Figure 13.7.2.7.11 Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores Physical Symptoms Intention-to-Treat Population	827

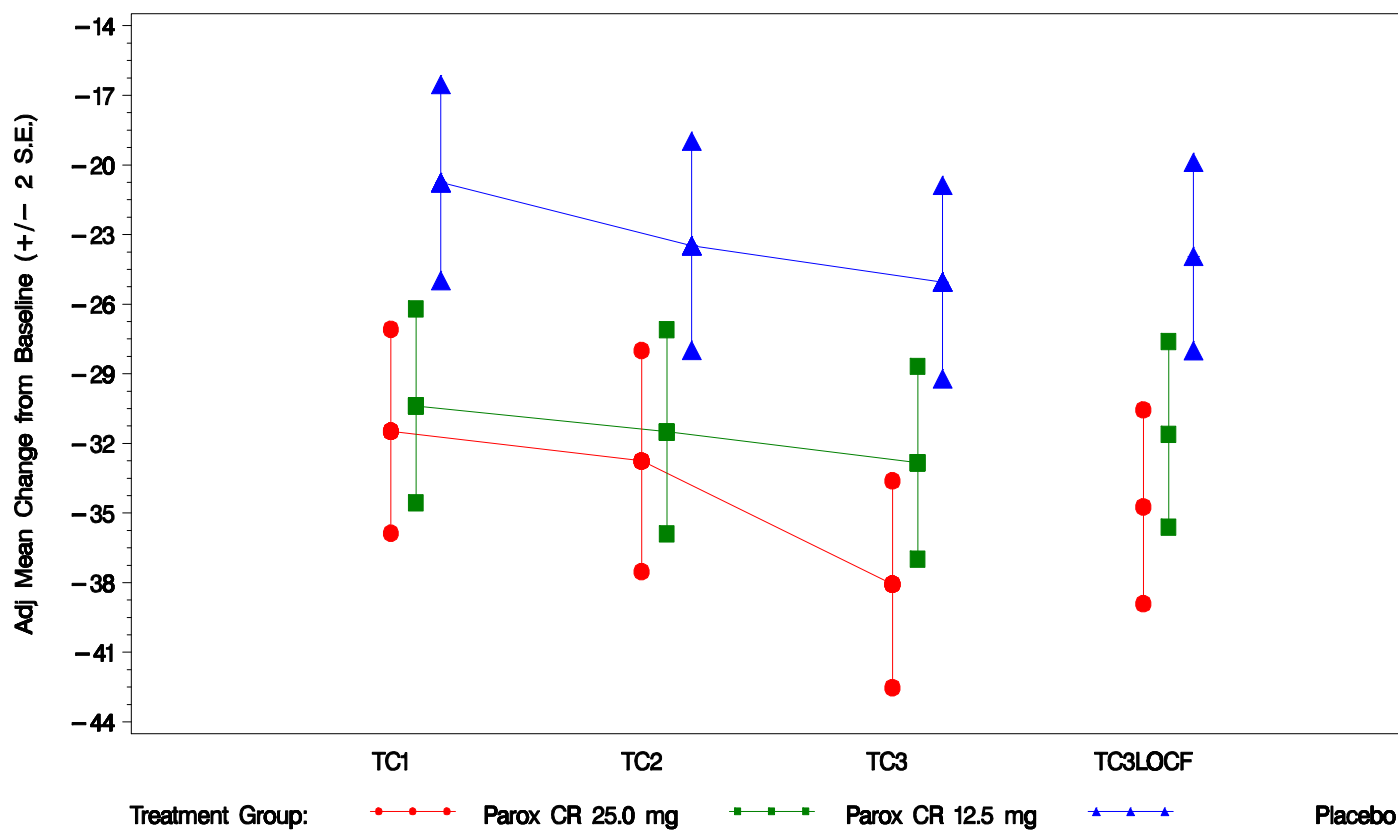
Figure 13.8.1.1 Adjusted Mean Change from Baseline (+/- 2 S.E.) in Sheehan Disability Scale Items Social Score Intention-to-Treat Population	828
Figure 13.8.1.2 Adjusted Mean Change from Baseline (+/- 2 S.E.) in Sheehan Disability Scale Items Work Score Intention-to-Treat Population	829
Figure 13.8.1.3 Adjusted Mean Change from Baseline (+/- 2 S.E.) in Sheehan Disability Scale Items Family Score Intention-to-Treat Population	830
Figure 13.8.2 Adjusted Mean Change from Baseline (+/- 2 S.E.) in Sheehan Disability Scale Total Score By Treatment Group Intention-to-Treat Population	831
Figure 13.9 Adjusted Mean Change from Baseline (+/- 2 S.E.) in the Observer Rated Premenstrual Tension Scale Total Score Intention-to-Treat Population.	832
Figure 13.10 Adjusted Mean Change from Baseline (+/- 2 S.E.) in the CGI - Severity of Illness Item Intention-to-Treat Population	833
Figure 13.11 Odds Ratio (95% C.I.) for Responders defined as a Score of 1 or 2 on the CGI - Global Improvement Item Intention-to-Treat Population	834
Figure 13.12 Odds Ratio (95% C.I.) for Responders defined as a Score of 1 or 2 on the Patient Global Evaluation Intention-to-Treat Population	835
Figure 14.1 Distribution of EuroQol EQ-5D Health Profile Items at Baseline Intention-to-Treat Population.	836
Figure 14.2 Distribution of EuroQol EQ-5D Health Profile Items at Treatment Cycle 3 Intention-to-Treat Population	837

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Figure 13.1

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in Mean Luteal Phase VAS–Mood Score
By Treatment Group
Intention-to-Treat Population



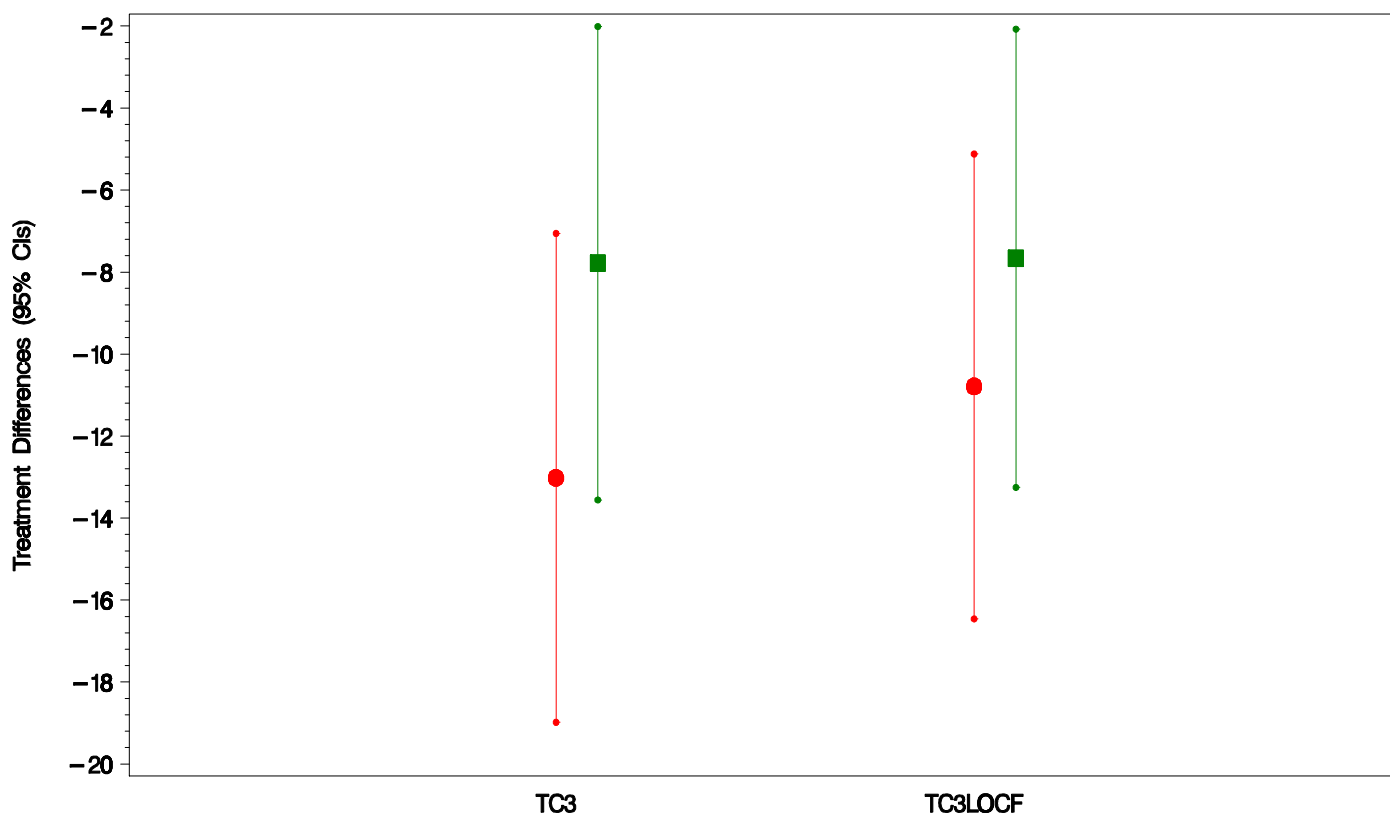
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3
Adjusted for Centre Group, Baseline Score and Age

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Figure 13.2

Treatment Difference (95% CI) for Change from Baseline in Mean Luteal Phase VAS–Mood Score
Intention–to–Treat Population



● = Paroxetine CR 25mg vs Placebo ■ = Paroxetine CR 12.5mg vs Placebo

Adjusted for Centre Group, Baseline Score and Age
Differences in adjusted means shown (Paroxetine CR minus placebo)

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Figure 13.3

Individual Subject Profile Plots of the Daily VAS – Mood Score (ITT)

This section contained data from each individual patient, rather than in aggregate. They have been excluded to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the Sponsor Clinical Study Register.

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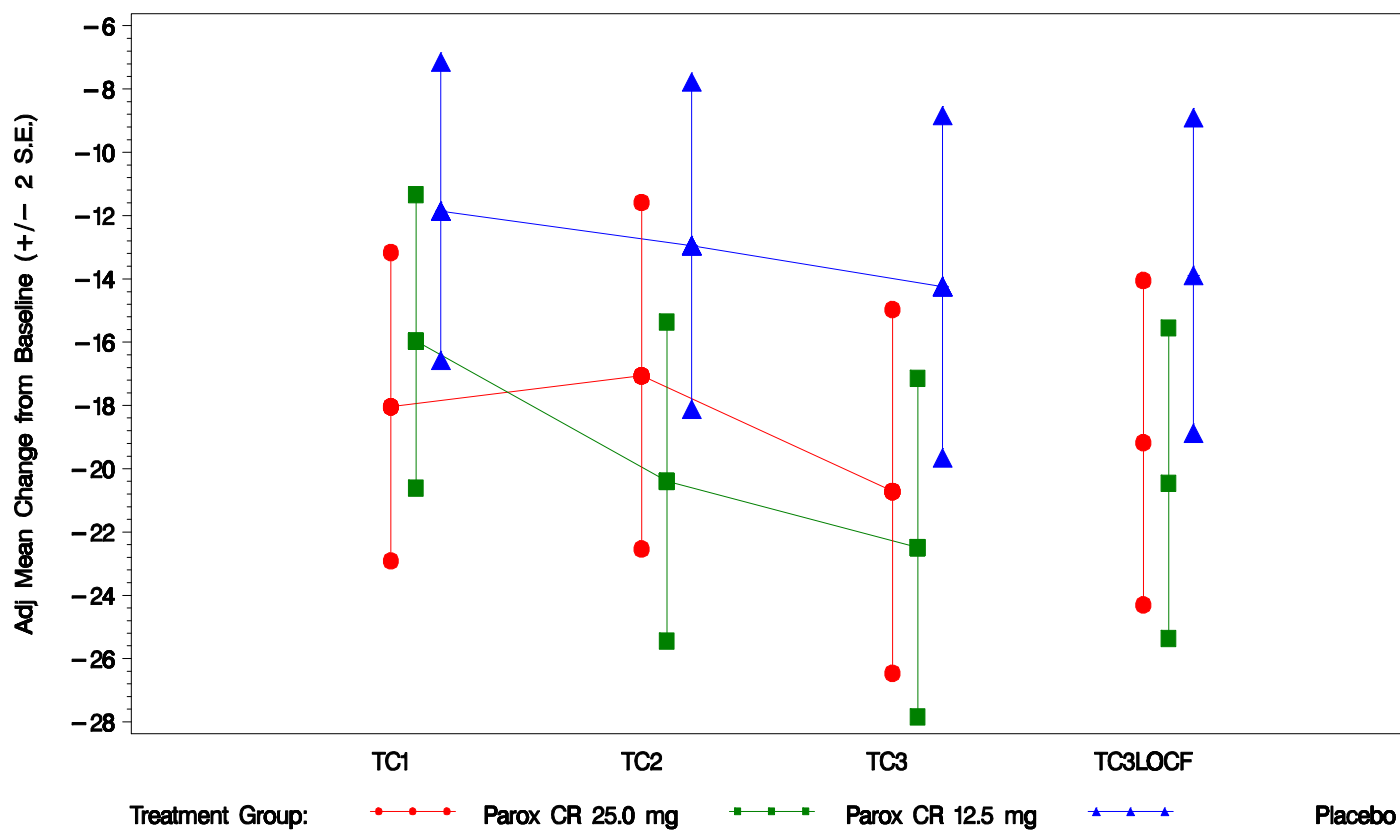
BRL-029060/717

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Figure 13.4

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in Mean Luteal Phase VAS Physical Symptom Score
By Treatment Group
Intention-to-Treat Population



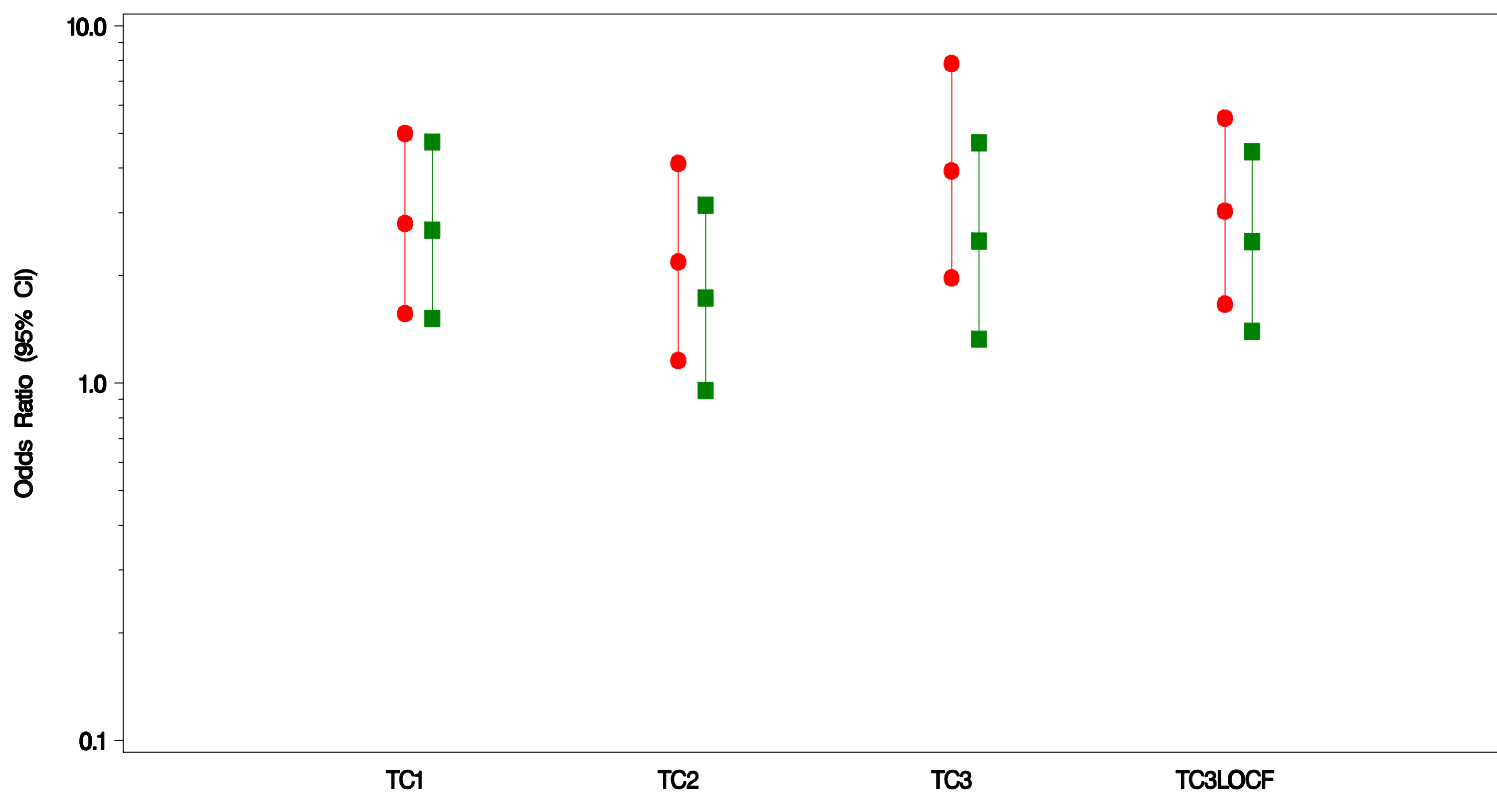
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3
Adjusted for Centre Group, Baseline Score and Age

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Figure 13.5

Odds Ratio (95% CI) for Responders defined by a 50% Reduction in their Baseline Mean Luteal Phase VAS–Mood Score
Intention-to-Treat Population



TC1=Treatment Cycle 1 TC2=Treatment Cycle 2 TC3=Treatment Cycle 3

● = Paroxetine CR 25mg vs Placebo ■ = Paroxetine CR 12.5mg vs Placebo

Adjusted for Centre Group, Baseline Score and Age

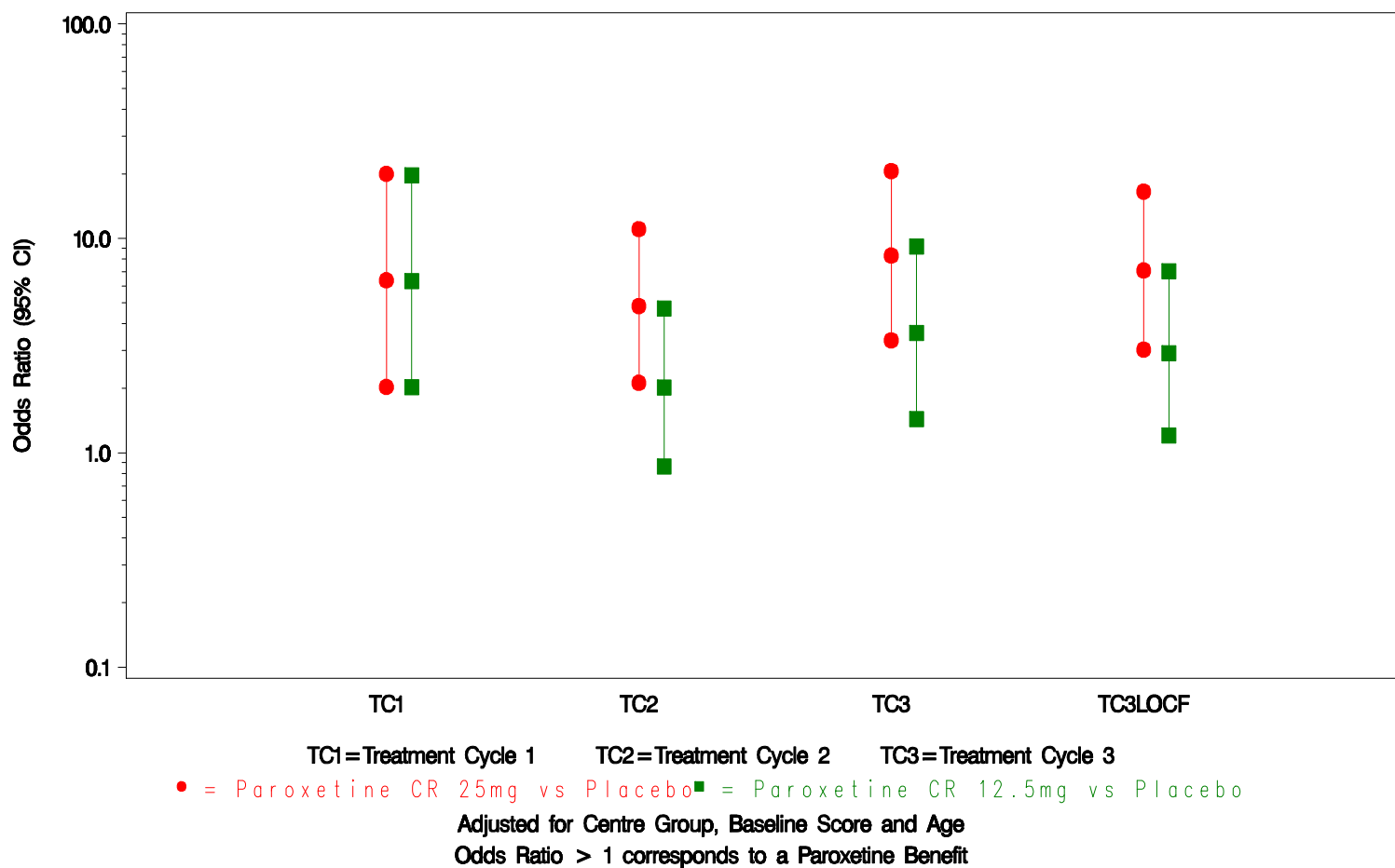
Odds Ratio > 1 corresponds to a Paroxetine Benefit

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Figure 13.6

Odds Ratio (95% CI) for Responders
 Defined by a Return to a Score Less Than or Equal to Baseline Mean Follicular VAS–Mood Score
 Intention-to-Treat Population

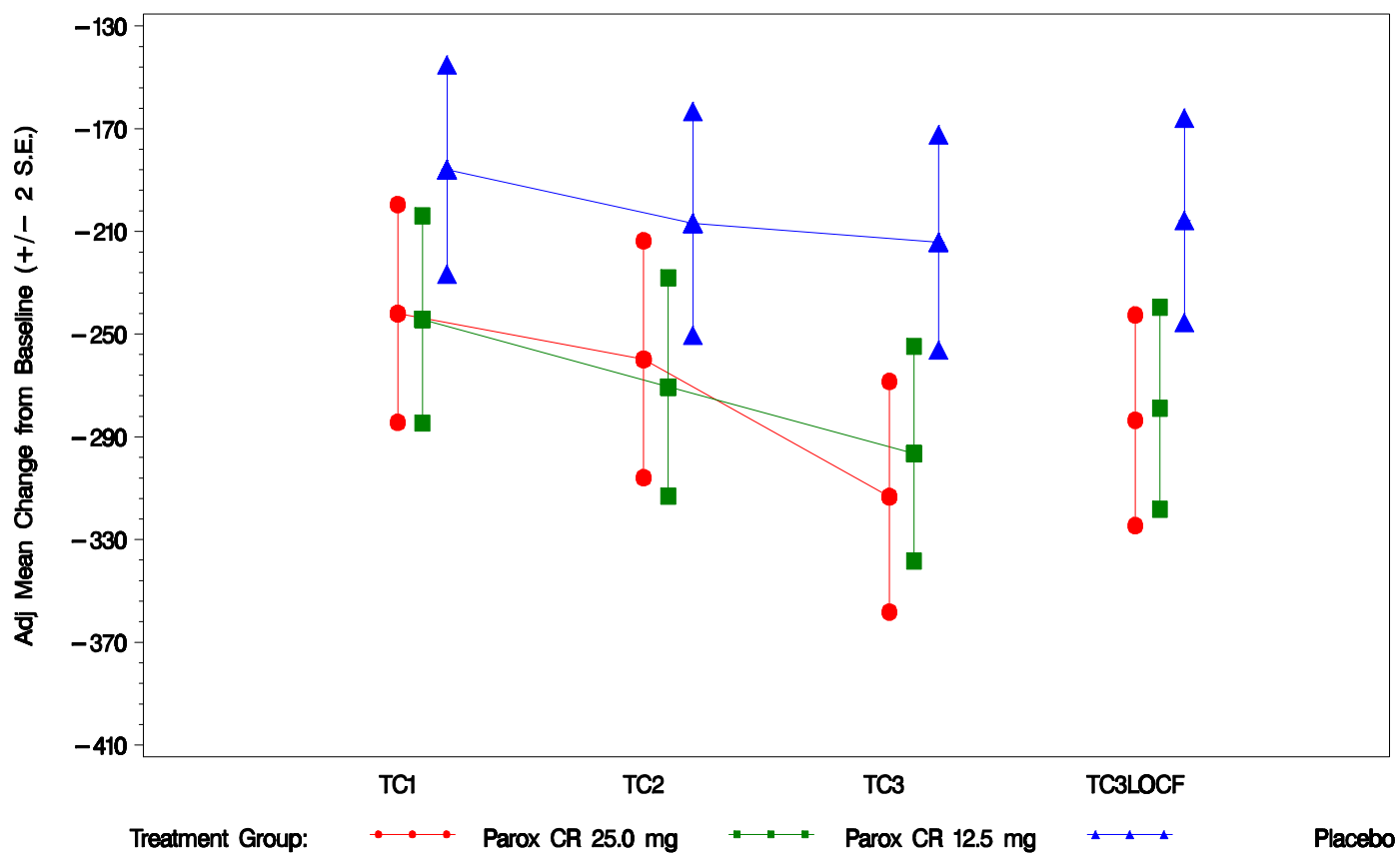


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Figure 13.7.1

Mean Change from Baseline ($\pm$ 2 S.E.) in Mean Luteal Phase VAS Total Score by Treatment Group
Intention-to-Treat Population



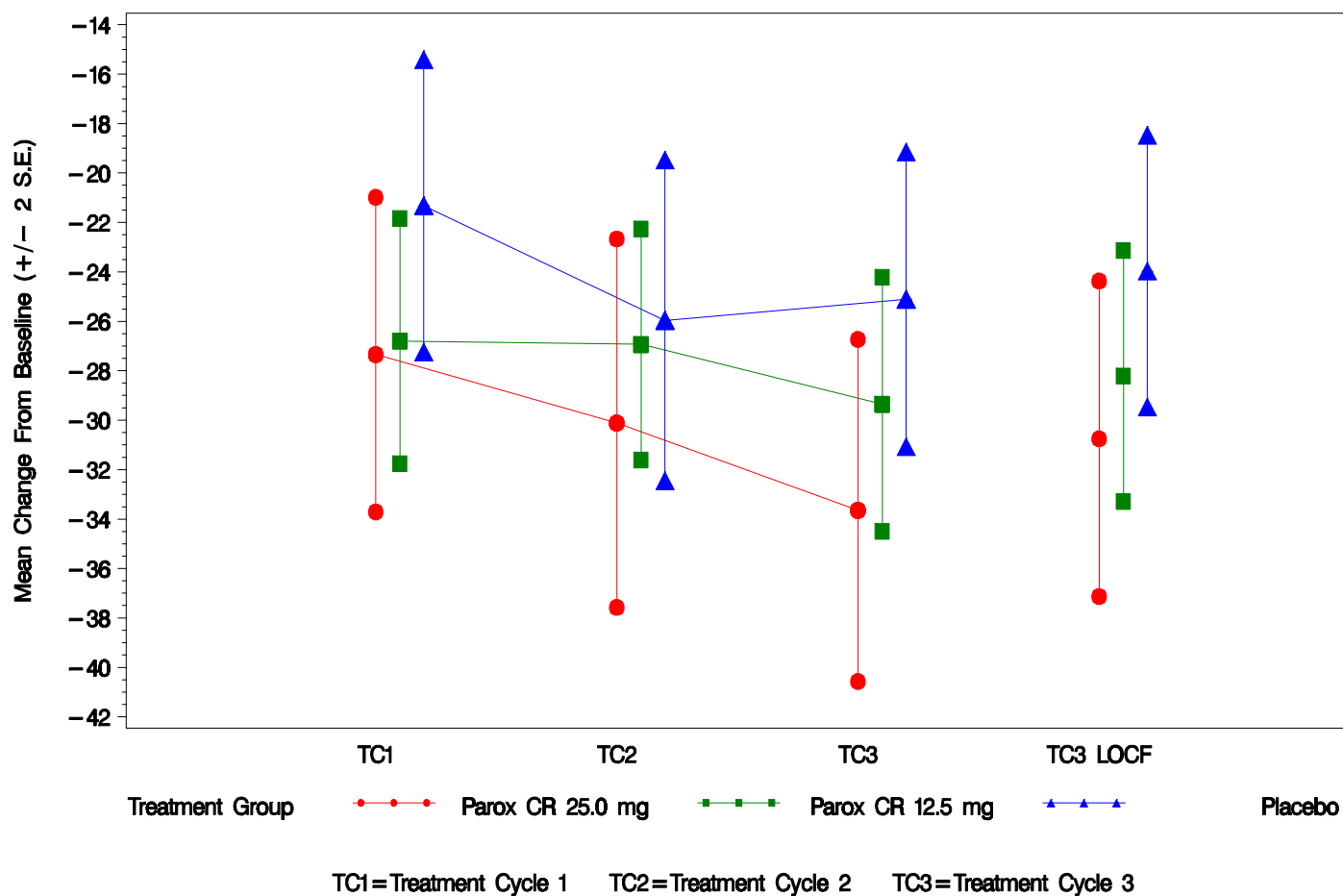
TC1=Treatment Cycle 1 TC2=Treatment Cycle 2 TC3=Treatment Cycle 3
Adjusted for Centre Group, Baseline Score and Age

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Figure 13.7.2.1

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Depressed Mood
Intention-to-Treat Population

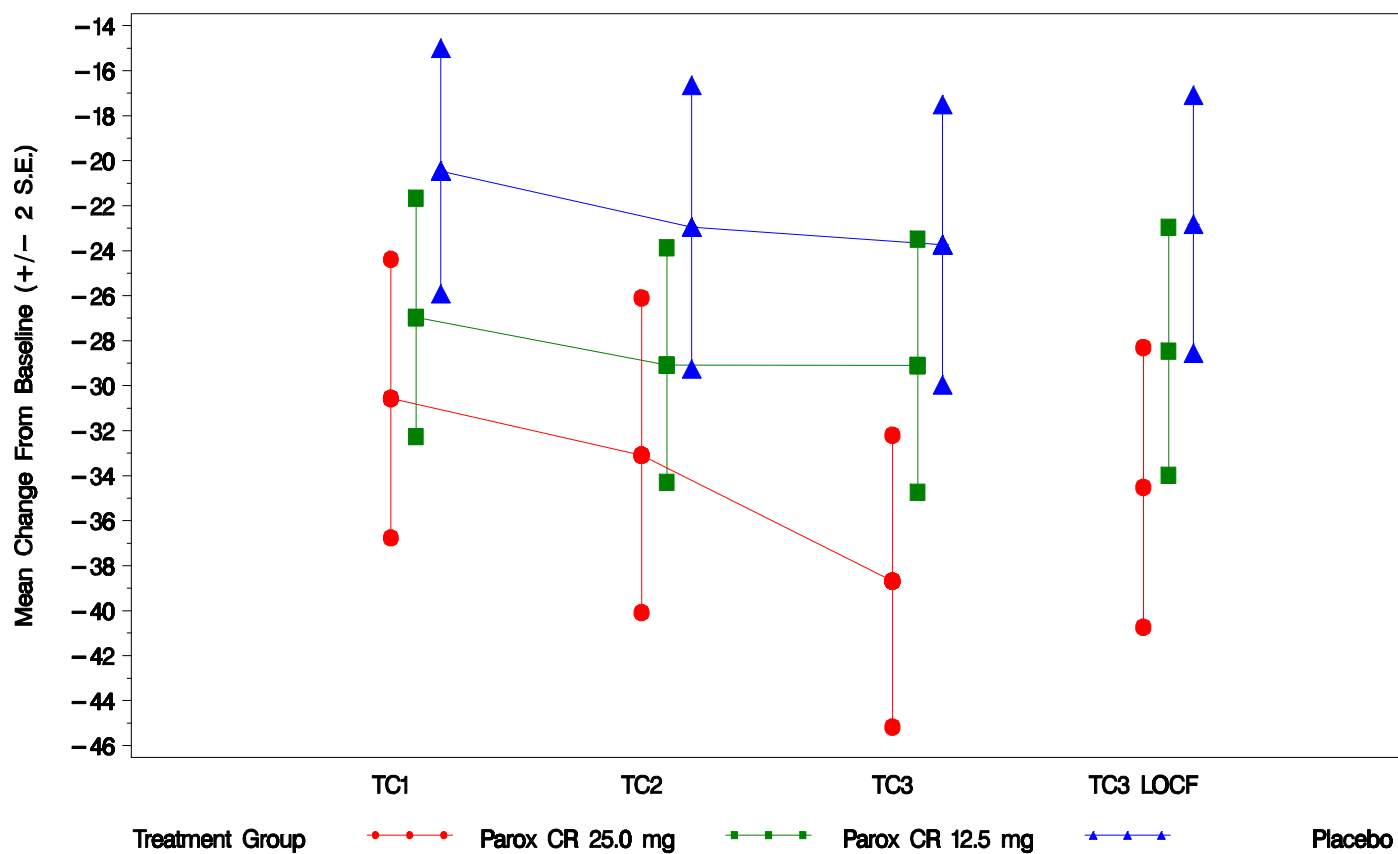


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Figure 13.7.2.2

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Tension
Intention-to-Treat Population



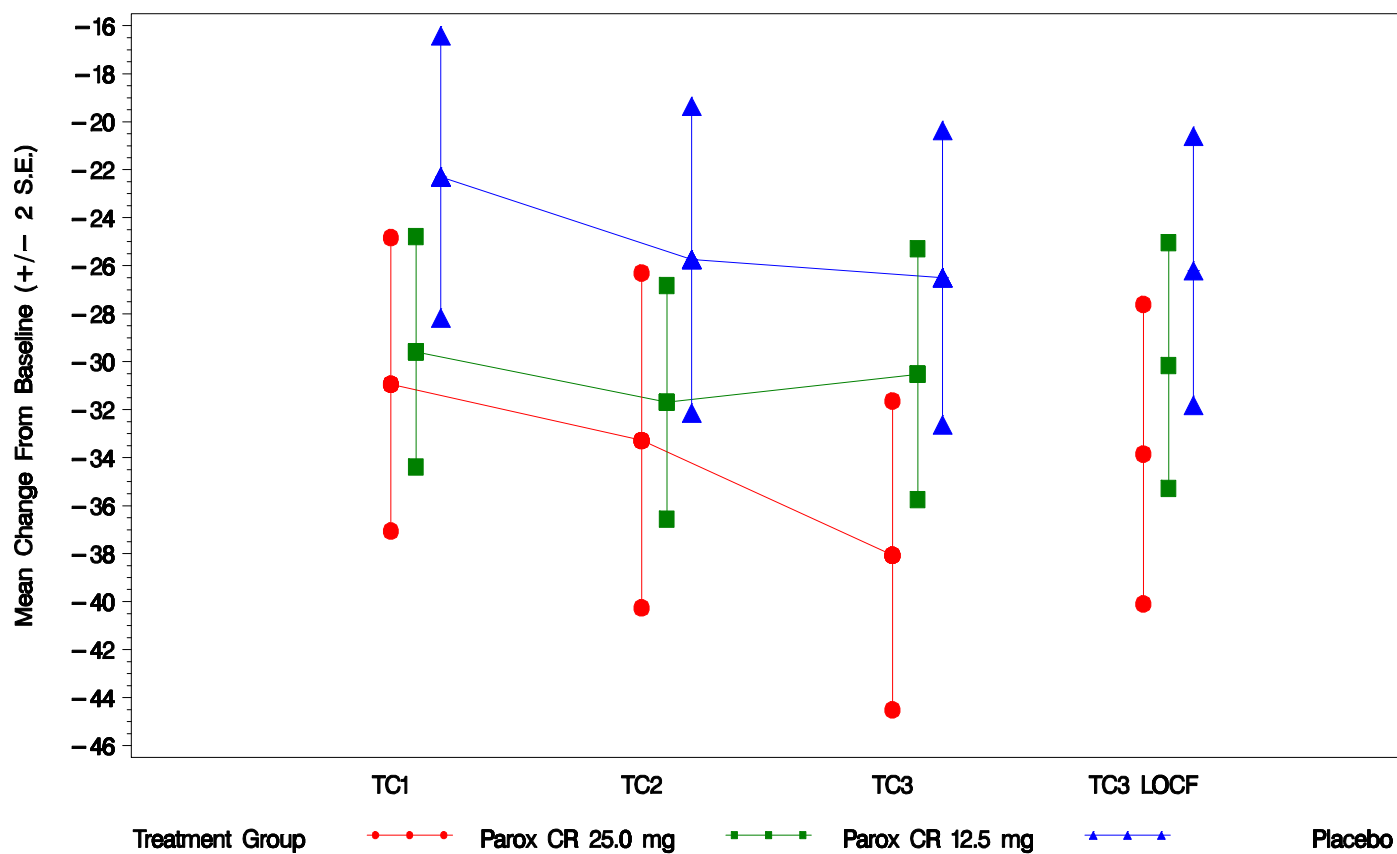
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.3

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Affective Lability
Intention-to-Treat Population



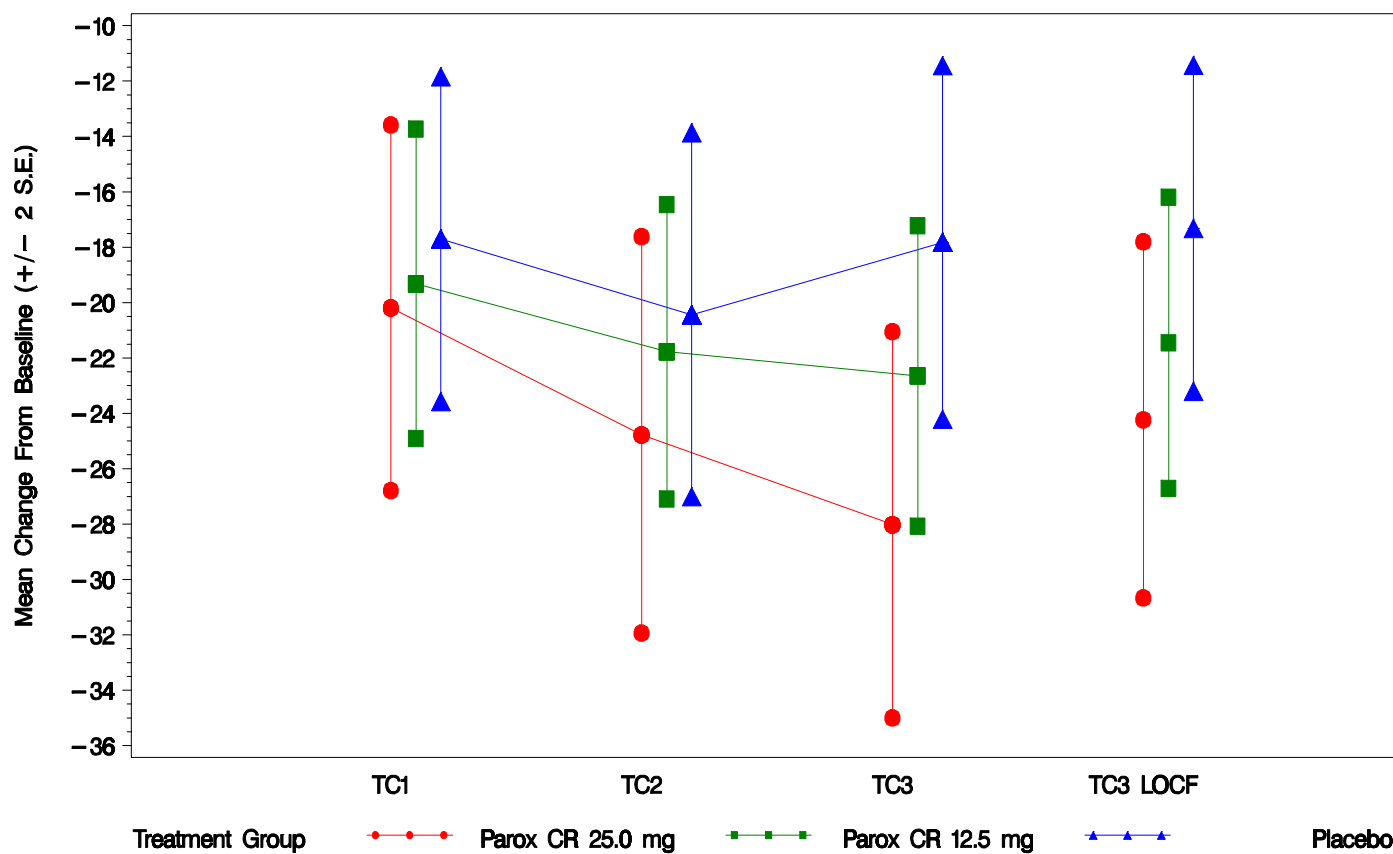
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.4

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Irritability
Intention-to-Treat Population



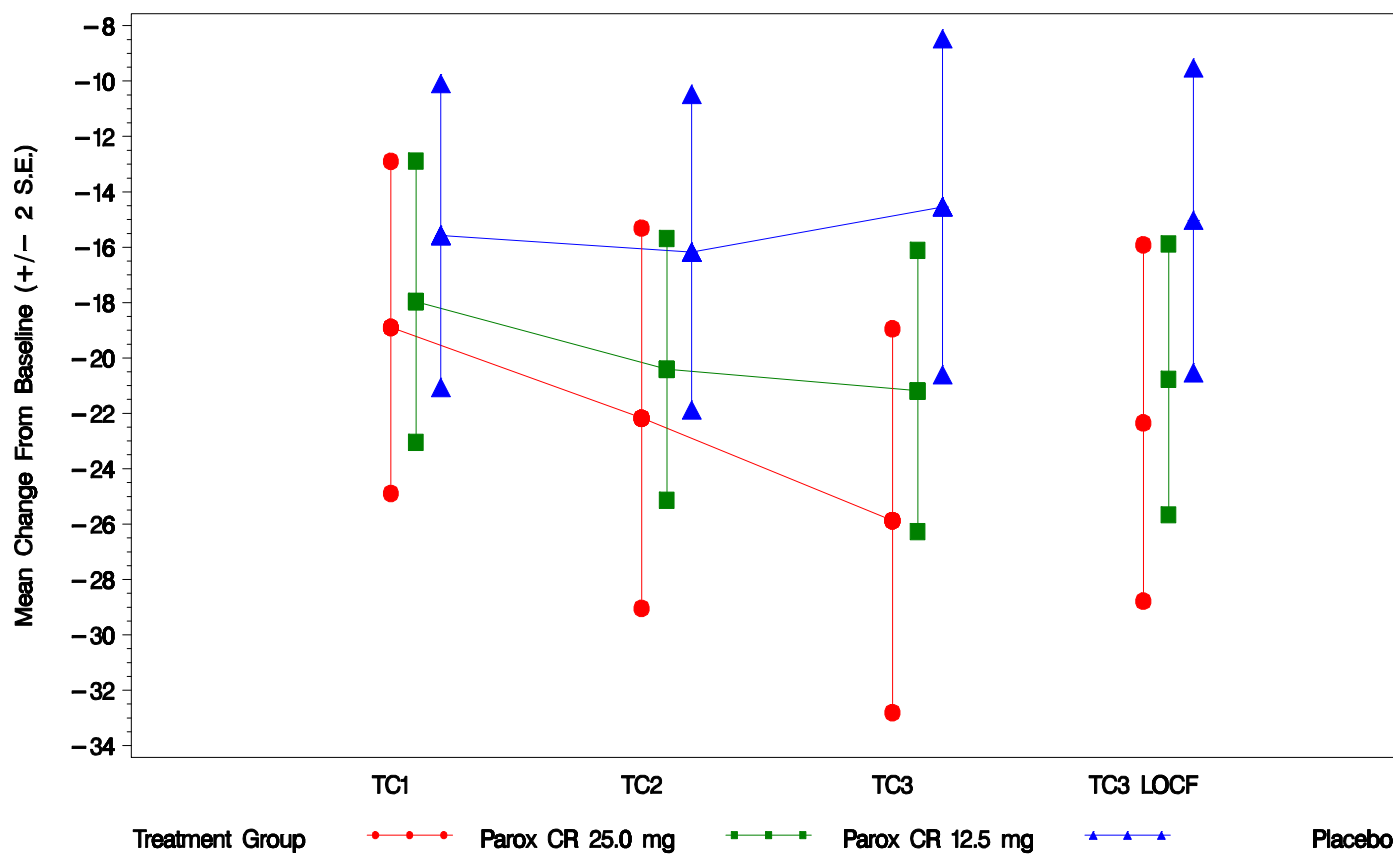
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.5

Mean Change from Baseline ($\pm$ 2 S.E.) in the 11 Individual VAS Item Scores
Decreased Interest
Intention-to-Treat Population



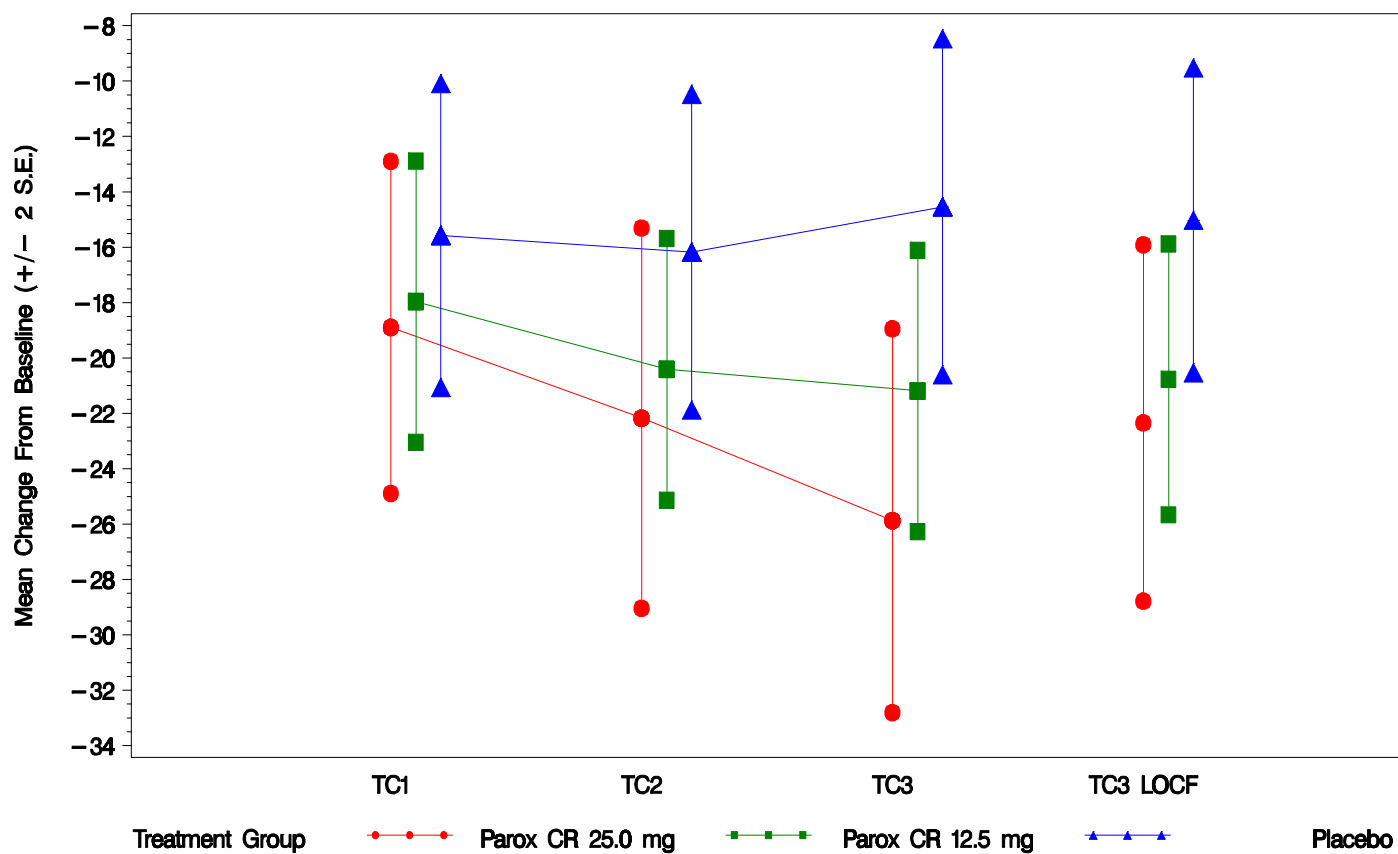
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.6

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Difficulty Concentrating
Intention-to-Treat Population



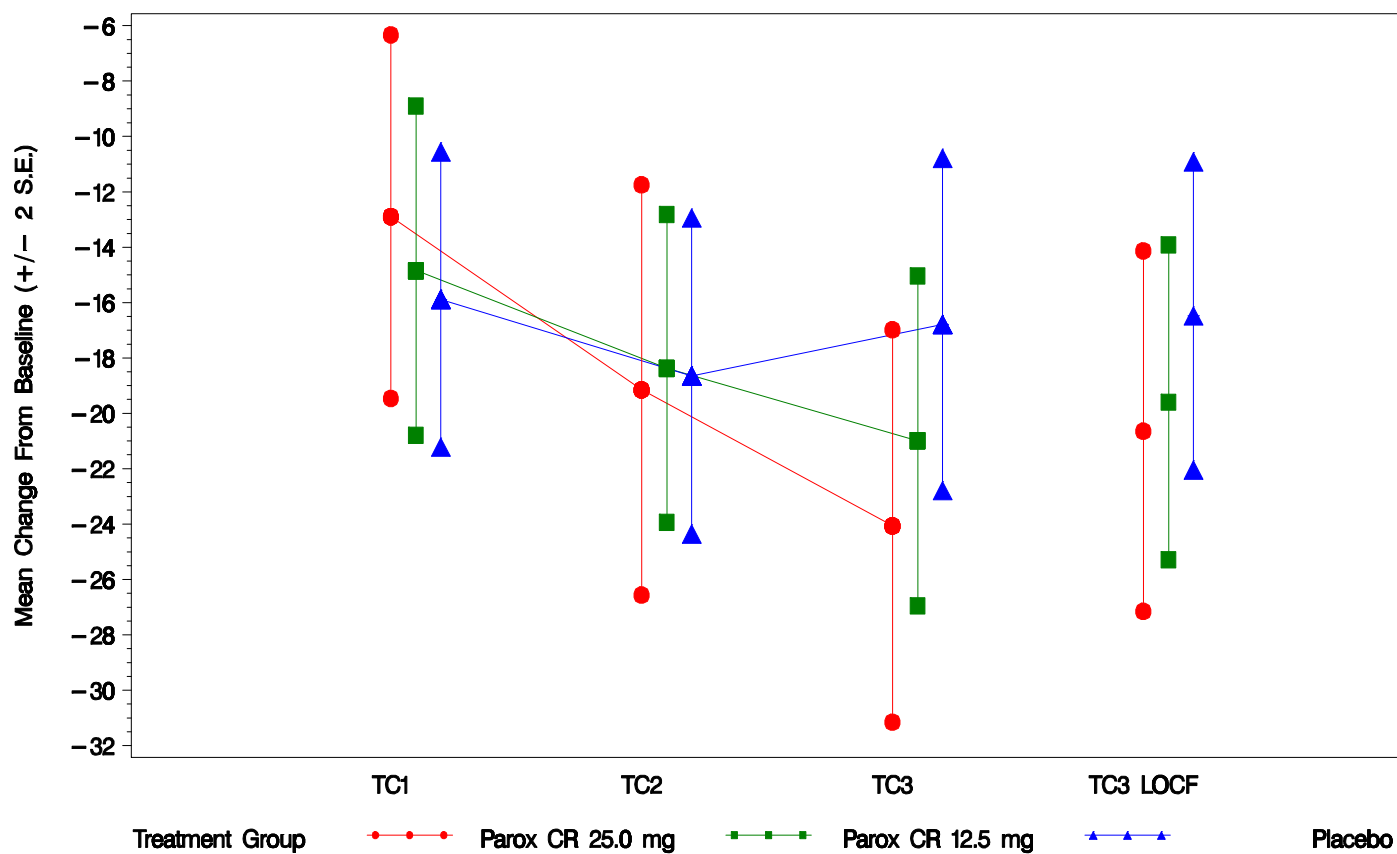
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.7

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Lack of Energy
Intention-to-Treat Population



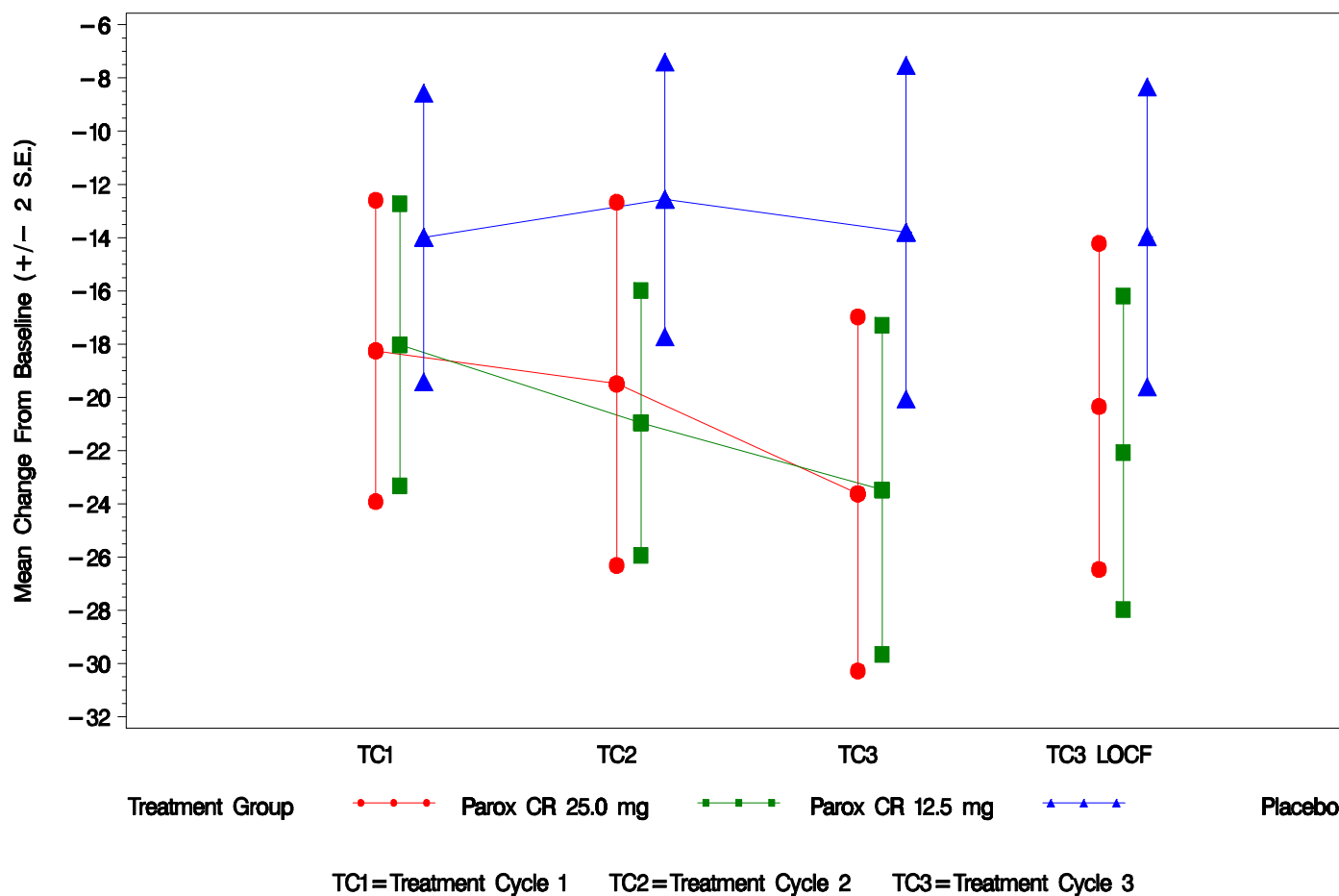
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.8

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Change in Appetite
Intention-to-Treat Population

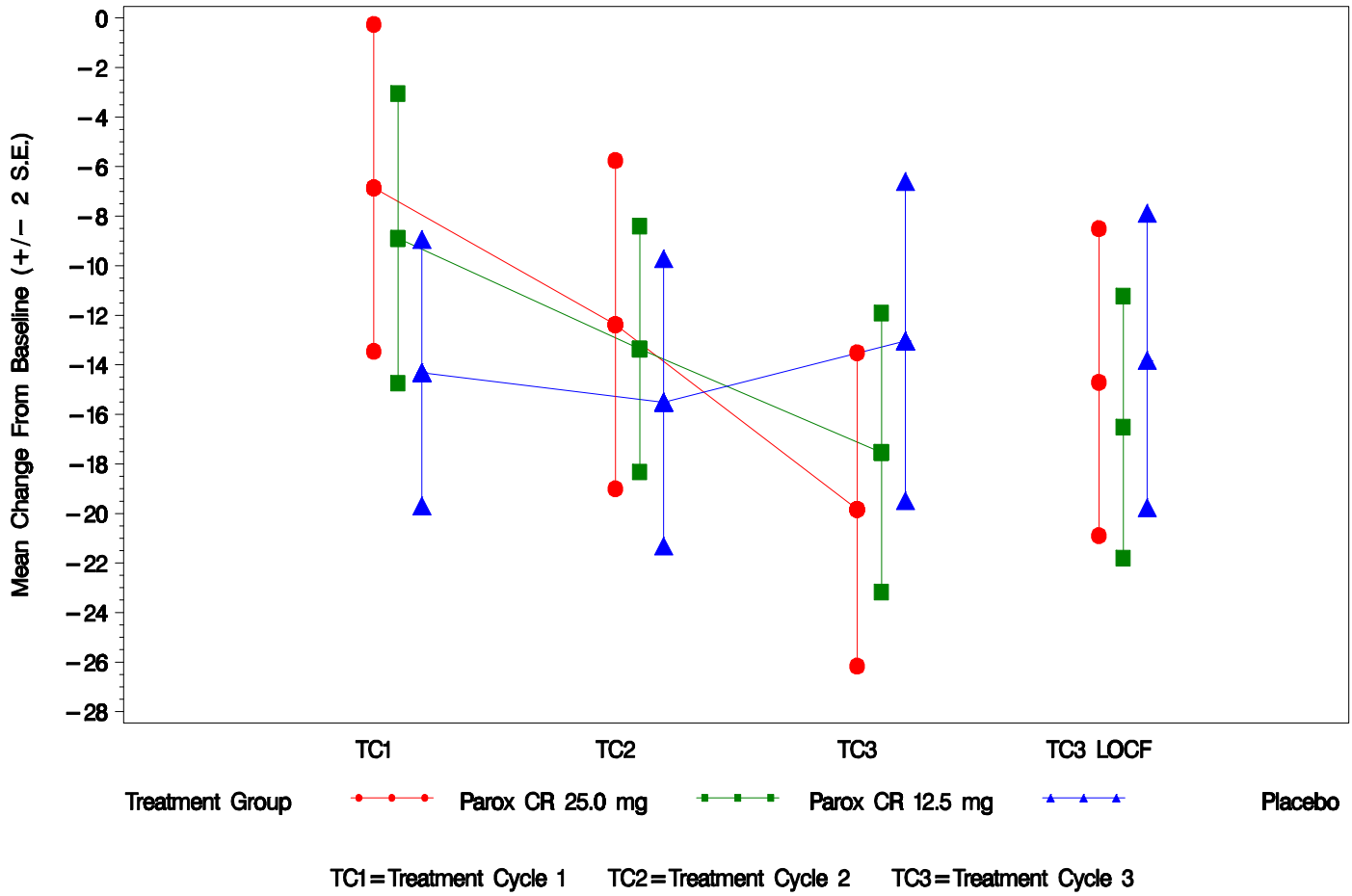


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Figure 13.7.2.9

Mean Change from Baseline (+/- 2 S.E.) in the 11 Individual VAS Item Scores
Change in Sleep Pattern
Intention-to-Treat Population

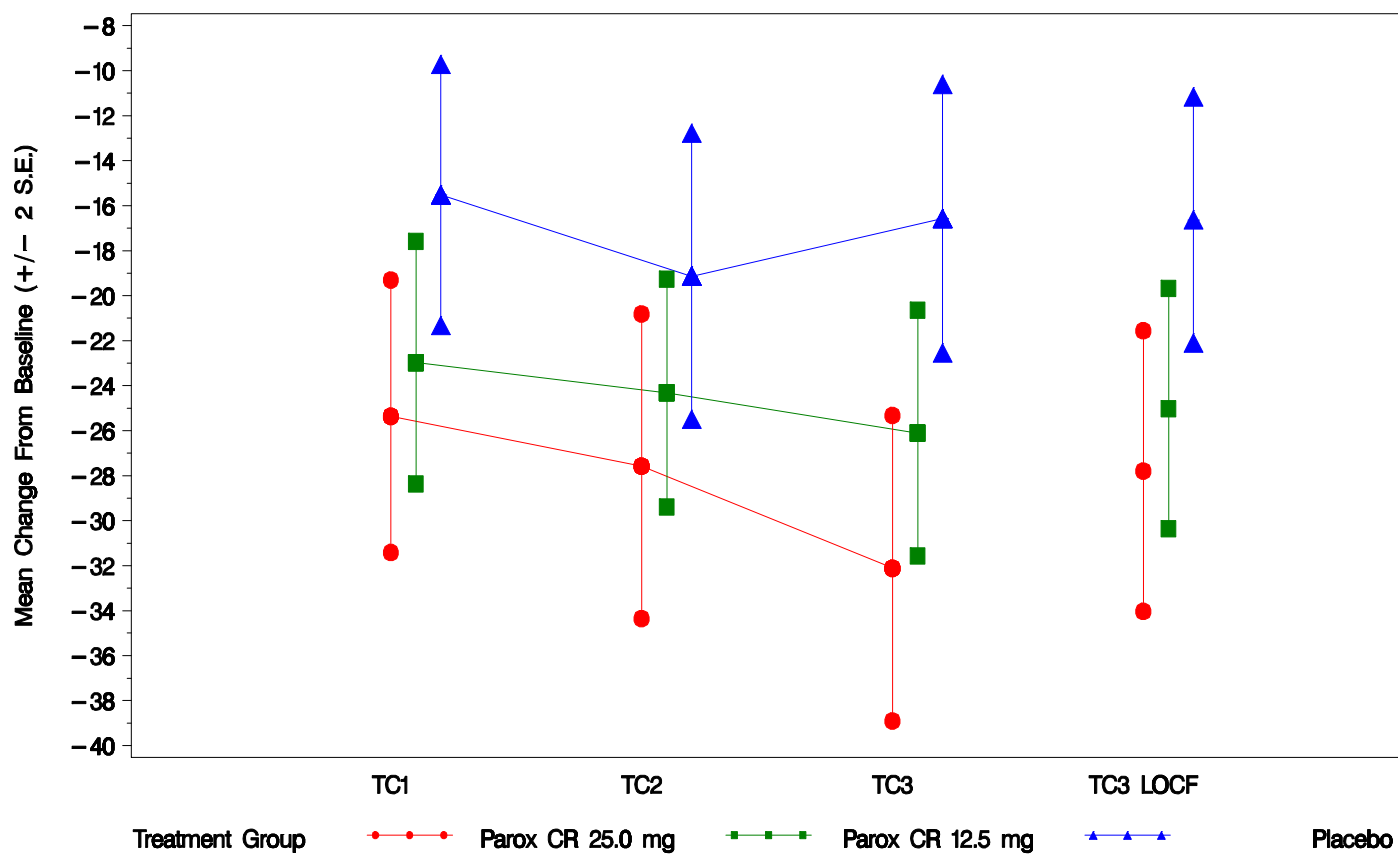


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Figure 13.7.2.10

Mean Change from Baseline ($\pm$ 2 S.E.) in the 11 Individual VAS Item Scores
Feeling out of Control
Intention-to-Treat Population



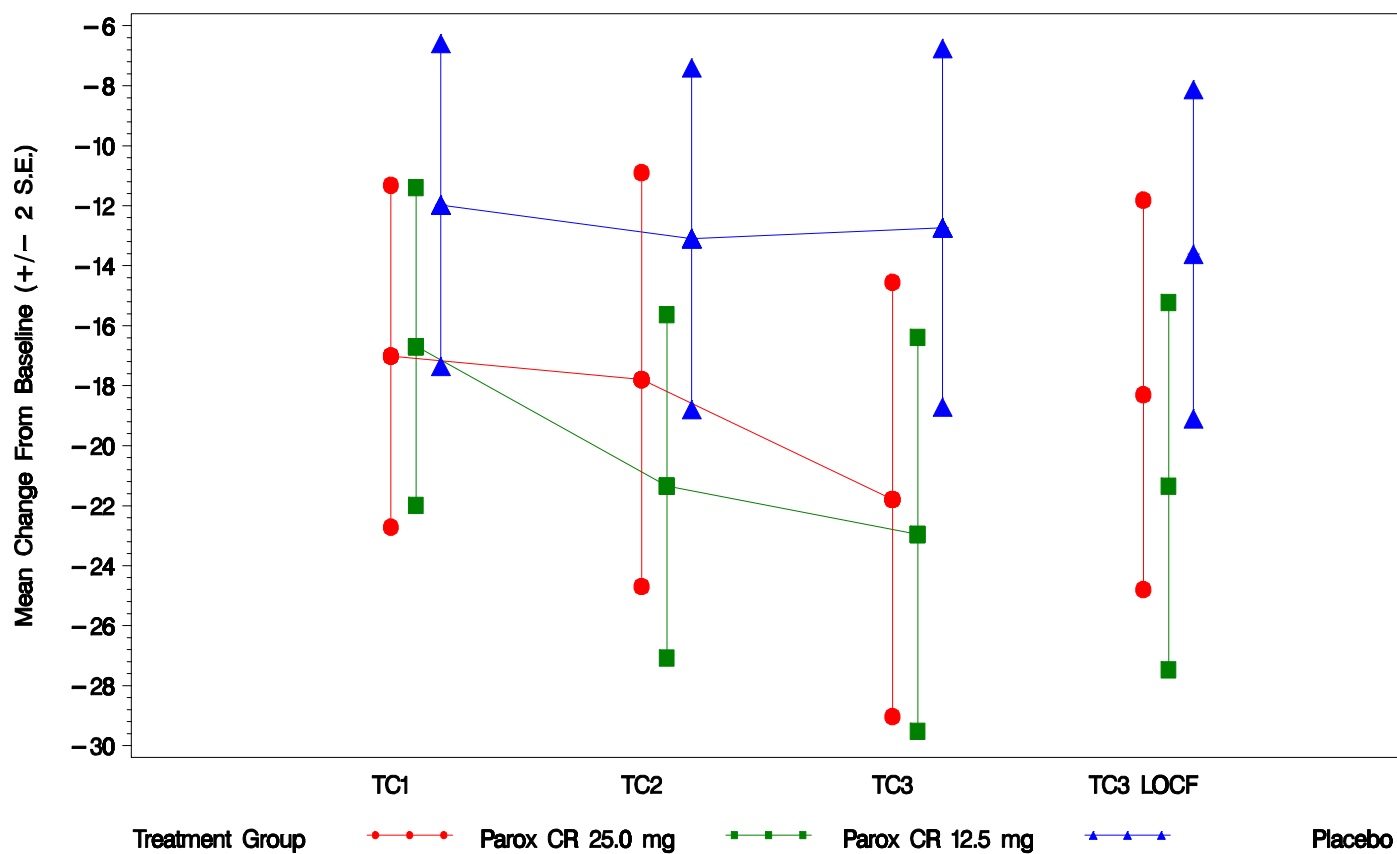
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.7.2.7.11

Mean Change from Baseline ($\pm$ 2 S.E.) in the 11 Individual VAS Item Scores
Physical Symptoms
Intention-to-Treat Population



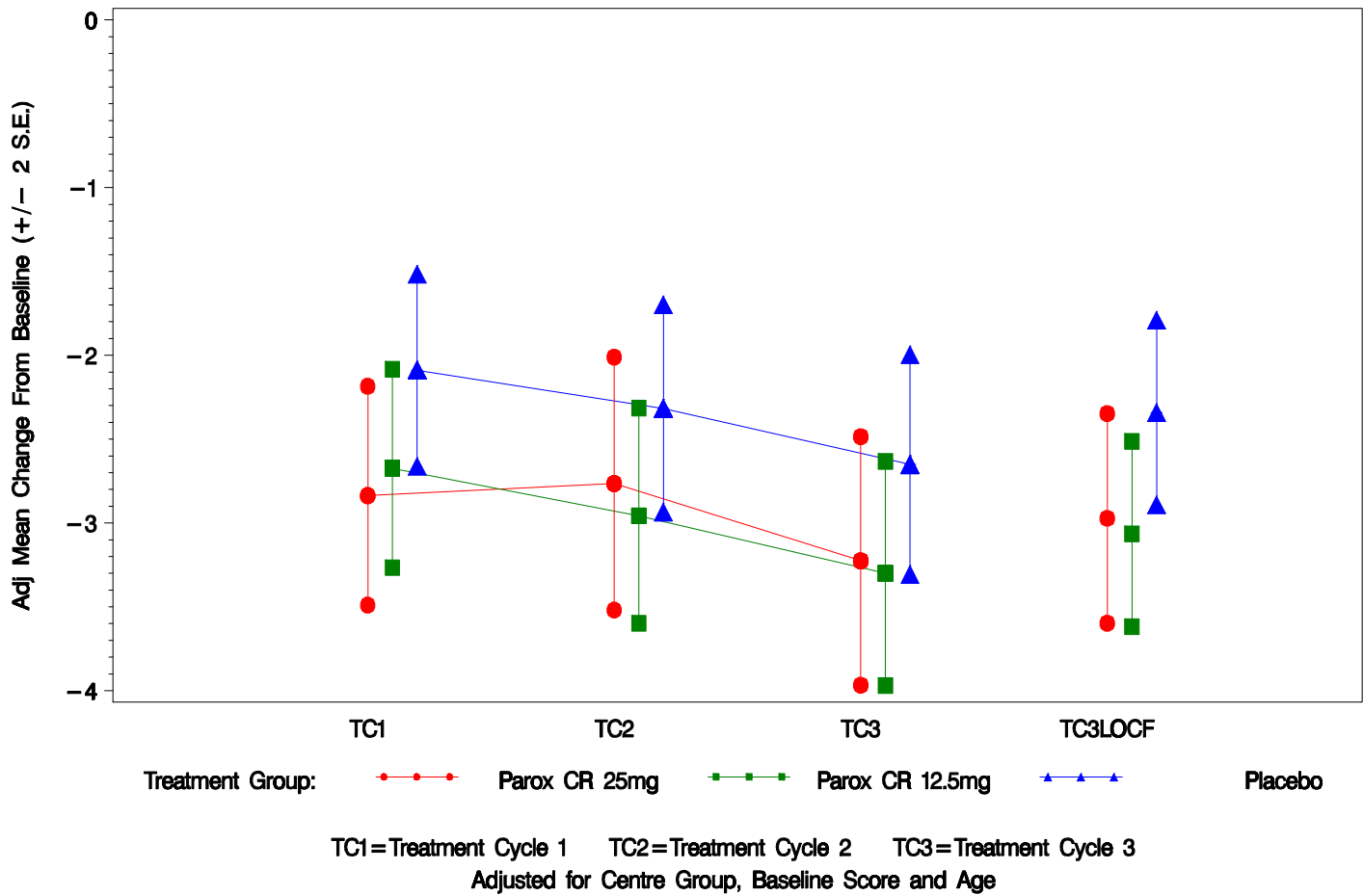
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3

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Figure 13.8.1.1

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in Sheehan Disability Scale Items
Social Score
Intention-to-Treat Population

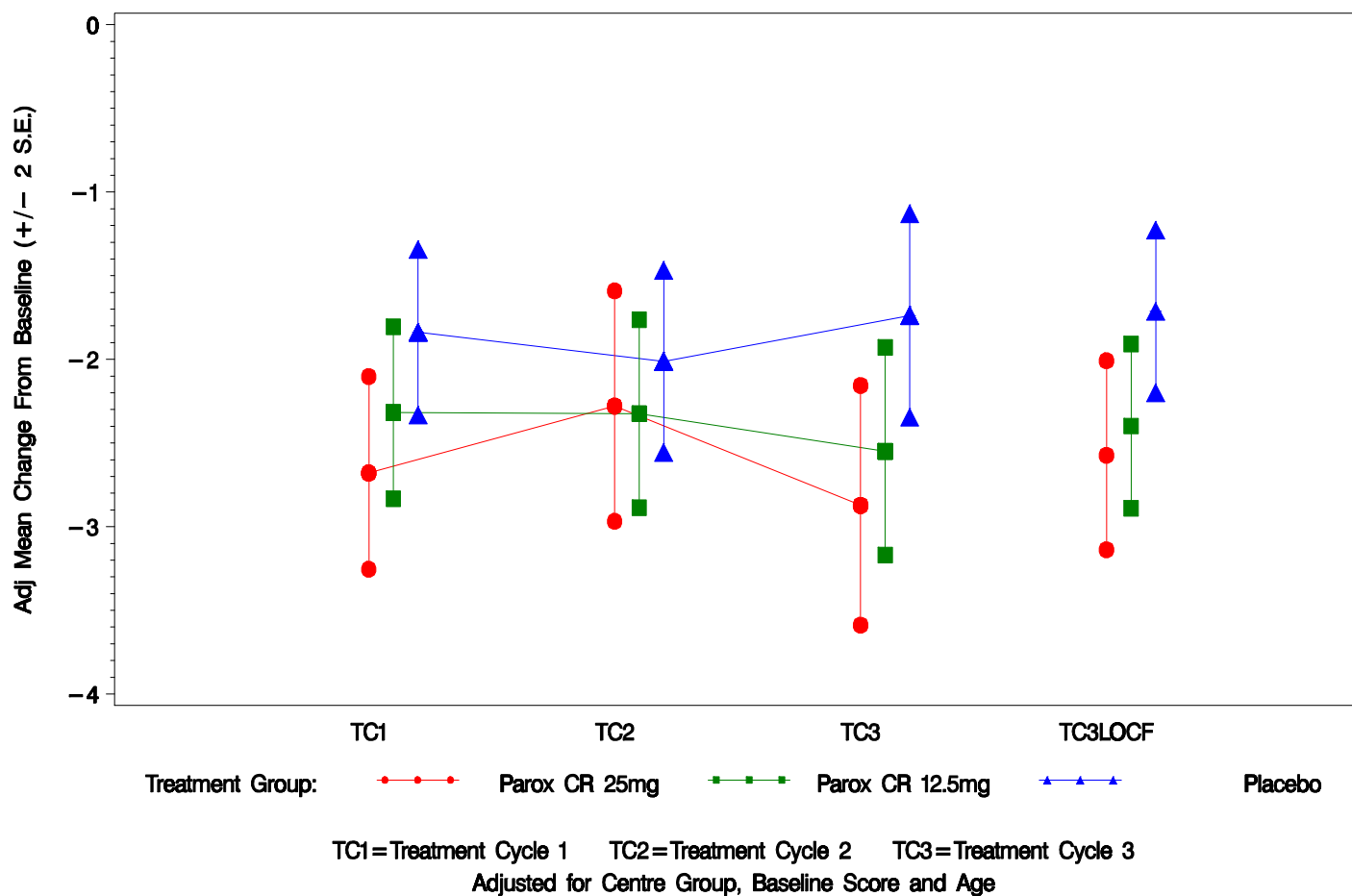


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Figure 13.8.1.2

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in Sheehan Disability Scale Items
Work Score
Intention-to-Treat Population

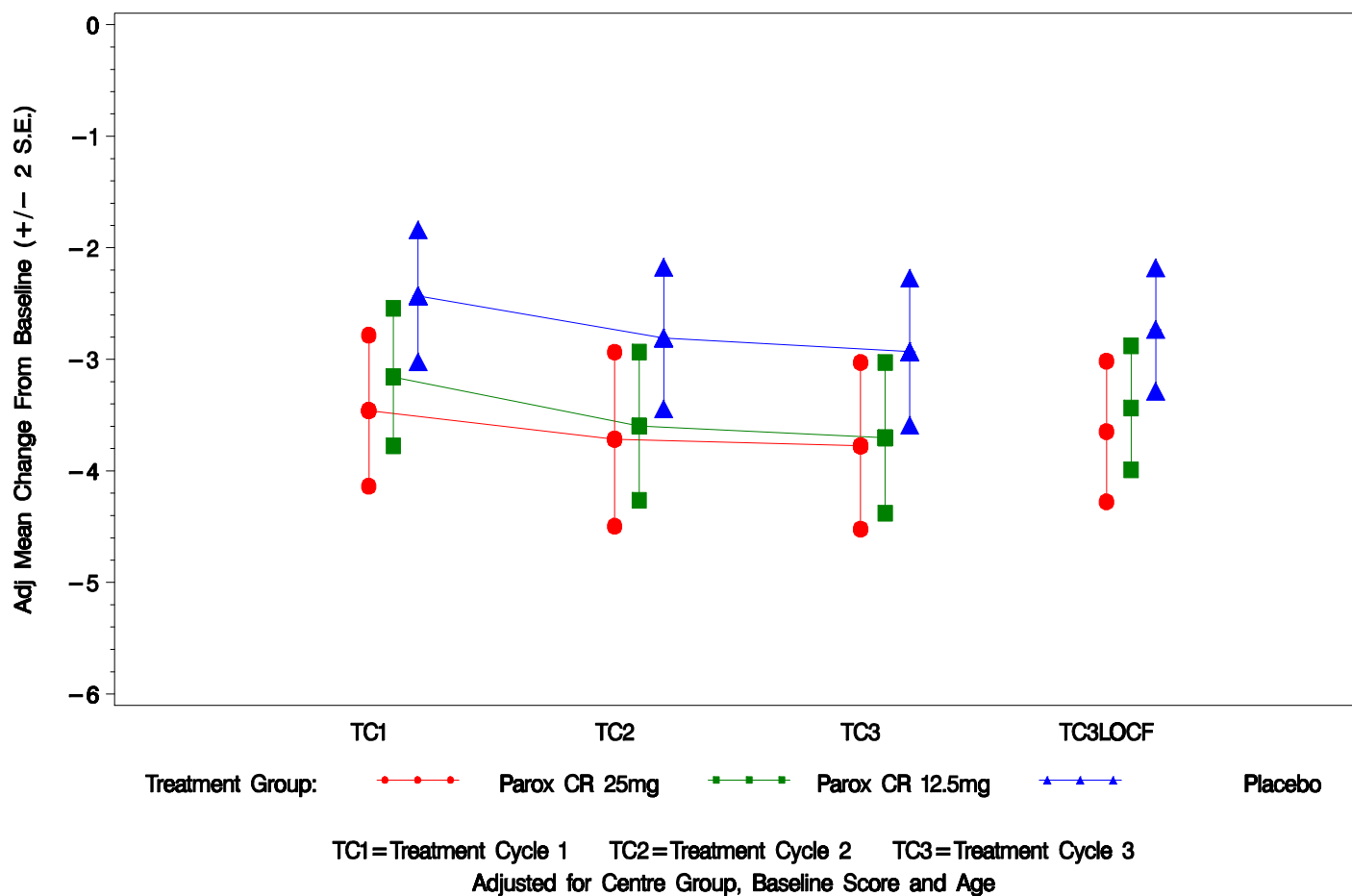


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Figure 13.8.1.3

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in Sheehan Disability Scale Items
Family Score
Intention-to-Treat Population



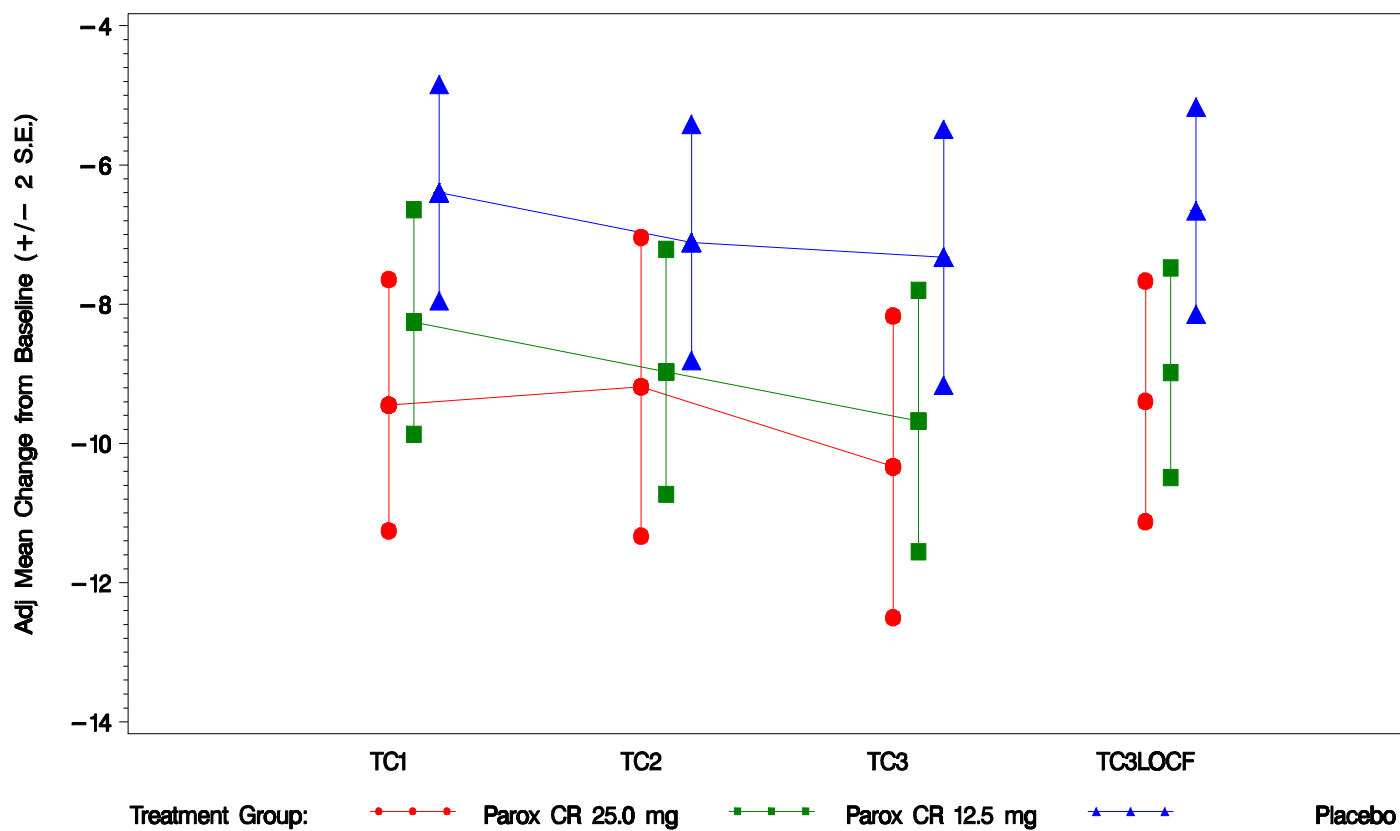
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Figure 13.8.2

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in Sheehan Disability Scale Total Score

Intention-to-Treat Population



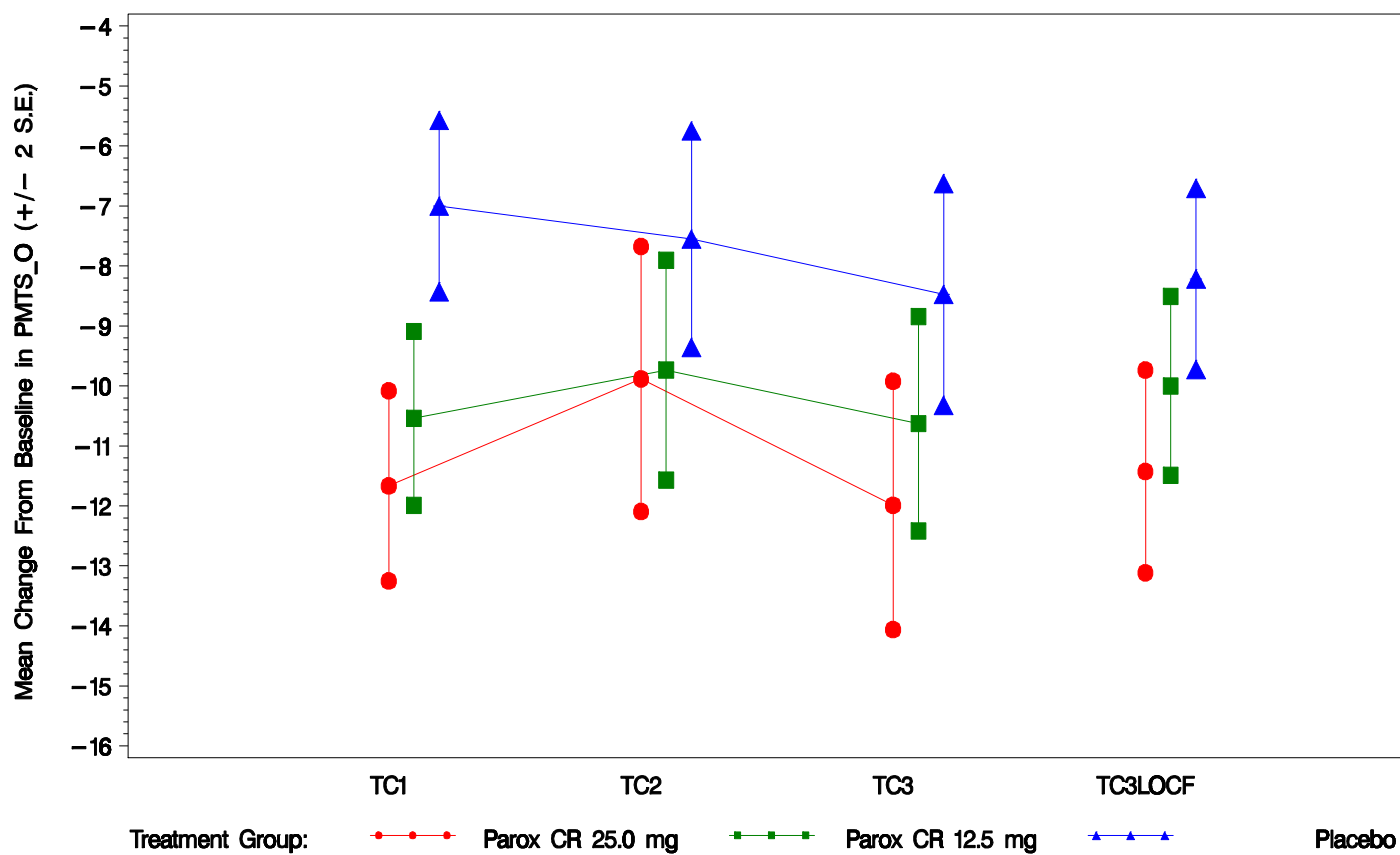
TC1= Treatment Cycle 1 TC2= Treatment Cycle 2 TC3= Treatment Cycle 3
 Adjusted for Centre Group, Baseline Score and Age

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Figure 13.9

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in the Observer Rated Premenstrual Tension Scale Total Score
Intention-to-Treat Population



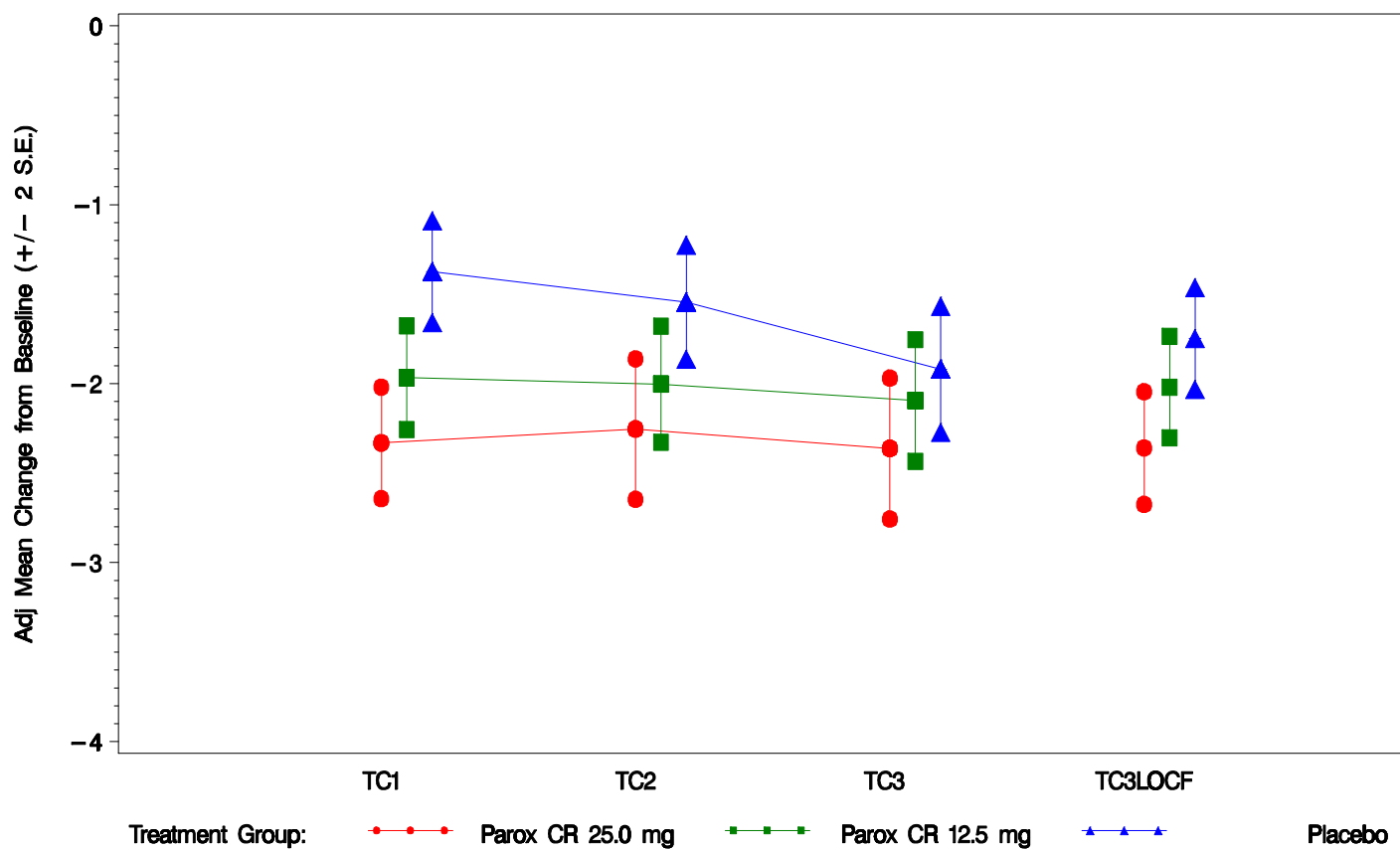
TC1=Treatment Cycle 1 TC2=Treatment Cycle 2 TC3=Treatment Cycle 3
Adjusted for Centre Group, Baseline Score and Age

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Figure 13.10

Adjusted Mean Change from Baseline ($\pm$ 2 S.E.) in the CGI – Severity of Illness Item.
Intention-to-Treat Population



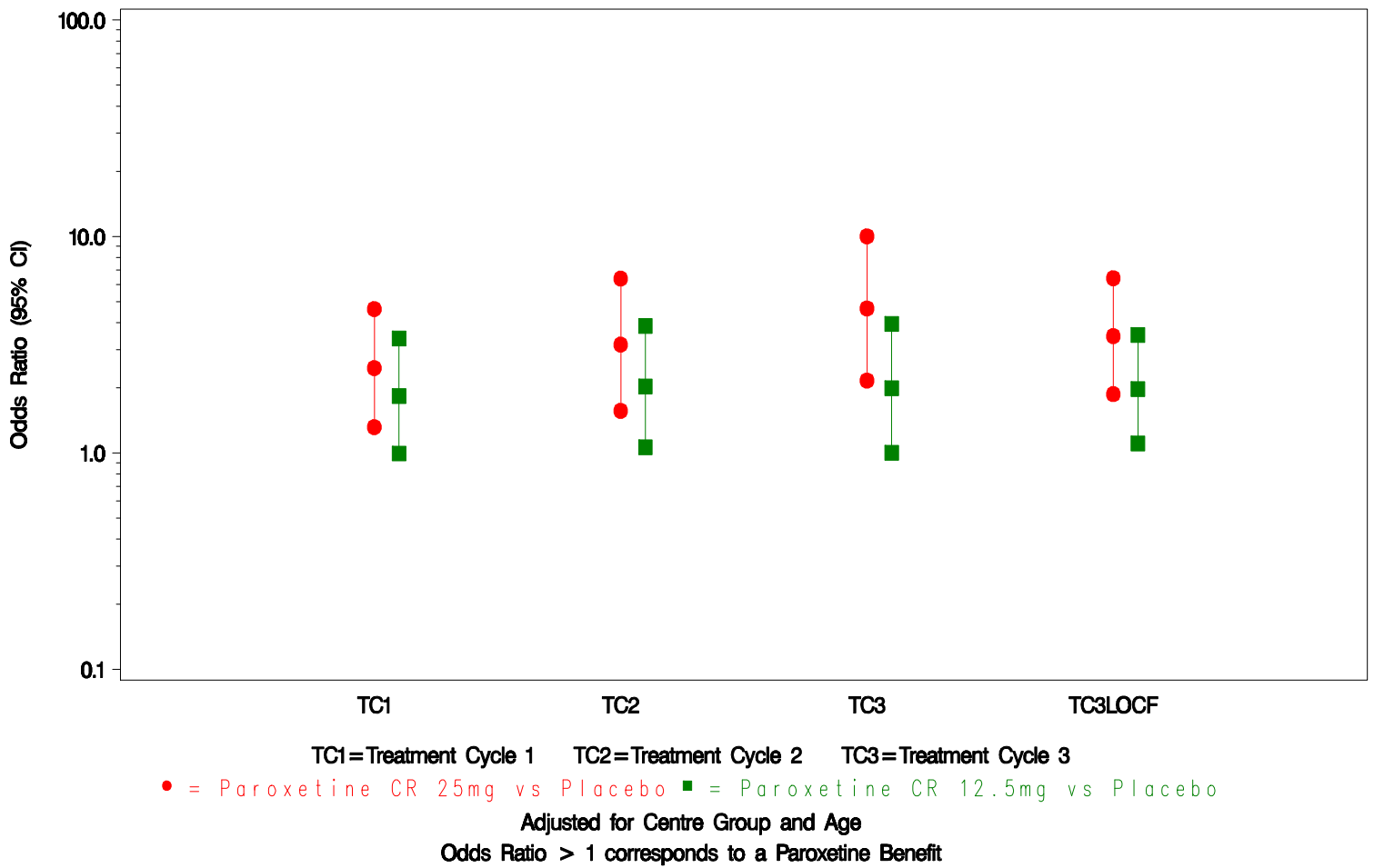
TC1=Treatment Cycle 1 TC2=Treatment Cycle 2 TC3=Treatment Cycle 3
Adjusted for Centre Group, Baseline Score and Age

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Figure 13.11

Odds Ratio (95% C.I.) for Responders defined as a Score of 1 or 2 on the CGI – Global Improvement Item.
Intention-to-Treat Population

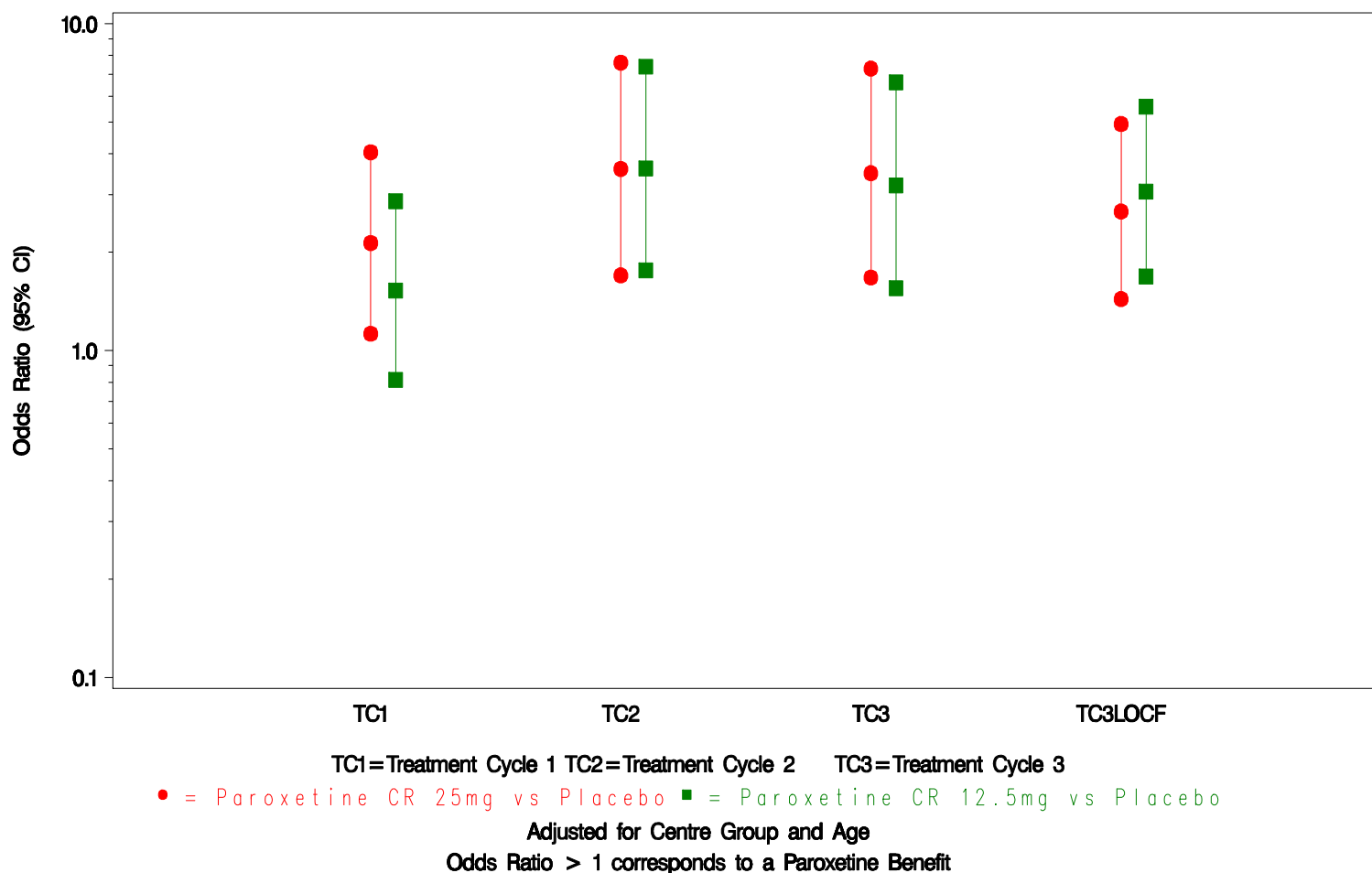


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Figure 13.12

Odds Ratio (95%CI) for Responders defined as a Score of 1 or 2 on the Patient Global Evaluation.
Intention-to-Treat Population

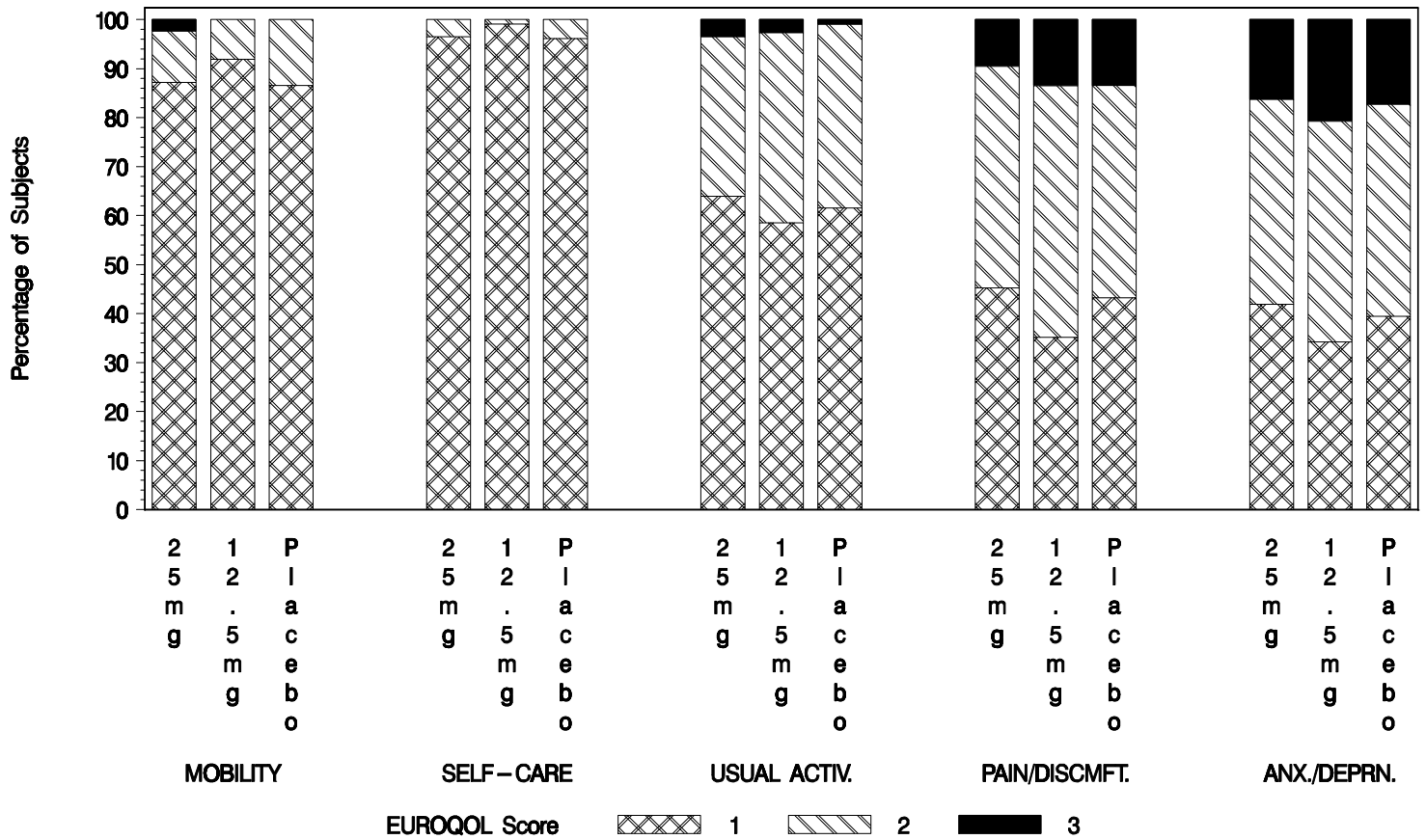


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Figure 14.1

Distribution of EuroQol EQ-5D Health Profile Items at Baseline
Intention-to-Treat Population



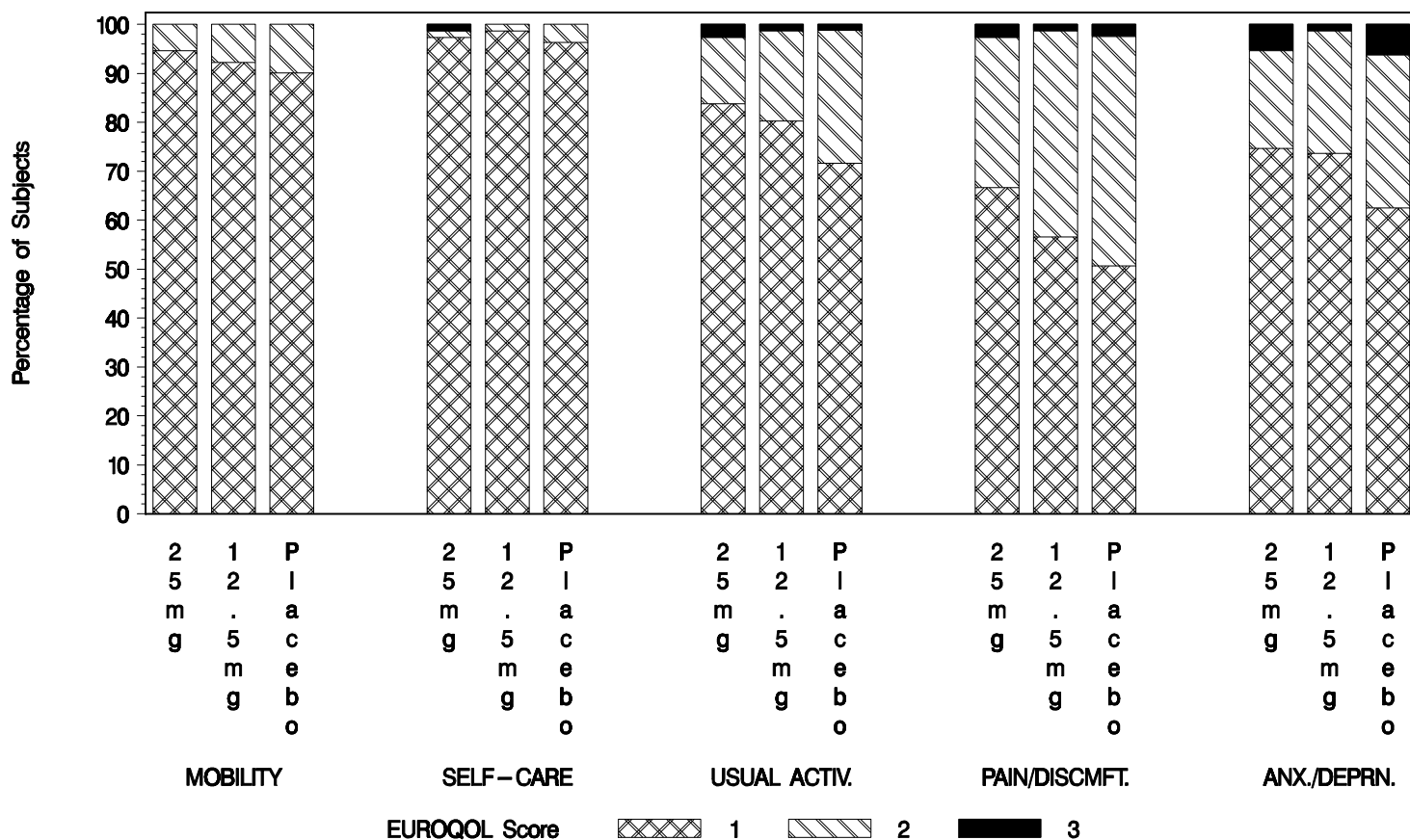
1 = No Problems, 2 = Some Problems, 3 = Severe Problems

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Figure 14.2

Distribution of EuroQol EQ-5D Health Profile Items at Treatment Cycle 3
Intention-to-Treat Population



1 = No Problems, 2 = Some Problems, 3 = Severe Problems

Attachment – Statistical Appendix

Confidential



Paroxetine

29060

**A double-blind, placebo-controlled, 3-arm fixed dose study of paroxetine CR
intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric
Disorder**

717

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29060/717 Statistical Analysis Plan

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*Biomedical Data Sciences

SB Document Number: SB-BRL-029060/RSD-101HGC/1

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Table of Contents

	Page
List of Appendices	842
1 Introduction	843
2 Objectives	845
2.1 Primary Objective	845
2.2 Secondary Objectives	845
3 Hypothesis	845
3.1 Null Hypothesis	845
3.2 Alternative Hypothesis	845
4 Key Definitions and Data Handling Conventions	846
4.1 Key Derivations and Calculations	846
4.1.1 Menstrual Cycle Phases	846
4.1.2 PMDD Symptoms and Measurements	846
4.1.3 Patient Disposition, Sessions and Visit Slotting	846
4.1.4 Derived Variables	848
4.1.5 Adjusting for Centre or Investigator type	849
4.1.6 Study Medication Capsule Compliance	850
4.1.7 Prior and Concomitant Medications	851
4.2 Values of Clinical Concern	852
4.3 Protocol Violations	852
4.4 Biometrics QC of Output	858
5 Analysis Populations and Analysis Datasets	859
5.1 Populations	859
5.2 Datasets	860
5.2.1 Missing data	860
6 Comparisons of Interest	863
6.1 Primary Comparisons of Interest	863
6.2 Other Comparisons of Interest	863
7 Targeted Sample Size	864
7.1 Sample Size Assumptions	864
7.2 Sample Size Sensitivity	864
8 Definition of Variables/Assessments	865
8.1 Primary Variable	865
8.2 Other Variables	865
8.2.1 Secondary Variables	865
8.2.2 Other Variables	867
9 Statistical Methodology	867
9.1 Patient Disposition, Baseline Characteristics and Demography	867
9.1.1 Prior and Concomitant Medications	869
9.1.2 Study Medication Compliance	869

9.2 Efficacy Analysis	869
9.2.1 Multiplicity	869
9.2.2 Analysis of Primary Efficacy	870
9.2.3 Analysis of Secondary Efficacy	872
9.2.4 Pharmacoeconomic Analysis	874
9.2.5 Interim Analyses	875
9.3 Safety Analyses	875
9.3.1 Adverse Experiences	875
9.3.2 Clinical Laboratories	877
9.3.3 Vital Signs	877
10 References	878
11 Appendices	879

List of Appendices

	Page
Appendix A1 Laboratory Normal Ranges and Predetermined Values of Clinical Concern	879
Appendix A2 Limits for the Vital Signs data	882
Appendix A3 EuroQol Tariffs	883
Appendix A4 Examples of emergent Adverse Events	884

1 Introduction

In most trials investigating the effect of serotonin reuptake inhibition in PMDD, the SSRI has been administered continuously throughout the menstrual cycle. Studies investigating the effect of continuous dosing with paroxetine CR in the treatment of PMDD are currently ongoing. However, several recent trials suggest that PMDD may also be effectively treated by administration of an SSRI intermittently, during luteal phases only. This is consistent with reports that the time lag between the start of dosing with SSRIs and clinical efficacy in PMDD is much shorter than seen in other disorders such as Depression, Panic and OCD.

The study is a double-blind, placebo-controlled, three-arm parallel group clinical trial comparing the efficacy of intermittent dosing with paroxetine CR (12.5mg and 25mg) with that of placebo in the treatment of PMDD. Study drug is administered during the luteal phase only (i.e. the last 14 days) of the menstrual cycle.

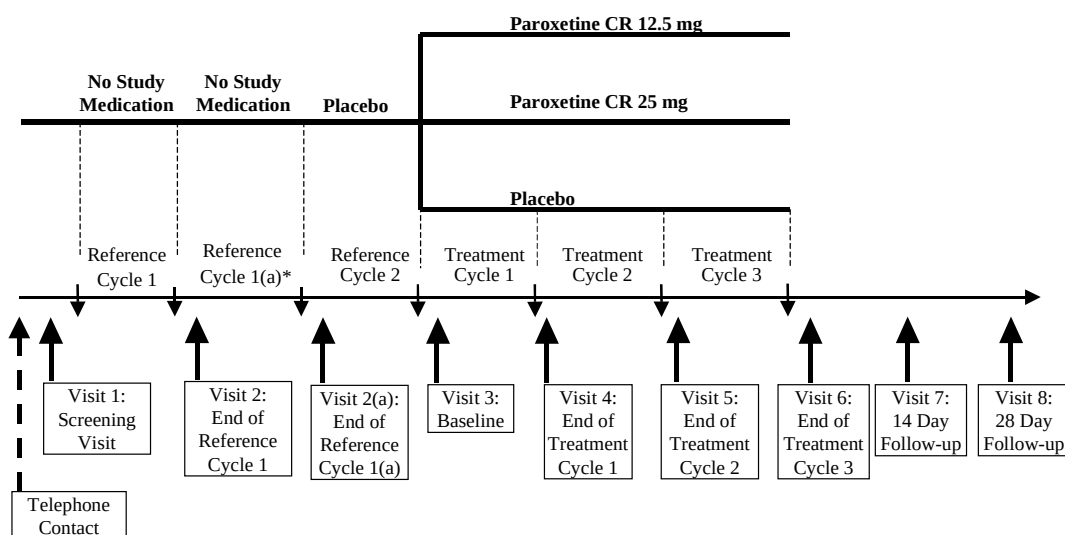
As shown in the schema below patients are initially contacted about the study by telephone. A proportion of these will then attend a screening visit and may participate in up to three reference cycles which correspond to their menstrual cycles. During the luteal phase of the last cycle single-blind placebo medication is administered.

In addition to satisfying other criteria, patients will only be randomised into the double-blind treatment phase if they rate at least a 200% higher (i.e. worse) on one, or at least 100% higher on two or more, of the four core DSM-IV symptoms (irritability, tension, depressed mood and affective lability) for the mean luteal phase score compared with the mean follicular phase score during two consecutive reference cycles. Additionally, the mean follicular phase score must be ≤ 20 mm and the mean luteal phase score must be ≥ 40 mm for the qualifying symptoms.

Those patients who are not eligible for inclusion on the basis of their reference cycle 1 VAS scores (checked at visit 2) may complete an additional cycle, reference cycle 1(a), and an additional clinic visit (visit 2(a)). Those individuals eligible following reference cycle 1, or the additional 1(a) cycle, will then proceed to reference cycle 2, taking placebo during the luteal phase of the cycle.

During the double-blind phase patients enter up to three treatment cycles receiving intermittent treatment during the luteal phase of each cycle. On permanently stopping randomised study medication patients are requested to attend a follow-up visit 14 days later, and those with ongoing AE's or abnormal laboratory results are required to attend an additional 28-day follow-up visit.

STUDY SCHEMA



* = Patients who did not qualify for inclusion in the study on the basis of their reference cycle 1 diary scores may, at the discretion of the investigator, enter an optional reference cycle 1(a) rather than being withdrawn from the study.

2 Objectives

2.1 Primary Objective

To compare the efficacy of intermittent dosing with paroxetine CR (12.5mg and 25mg) with that of placebo for the treatment of PMDD. The hypothesis to be tested is that paroxetine treatment results in a greater improvement in symptoms of PMDD compared with placebo treatment.

2.2 Secondary Objectives

To evaluate the safety and tolerability of intermittent dosing with paroxetine CR (12.5mg and 25mg) for the treatment of PMDD.

3 Hypothesis

3.1 Null Hypothesis

The null hypothesis is that there is no difference between each dose level of paroxetine CR (12.5mg and 25mg) and placebo in the change from baseline in the VAS – MOOD score at the treatment cycle 3 LOCF endpoint in the intent-to-treat (ITT) population.

3.2 Alternative Hypothesis

The alternative hypothesis is that there is a difference between either dose level of paroxetine and placebo.

The null hypothesis will be rejected, and the study judged a success, if there is sufficient evidence for either of the alternative hypotheses. The study has been powered to detect a difference of 16.3 mm between either dose level of paroxetine and placebo.

4 Key Definitions and Data Handling Conventions

4.1 Key Derivations and Calculations

4.1.1 Menstrual Cycle Phases

Day one of the menstrual cycle: is defined as the first day of continuous menses/bleeding (not spotting).

Follicular Phase: is defined as the period from day one of the cycle up to the luteal phase. Eligibility and efficacy calculations based on VAS symptom scores for the follicular phase will be restricted to data from days 6-10 of the cycle.

Luteal Phase: is defined as the 14 days prior to the onset of continuous menstrual bleeding. Eligibility and efficacy calculations based on VAS symptom scores during the luteal phase will be based on data from the last 5 days of the cycle.

4.1.2 PMDD Symptoms and Measurements

DSM-IV symptoms of PMDD: These comprise of eleven symptoms: irritability, tension, depressed mood, affective lability, decreased interest, difficulty concentrating, lack of energy, change in appetite, change in sleep pattern, feeling out of control and physical symptoms. Of these, irritability, tension, depressed mood and affective lability are considered as core symptoms which are used to construct the composite VAS – MOOD score.

Visual Analogue Scale (VAS) for PMDD symptoms: For each of the eleven PMDD symptoms the patient records a daily rating on a visual analogue scale. This is a unipolar scale ranging from "not at all" = 0mm to "extreme symptoms" = 100mm.

Patient Diary: Each patient records their VAS scores in a diary which they complete each night, starting a new diary on the first day of the next menstrual cycle.

4.1.3 Patient Disposition, Sessions and Visit Slotting

Patient Disposition: *Screen-only* patients are those patients who were screened but not randomised who provided written, dated informed consent.

Patients who are randomised but fail to meet the ITT definition are **not** considered to be screen-only patients. These patients should be withdrawn from the study and an eCRF completed for each. These patients will be listed under their randomised group but not tabulated.

Among the ITT population, a patient is considered to be a *study completer* if they progress through the study up to and including the end of the Treatment Cycle 3 visit. Otherwise patients are considered to be *early withdrawals*. This will be based on the investigator's response to the study conclusion question in the study conclusion panel of the eCRF.

NB. The data for patients who do not provide informed consent will not be used within the tables and listings.

Sessions: In this study the sessions are pre-treatment, on-treatment and post-treatment.

Pre-treatment: This is split into two periods: i) prior to placebo run-in and ii) from the start date of taking placebo run-in study medication to the day before the first dose of randomised study drug medication is taken.

For tabulations and analyses, the baseline visit is defined as visit 2 or visit 2(a) (end of reference cycle 1 or 1(a)) for the laboratory and height data, and as the visit 3 assessment (end of the reference cycle 2) for the remaining visit-type data.

Because of the long intervals between visits, and use of placebo run-in study drug during reference cycle 2, efficacy data from earlier visits will not be carried forward if the baseline data is missing. This will also apply to all other types of data.

On-treatment: This period runs from the day that the first dose of randomised study medication was taken up to the day that the study drug was permanently discontinued. Note, within this session the *active treatment phase* (i.e. when randomised study drug is taken) should occur only during the luteal phase of each menstrual cycle.

An assessment will be considered to be on-treatment if the assessment date (or the start date for "event" data) overlaps with the on-treatment interval.

Post-treatment: For efficacy, pharmacoeconomic and safety data this will be divided into follow-up and post follow-up as follows:

Follow-up: Efficacy and pharmacoeconomic data are considered to be in the follow-up period if the assessment was ≤ 7 days after the last day of randomised treatment. For safety data this window is extended to ≤ 14 days (≤ 30 days for serious adverse events).

Post follow-up: Any efficacy, pharmaeconomic or safety assessment or event which takes place after the follow-up period will be considered post-follow-up. This data will not be tabulated but will be presented in data listings.

NB. The on-treatment and follow-up data will be combined in tabulations for the efficacy and pharmacoeconomic data whereas for safety data these periods will be treated separately (see [Section 9.3](#)).

Definitions for the assignment of prior and concomitant medications and "emergent" adverse experiences based on start and stop dates, are described in [Section 4.1.7](#) and [Section 9.3.1](#), respectively.

Diary card nomenclature: The nomenclature used for the patient diaries will be as follows: study cycle 1, study cycle 1a, study cycle 2, study cycle 3, study cycle 4 and study cycle 5 corresponding to reference cycle 1, reference cycle 1(a), reference cycle 2, treatment cycle 1, treatment cycle 2, and treatment cycle 3, respectively. This will prevent the patients deducing whether a particular diary is for a "reference cycle" or for a "treatment cycle".

Handling multiple assessments: If there is more than one assessment of a given type assigned to a given menstrual cycle then the latest evaluation will be used in the data summaries and analyses. Details on handling repeat laboratory data are given in the Output Specifications Document.

Definition of Summary Statistics: Where summary statistics are to be presented then the number of patients, mean, standard deviation, median, maximum and minimum values will be presented.

4.1.4 Derived Variables

VAS – MOOD: For each patient, the VAS –MOOD score is the mean of VAS symptom scores for the four core PMDD symptoms. Each symptom score is the mean of the scores for the designated days of the follicular or luteal phase (i.e. days 6-10 or the last five days) of the cycle.

Body Mass Index: This is defined as weight/height^2 (kg/m^2).

Area Under the Curve: Each patient's VAS – MOOD profile will be summarised by calculating the AUC at baseline and the treatment cycles during the last five days of the luteal phase based on available data using the trapezoidal rule [1]:

$$\frac{1}{2} \sum_{i=0}^{n-1} (t_{i+1} - t_i)(y_i + y_{i+1})$$

for $n+1$ measurements of y_i VAS – MOOD scores at day t_i (i runs from 0 to n).

For each patient the AUCs derived from the separate post-baseline visits will be added together. This total will then be standardised by dividing by the total number of luteal phase days used in the calculation to obtain an average level over the 1-3 luteal phases considered. The patient's AUC at baseline will similarly be standardised. Note, these weighted mean scores are on the same scale as the VAS – MOOD.

4.1.5 Adjusting for Centre or Investigator type

It is anticipated that this will be a transnational study carried out in approximately 40 centres.

Any centre which recruits less than 12 patients will be assigned to a type according to the speciality of the primary investigator as follows:

- Obstetrics/Gynaecological Specialist
- Psychiatric Specialist
- GP or Primary Health Care

The speciality type will be requested during the site survey prior to study start. Note, these categories were chosen in an attempt to achieve reasonable homogeneity in factors which might affect the primary response. They are likely to account for more variation in response than groupings based solely on geographical location.

Within each investigator type, these low recruiting centres will be combined with each other to obtain an aggregated centre type. This will be achieved by ranking each of these centres on the basis of the number of patients randomised to study treatment, the centre with the smallest number of patients being ranked one. Centres with equal numbers of patients will be ranked depending on centre

number, the lowest centre number being allocated the lowest rank. The centre with the lowest rank will then be combined with the centre with the highest rank. The centre with the second lowest rank will be combined with the centre with the second largest rank and so on. This procedure will be repeated until there are no aggregated centres with less than 12 patients.

For those centres with at least 12 patients the individual centres, along with any pooled centres, will be used as the adjustment factor in all statistical analyses.

NB. The assignment method will be performed on the ITT population and repeated on the PP population.

4.1.6 Study Medication Capsule Compliance

The patient is instructed to take one capsule each morning during the luteal phase (i.e. last 14 days) of their menstrual cycle. The compliance of patients with respect to their assigned treatment regimen will be assessed in three ways:

i) *Capsule compliance*: This will be calculated programatically for each cycle using the following formula:

$$\% \text{ compliance} = \frac{\# \text{ capsules dispensed} - \# \text{ capsules returned}}{\text{days}} \times 100$$

where days is the interval from the first to last dose of study medication during the cycle i.e. stop date – start date +1. This calculation will be based only on data recorded in the study medication panel of the eCRF. For a given cycle, patients are considered to be compliant if this calculation is within 80-120%.

ii) *Interruption in Study drug*: To be compliant patients must not have had a break in study medication for more than 3 consecutive days between the medication start and stop dates in a given dosing period. This will be based on the investigator question in the study medication panel of the eCRF.

iii) *Adherence with regard to taking medication during the luteal phase*: A patient will be considered compliant if they start taking study drug at least seven days prior to Day 1 and have discontinued before Day 3 of the next cycle. Here the medication start and stop dates will be based on data in the study medication panel of the eCRF, and the dates for Days 1 and 3 of the next menstrual cycle will be taken from the patient diary.

For each patient, compliance will be calculated for each menstrual cycle they completed on-study. A patient will be assigned as compliant or non-compliant (or as "unknown" in the unlikely situation where a required component data item is missing) for each of these criteria. An individual will be considered to be **overall compliant** for a given cycle if they meet all three compliance definitions. Otherwise, if a patient is non-compliant on at least one of the three criteria then they will be assigned as non-compliant overall (or "unknown" if one or more component items were "unknown").

4.1.7 Prior and Concomitant Medications

At the screening visit investigators are requested to record medications taken within the last month. Prior and concomitant medication and usage during the post-treatment period will be defined using the start and stop dates, and ongoing fields recorded in the eCRFs relative to the first and last dose dates of randomised study medication.

The definitions for prior, concomitant and post-treatment are shown schematically in the diagram below:

Pre-treatment	On-treatment	Post treatment			
start and stop dates (?=missing date)			Prior	Conco- mitant	Post
x—————x			Y	N	N
x—————	—————x		Y	Y	N
x—————	—————	—————x	Y	Y	Y
	x————x		N	Y	N
	x—————	—————x	N	Y	Y
		x—————x	N	N	Y
?			Y	N	N
—————x			Y	Y	N
	?		Y	Y	Y
	—————x				
		?			
		—————x			
x—————?			Y	Y*	Y*
	x—————?		N	Y	Y*
		x—————?	N	N	Y

Note, where medication is stopped on-treatment or post-treatment and no start date is recorded it will be assumed that the medication was ongoing from the pre-treatment phase. If a medication is started pre-treatment or on-treatment and no stop date is recorded then usage will be assumed to be ongoing provided that the

investigator has indicated that the medication is continuing into the relevant phase (see "*" in the above diagram).

If a medication is started or stopped on the same day of taking the first or last dose of randomised study drug then this will be considered as a concomitant medication. Note, a medication can be counted in more than one phase.

4.2 Values of Clinical Concern

The following flagging criteria are used for the selected laboratory parameters:

- *Above or below normal range:* These flags denote values that fall outside the normal range. Values above the normal range are flagged 'F1 High' and those below as 'F1 Low'.
- *Values of clinical concern:* The 'F3 High' flag denotes values at least as high as the upper cut-off for clinical concern and the 'F3 Low' flag denotes those which are at least as low as the lower-limit of clinical concern.

The F1 and F3 limits are given in [Appendix A1](#). Each laboratory value will be uniquely assigned to one of five categories: clinical concern-high, above the normal range but not of clinical concern, within the normal range, below the normal range but not of clinical concern, or of clinical concern-low. Note, values outside the normal range fall into one of four categories.

Limits for the vital signs data are given in [Appendix A2](#).

4.3 Protocol Violations

The inclusion and exclusion criteria (detailed in Sections 4.2 and 4.3 of the protocol) will be divided into major protocol violations (PVs) and minor protocol deviations (PDs). All eligibility violations will be listed but only PVs will lead to the patient being excluded from the Per Protocol population because the violation may have an influence on the effect of treatment. Minor PDs are considered to have little influence on the effect of treatment and hence do **not** warrant patient exclusion from the PP population. Protocol violations will only be documented for the ITT population. Details on those not meeting the ITT definition will be available in listings.

Protocol violations will, if possible, be validated against data recorded in the eCRF as described below. Note that where an answer for an inclusion/exclusion

tick box differs from the algorithmic check of the criteria, the algorithmic check will overrule the tickbox. For each criterion which requires a quantitative assessment (e.g. VAS, CGI Severity of illness) and a numeric value is not available (see [Section 5.2.1](#)) the criterion can not be checked. Therefore, such criteria will be considered not to be fulfilled (regardless of the tick-box response) and assigned as protocol violations/deviations.

Major Protocol Violations

Any patient satisfying one or more of the following criteria will be considered as having a major protocol violation and will not be included in the PP population.

Non-fulfillment of Inclusion Criteria

(i) No primary diagnosis of PMDD according to DSM-IV criteria (screening inclusion criterion 3 / baseline inclusion criterion 3)

1. Biometrics will derive the set of patients with this inclusion criterion not ticked as 'yes' at baseline i.e. after completion of the reference cycles.
2. In addition, biometrics will provide a listing of in-eligible patients based on the 4 DSM-IV Criteria (Criteria A, B & C collected at Screening and D collected at Baseline).

(ii) PMDD symptoms not present in the majority of cycles in the past 12 months (screening inclusion criterion 4)

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes' at screening.

(iii) Insufficient 'on-offness' of premenstrual symptoms (baseline inclusion criterion 2)

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes' at baseline.
2. Biometrics will derive and provide a listing of the set of patients who fail to show at least a 200% higher (i.e. worse) on one, or at least 100% higher on two or more, of the four core DSM-IV symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score during two consecutive reference cycles,

and fail to have both a mean follicular phase score of ≤ 20 mm and a mean luteal phase score of ≥ 40 mm for the 1-4 qualifying symptoms.

(iv) Insufficient score on CGI-Severity of Illness at baseline (baseline inclusion criterion 1)

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes' at baseline.
2. Biometrics will derive the set of patients who have a CGI-Severity of Illness score < 3 at baseline.

(v) Hormonal contraception use (screening inclusion criterion 5; see inclusion criterion item (iii) under minor protocol violations).

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of prior and concomitant medication to identify women who have used a hormonal form of contraception within one month prior to screening and/or at any point in the study (oral contraceptives or systemic method of contraception) which the GMA will review and document any protocol violators.

Note, patients will be excluded from the per protocol population if they meet the second criterion.

Exclusion Criteria

(i) History of Axis I disorder (other than specific phobias) within 6 months prior to screening (screening exclusion criterion 1/ baseline exclusion criterion 4)

1. Biometrics will provide a listing of patients with either of these exclusion criteria not ticked as 'no' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of psychiatric history records which the GMA will review and document any protocol violators.

(ii) Patients with diagnosed gynaecological diseases (screening exclusion criterion 3)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of medical history and AEs which the GMA will review and document any protocol violators who are diagnosed with gynaecological diseases at any time during the study (i.e. uterine fibroids, ovarian/uterian/cervical carcinoma, or endometriosis).

(iii) Out of range score on MADRS at Screening (screening exclusion criterion 4)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at screening.
2. Biometrics will derive and provide a listing of patients who have a MADRS score ≥ 10 during the follicular phase of the menstrual cycle at Visit 1.

(iv) Ongoing medication which may affect PMDD symptomatology (screening exclusion criterion 6)

1. Biometrics will derive the set of patients with this exclusion criterion not ticked as 'no'.
2. In addition, biometrics will provide a PV excel spreadsheet of all ongoing mediations (with start and stop dates, and ongoing flags) which were used within one month prior to screening and/or at any time during the study which the GMA will review and document any protocol violators. The study medication start and stop dates will also be provided.

(v) Pregnant or lactating women (screening exclusion criterion 10 / baseline exclusion criterion 2)

1. Biometrics will provide a listing of patients with either of these exclusion criteria not ticked as 'no'.
2. In addition, biometrics will provide a listing of women who have a positive result for the serum pregnancy test, at any laboratory assessment during the study.

(vi) Study medication non-compliance

1. For a given treatment cycle, up to and including the last one completed on-study, patients are considered non-compliant if they do not satisfy one or more of the three compliance definitions given in [Section 4.1.6](#).

Minor Protocol Deviations

The following criteria will be considered as minor protocol deviations. Patients without a major protocol violation but with one or more minor protocol deviations will still be included in the PP population.

Non-fulfillment of Inclusion Criteria**(i) Outside permitted age range** (screening inclusion criterion 1)

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes'.
2. In addition, biometrics will derive the set of patients with age <18 and >45 (as defined by the DART, and assessed by algorithm by consideration of the date of birth with respect to the date of the screening visit).

(ii) Irregular or out of range menstrual cycles (screening inclusion criterion 2)

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes' at screening.
2. In addition, biometrics will provide a listing of all patients with menstrual cycles outside the range 22-35 days at any point during the study.

(iii) Inadequate or non-use of contraception for women of child bearing potential (screening inclusion criterion 5, see inclusion criterion [\(v\)](#) under major protocol violations).

1. Biometrics will provide a listing of patients with this inclusion criterion not ticked as 'yes' at screening.

Note, patients will be classified as having a protocol deviation if they meet this criterion provided that the woman was not identified as a PV for hormonal contraception usage.

Exclusion Criteria**(i) Severe, clinically significant, concurrent disease** (screening exclusion criterion 2)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of medical history and physical exam records for the duration of the study which the GMA will review and document any protocol deviations.

(ii) Suicidal risk (screening exclusion criterion 5)

1. Biometrics will provide a listing of patients who have this exclusion criterion ticked 'yes'.
2. Patients will also be identified as having risk of suicide from the Psychiatric History - Item N (collected at the end of Reference Cycle 1A visit).

(iii) Previous adequate treatment with SSRI's for premenstrual symptoms (screening exclusion criterion 7)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of prior and concomitant medication records which the GMA will review and document any protocol deviations.

(iv) Intolerance to paroxetine or other SSRIs (screening exclusion criterion 8)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of medical history and physical exam records which the GMA will review and document any protocol deviations.

(v) Participation in a psychiatric drug trial within 6 months of screening
(screening exclusion criterion 9)

1. Biometrics will provide a listing of patients who have this exclusion criterion not ticked 'no'.

(vi) Abnormal laboratory test (baseline exclusion criterion 1)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at baseline.
2. In addition, biometrics will produce a PV excel spreadsheet of all screening and baseline laboratory values identified as clinically significant abnormal by the extended ranges (F3 flags) for review by the GMA who will document any protocol deviations.

(vii) Use of an investigational drug within 30 days or 5 half-lives prior to screening (screening exclusion criterion 11)

1. Biometrics will provide a listing of patients with this exclusion criterion not ticked as 'no' at screening.
2. In addition, biometrics will provide a PV excel spreadsheet of investigational drug entries in the prior and concomitant medication records, identified by the Anatomical Therapeutic Chemical (ATC) code, which the GMA will review and document any protocol deviations.

(viii) Unable to comply with study procedures or assessments (screening exclusion criteria 12 / baseline exclusion criterion 3)

1. Biometrics will provide a listing of patients with either of these exclusion criteria not ticked as 'no'.

NB. The listings detailed above are only used to identify the protocol violations/deviations prior to unblinding the data so are not sorted by treatment.

4.4 Biometrics QC of Output

The quality control (QC) of the tables and listings generated for the statistical reporting and analysis of this study is the responsibility of the Biometrics department. While it is anticipated that Biometrics will work from a fully quality assured database, any data anomalies discovered during final analysis will be

notified to the Data Management and Clinical groups. Biometrics will perform a QC review of the results prior to release in accordance with Biometrics IOP 7.09.00.02. The exact tables to be used in the metric for Biometrics QC will be specified in the Output Specifications Document.

5 Analysis Populations and Analysis Datasets

5.1 Populations

Two patient populations will be analysed; primary inference for efficacy and safety will be based on the ITT population.

Intent-to-Treat (ITT): The modified ITT population, referred to as the ITT population, consists of all randomised patients who received at least one dose of study medication and have at least one post-baseline assessment.

Per protocol (PP): This population comprises the subset of the ITT population who meet all the following criteria:

- Have no major protocol violation with regard to inclusion or exclusion criteria.
- Have no major protocol violation between randomisation and completion of the active treatment phase of the study (treatment cycles 1-3).
- Have no break in study medication for more than 3 consecutive days, are 80-120% compliant and adherent with regard to taking medication during *each* active treatment phase of the study (i.e. luteal phase of treatment cycles 1-3) as defined in [Section 4.1.6](#).

Only the primary efficacy variable (i.e. no secondary efficacy measures) will be analysed using the PP population. The PP population will not be analysed if it comprises more than 95%, or less than 50%, of the patients in the ITT population. Patients to be excluded from the PP efficacy analysis will be identified prior to unblinding of the study.

5.2 Datasets

Three dataset definitions apply for this study:

<i>Last Observation Carried Forward (LOCF)</i>	On-treatment observations are carried forward to estimate subsequent missing data points for a patient.
<i>70% Last Observation Carried Forward (70% LOCF)</i>	This comprises the LOCF dataset at the latest timepoint where at least 70% of the patients in each treatment group remain in the study.
Observed Cases (OC)	In this dataset data are evaluated only at the time-point at which they were collected with no missing values filled in with estimates.

These datasets will be used for both the ITT and PP populations. For the OC dataset any efficacy assessment performed more than seven days after the last dose of double-blind study medication will be excluded from the analyses, but will be presented in data listings. The LOCF dataset will be constructed from the OC dataset.

5.2.1 Missing data

Data can be missing because of early study withdrawal or because of a missed assessment while on-study. Also, although available, data can be excluded programatically from the analyses either because of insufficient data to compute a value for derived variables (e.g. the VAS - MOOD composite score) or, as described in [Section 4.1.3](#), the assessment took place more than the allowed number of days after the last study dose.

5.2.1.1 Handling Missing Efficacy Data

Composite Scores

The efficacy variables based on composite scores are listed below. Rather than discard a value if component items are missing at a given timepoint the methods described next will be used to derive a score, provided that the criteria for the number of allowable missing items is satisfied.

For items 3, 4 and 5 below, if a value is imputed because of missing data the derived score will be rounded to one decimal place prior to any analyses, and presented with this level of precision in tables and listings.

1. Visual Analogue Scale (VAS) individual symptom items: For each of the eleven VAS items a mean score for the luteal or follicular phase will only be calculated if scores are available for at least four of the five designated days.

2. VAS – MOOD score: If mean symptom scores are available for at least three of the four core symptoms then a composite VAS-MOOD score will be derived as the average of the mean item scores; otherwise the VAS-MOOD score will be assigned as missing at this timepoint.

3. Area Under the Curve (AUC) for VAS – MOOD : For a given baseline or treatment cycle the VAS – MOOD AUC will be calculated only if data are available for at least four of the five designated luteal days. If there is one missing score, and this occurs on the first or the last day then the AUC calculation will be based on the available data from the other four days with i running from 0 to 3. Otherwise, if the missing score occurs on the second, third or fourth day then this value will be imputed as the average of the observed values from the day before and the one after this missed data point. In this instance it will be assumed that there are 5 days-worth of data (i.e., i runs from 0 to 4).

4. Montgomery-Asberg Depression Rating Scale (MADRS): This scale, collected only at screening (i.e. visit 1), comprises ten individual questions each rated on a 7 point scale from 0 (mild or not present) to 6 (severe). Provided that at least 9 of the 10 questions were answered the total score will be calculated as:

$$\frac{\text{No. items in the scale} * \text{Total score for answered items}}{\text{No. items answered}}$$

i.e. the mean of the observed data multiplied by the total number of items in the scale.

5. Premenstrual Tension Scale - Observer rated (PMTS-O): The PMTS-O consists of 10 questions from which the total score is calculated. Items 1-6, 9 and 10 consist of 5 response categories: 0 = *No symptoms* to 4 = *Severe symptoms*; Items 7 and 8, 'Eating Habits' and 'Sexual Drive and Activity' consist of only 3 response categories: 0 = *No symptoms* to 2 = *Severe symptoms*.

If a single item is missing the total will be calculated using the following formula:

$$\text{Total Score} = \text{Observed Total Score} * \left(1 + \frac{\text{Denominator of the missing value}}{\text{Sum of denominators of the non-missing values}}\right)$$

Here the total score is adjusted for the missing value by assuming that this value is a weighted average of the answered questions. Since this total will only be imputed when there is one missing value, the formula can be simplified to:

- 3 item missing question: i.e. Observed total score * (1 + 2/34)
- 5 item missing question: i.e. Observed total score * (1 + 4/32)

Note, the 2/34 and 4/32 can be considered as correction factors which allow for the scale on which the missing question was rated.

If more than 1 response is missing then the patient's PMTS-O data will be excluded at that particular timepoint.

6. EQ-5D health profiles: If at a given timepoint one or more of the five dimensions is missing then the digit summary and weighted tariff will not be derived for that timepoint.

Other variables

1. Clinical Global Impression (CGI, Global Improvement and Severity of Illness) and Patient Global Evaluation (PGE): For these variables, data on patients who have a score of 0 (i.e. not assessed) or missing data will not be included for that particular timepoint. For LOCF analyses, the last non-zero post-baseline score will be carried forward.

2. Sheehan Disability Scale: If an individual item (i.e. work, social life or family life) is missing or unassessed at a visit, then that patient's data will be excluded from the analysis of that particular SDS item score at that timepoint.

3. Work Productivity and Activity Impairment Questionnaire (WPAI): For each question, patients with no data will be excluded from the denominator in the summary tables.

4. International Standard Classification of Occupations (ISCO-88): Patients with no data for this question will be excluded from the denominator in the summary tables.

5. EuroQol VAS: Patients with missing data will be excluded from summary tables and analyses at that timepoint.

5.2.1.2 Evaluability and Missing Baseline Data

Having applied these rules, a patient will be considered evaluable for a given change from baseline efficacy analysis if they have a baseline and a post-baseline non-missing value (at least one for the LOCF analysis or at a specific timepoint for the OC analysis) i.e. baseline values will not be carried forward. Note, the number of subjects included is likely to vary across efficacy endpoints.

NB. See the pre-treatment session details in [Section 4.1.3](#) for handling missing baseline data.

6 Comparisons of Interest

6.1 Primary Comparisons of Interest

The paroxetine arms versus placebo comparisons of change from baseline in the luteal phase VAS-MOOD score at the treatment cycle 3 LOCF endpoint in the ITT population are the primary comparisons of interest in this study.

For this study to be considered a success a clinically and statistically significant difference must be observed (after adjustment for multiple comparisons) between the placebo arm and either of the paroxetine arms.

6.2 Other Comparisons of Interest

Other comparisons of interest include a LOCF analysis of the secondary endpoints at the treatment cycle 3 visit. In addition, an analysis of the primary and secondary efficacy variables based on the 70% LOCF dataset and the observed cases (OC) dataset at the treatment cycle 3 visit will be performed. A per protocol (PP) analysis of the primary endpoint only will be performed.

The difference between the two paroxetine arms is not of central scientific interest and this comparison will not be considered when adjusting for multiple comparisons. This comparison will be presented for the primary variable alone for information only.

7 Targeted Sample Size

7.1 Sample Size Assumptions

This study is powered to demonstrate a difference of 16.3mm between paroxetine CR (12.5mg and 25mg) and placebo, in mean change from baseline to treatment cycle 3 in VAS - MOOD score. Based on data presented from an earlier study of fluoxetine continuous dosing [2] [3] and from a sample size re-estimation procedure applied to the three trials in the continuous paroxetine treatment program for PMDD[4], a common standard deviation of 30mm was assumed for the change in VAS - MOOD score at the treatment cycle 3 LOCF endpoint. A total of 86 evaluable patients in each of the three study arms will provide 90% power to detect a difference of 16.3mm. To adjust for the two treatment comparisons a two-sided alpha level of 0.025 has been used. Assuming a 20% attrition rate, the total number of patients randomised to each treatment group is increased to 108, a total of 324 patients overall.

Note, the sample size of 108 randomised patients per regimen has a 95% probability of observing at least one adverse event for those events that occur at the rate of 2.7% or greater.

7.2 Sample Size Sensitivity

The robustness and sensitivity of the sample size calculation has been considered in order to assess the impact on the power of the study should the observed standard deviation be higher or lower than expected.

Given a fixed sample size and a difference of 16.3mm the size of the standard deviation will affect the power of the study to detect this difference between the treatment groups, as shown in the table below.

The minimum standard deviation value of 20 was chosen based on data from the placebo and intermittent paroxetine dosing arms from a recent study [5], and the maximum value was chosen in order to be symmetric about the assumed value.

Standard Deviation	Power (%) with 86 evaluable patients per group	Evaluable patients required per group for 90% Power
SD maximum 40	65	151
35	78	116
SD best 30	90	86
25	97	60
SD minimum 20	>99	39

8 Definition of Variables/Assessments

Change from baseline: For a given variable this is defined as the value at a particular treatment visit minus the patient's baseline measurement. For example, on the individual VAS symptom scales (or the composite VAS – MOOD score) the range would be from –100mm to + 100mm; a negative score representing an improvement and a positive score showing a worsening.

The efficacy variables are listed next. The secondary variables are presented according to type of response i.e. continuous or binary data which determines the type of model to be fitted as described in [Section 9.2.3](#). Although the pharmacoeconomic variables are also given the analyses are described separately (see [Section 9.2.4](#)).

8.1 Primary Variable

- Change from baseline in luteal phase VAS - MOOD score at treatment cycle 3 endpoint.

8.2 Other Variables

8.2.1 Secondary Variables

Continuous endpoints

- Change from baseline in the luteal phase VAS Physical Symptoms score at the treatment cycle 3 endpoint.
- Change from baseline in area under the curve (AUC) for treatment cycles 1-3 in daily luteal phase VAS – MOOD scores, adjusting for the total number of luteal days.
- Change from baseline in the observer rated Premenstrual Tension Scale (PMTS-O) total score at the treatment cycle 3 endpoint.
- Change from baseline in the CGI - Severity of Illness score at the treatment cycle 3 endpoint.
- Change from baseline in the individual items of the Sheehan Disability Scale (SDS; work, social life and family life) at the treatment cycle 3 endpoint.
- Change from baseline in the EuroQol VAS at treatment cycle 3 endpoint.

Binary endpoints

- The proportion of responders defined by a 50% reduction in their baseline luteal phase VAS- MOOD score at the treatment cycle 3 endpoint.

Percentage change is defined as:

$$\% \text{ Change} = \frac{(VAS - MOOD_{\text{endpoint}} - VAS - MOOD_{\text{baseline}})}{VAS - MOOD_{\text{baseline}}} \times 100$$

- The proportion of responders defined by a mean luteal phase VAS - MOOD score at the treatment cycle 3 endpoint of less than or equal to their baseline mean follicular phase VAS-MOOD score.
- The proportion of patients who scored 1 or 2 (very much improved or much improved) on the CGI – Global Improvement item at the treatment cycle 3 endpoint.
- The proportion of patients who scored a 1 or 2 (very much improved or much improved, respectively) on the Patient Global Evaluation (patient-rated) at the treatment cycle 3 endpoint.

8.2.2 Other Variables

The following will be summarised by descriptive statistics with no formal statistical analysis performed:

- Change from baseline in each individual VAS item score, excluding the Physical Symptoms item, at the treatment cycle 3 endpoint.
- Patient evaluation of Study Medication (observer-rated) at treatment cycle 3 endpoint, or early withdrawal.
- Change from baseline in the weighted EQ-5D health profile score based on the EuroQol tariff (EQ-5D utility).
- EQ-5D health profiles at baseline and treatment cycle 3.
- Overall work productivity score from the Work Productivity and Activity Improvement Instrument.
- International Standard Classification of Occupations at baseline (visit 3).

9 Statistical Methodology

Unless otherwise specified the following analyses will be performed on the ITT population only.

9.1 Patient Disposition, Baseline Characteristics and Demography

The number of screen-only patients, randomised to treatment, completing the study, eligible for the intention-to-treat, and eligible for the per-protocol analysis will be tabulated for the three treatment groups. In this table the screen-only patients will be split according to whether they have received placebo run-in medication or not.

Patients excluded from the ITT population

The number and percentage of patients withdrawing for each reason by the withdrawal period (i.e. before placebo run-in medication, prior to first dose of randomised medication versus on or after the first dose of randomised medication) by treatment arm will be tabulated. Depending on withdrawal period

the following data, as requested in [Section 9.2](#) of the protocol, will be provided in listings:

1. For patients who withdraw from the study prior to receiving single-blind placebo medication in Reference Cycle 2: Patient demography (Date of Birth, Race), Reason for withdrawal (from the Patient Continuation/Withdrawal panel) and Eligibility based on the reference cycle VAS scores.
2. For patients who withdraw from the study after administration of any single-blind placebo medication: as in 1. above and additionally Medical History, Baseline AE and Prior/Concomitant Medications.

Patients in the ITT population

Unless otherwise stated the following tables and listings will be based on the ITT population.

The number and percentage of patients either completing the study or withdrawing early for each reason will be tabulated. This table will also be presented for the PP population. Withdrawal rates will also be summarised by visit.

The number and percentage of subjects by race and age group (18-25, 26-35, ≥ 36 , unknown) will be tabulated by treatment group. Summary statistics will be presented for the Montgomery and Asberg Depression rating scale (MADRS) at screening visit 1. Summary statistics will also be tabulated for age, weight, height and body mass index (BMI). These tables will also be presented for the PP population.

Selected medical and surgical history (excluding psychiatric disorders) will be tabulated for prior conditions by treatment group. Similar tables will be produced for active conditions. Tabulations of psychiatric history disorders, history of PMDD, prior treatment for PMDD, and obstetric/gynaecological history will also be provided.

The comparability of the treatment groups with respect to the above selected baseline and demographic characteristics will be assessed. If large differences are observed then these imbalances will be investigated. No formal hypothesis testing or interval estimation will be applied to baseline or demographic characteristics.

9.1.1 Prior and Concomitant Medications

All prior and concomitant medications and those taken during the post-treatment period will be listed by treatment group, showing the preferred and verbatim terms. Tables will be produced showing the number and percentage of subjects in each treatment group receiving prior medication by ATC code and preferred term, and also by preferred term ordered by decreasing frequency within the paroxetine CR 25mg treatment group. Similar tables will be created for the treatment and post-treatment phases.

9.1.2 Study Medication Compliance

For each treatment cycle, overall study medication compliance, along with each of the three component parts as defined in [Section 4.1.6](#), and dosing information (i.e. duration interval and number of capsules dispensed and returned) will be listed by treatment group. The number and percentage of patients who are overall compliant or non-compliant will be tabulated by visit and treatment group. In addition, a cross-tabulation of the compliant/non-compliant responses for the three components will be produced by visit and treatment. This breakdown will show the proportion that were compliant on all three criteria, compliant only on the 80-120% criterion etc.

9.2 Efficacy Analysis

9.2.1 Multiplicity

All confidence intervals (CIs) and hypothesis tests will be two-sided. For the primary variable the treatment effect will be considered statistically significant at the overall 5% level, with an adjustment for two treatment comparisons using Hochberg's modification to the Bonferroni inequality [\[6\]](#); adjusted 95% confidence intervals will be presented. For the purpose of applying Hochberg's method to the calculation of adjusted confidence intervals, comparisons will be ordered on the basis of the corresponding p-value. For secondary variables no multiplicity adjustment will be applied; the treatment effect will be considered statistically significant at the 5% level and confidence intervals will be presented at the 95% level.

9.2.2 Analysis of Primary Efficacy

9.2.2.1 Model Specification

The change from baseline VAS – MOOD response will be analysed using a normal, linear model. As described in Section 9.2.2.3 the assumptions underlying the statistical analysis will be checked. If these assumptions are not met, appropriate non-parametric methods will be used (i.e. the Wilcoxon Rank Sum test, WRST).

Since PMDD is a relatively new area of research there is limited information on the variables which affect response. For this reason, the statistical model on which the primary inference will be based will include terms for treatment group, centre, baseline VAS - MOOD score and age (in years) at entry to the study. In addition, the following candidate covariates will be entered separately into the model:

- baseline SDS work item
- duration of PMDD (years)
- baseline SDS social life item
- baseline SDS family life item
- number of previous pregnancies (0, 1, 2, 3, 4 or ≥ 5)

All those that achieve statistical significance at the 5% level will be included in the primary model. No interaction terms will be included in this primary model.

9.2.2.2 Robustness of the Primary Analysis

To assess the robustness of the primary model, interactions between treatment and each of the other main effects (continuous or categorical covariates) included in the primary model will be investigated in turn, the statistical significance of these terms being assessed at the 10% level. In the event that one or more interaction terms is found to be statistically significant, attempts will be made to establish the cause of the heterogeneity, e.g. joint modelling of significant interaction terms and investigation of other demographic characteristics. The significant treatment interactions will be tabulated and shown graphically; for those interactions with a continuous covariate the treatment effect will also be plotted by the following pre-defined categories:

- VAS -MOOD score at baseline: quartiles of the observed values

- Age: 18-25, 26-35, ≥ 36
- Duration of PMDD: <2, 2-5, 6-10, >10 years
- Work, social, and family life SDS items: 0, 1-3, 4-6, 7-9, 10

In the event that no other explanation can be found for the cause of the heterogeneity, and provided that the number of categories for the covariate is large, an overall estimate of the treatment effect will be obtained by considering the covariate and treatment by covariate interaction terms as random effects.

NB. Investigation of interaction terms will be confined to the primary variable using the treatment cycle 3 LOCF dataset for the ITT population.

9.2.2.3 Diagnostics

The assumptions of normality and homogeneity of variance will be assessed for the primary model by inspection of the following plots:

- Histogram of standardised residuals
- Normal probability plot with simulation envelope
- Standardised residual plot against fitted value with smooth line
- Absolute residual plot against fitted value with smooth line

In addition, the model will be re-fitted excluding observations with large residuals or which are strongly influencing the fit of the model to the data. The clinical importance of changes to the results on exclusion of these observations will be assessed and any important differences will be reported. However, the primary inference will be based on the primary model with any influential outliers included.

9.2.2.4 Presentation of the Primary Model Results

A table of summary statistics (adjusted mean, standard error of mean and N) for change from baseline in VAS – MOOD score by each treatment group, together with the estimates of differences in means (95% CI and P-values, adjusted for multiple comparisons) between each dose of paroxetine and placebo, adjusted for covariates will be presented. The difference in means between the two paroxetine dose groups will be presented for information only.

In addition, the regression coefficients (95% CI) of change in VAS - MOOD for the other covariates in the primary model will be presented in the [Statistical Appendix](#).

9.2.2.5 Summaries and Further Analyses of VAS - MOOD

Summary statistics of the observed (absolute) and change from baseline VAS – MOOD values at each timepoint will be provided.

In order to address the issue of potential bias in estimating the treatment effect on VAS – MOOD resulting from missing VAS data, the percentage of missing VAS - MOOD responses will be tabulated by visit and treatment group using the OC dataset. The percentage of missing data for the individual VAS – MOOD items will also be tabulated by visit and treatment.

To assess the within and between-subject variability in VAS - MOOD individual patient response profiles will be plotted for each day of the menstrual cycle. Connected lines will show an individuals sequence of scores over time, with breaks in the sequence indicating missing data. These will be plotted by treatment group, and within each arm ordered according to the last visit attended. This ordering was chosen to aid detection of any unusual patterns in scores prior to premature withdrawal.

9.2.3 Analysis of Secondary Efficacy

Continuous Variables

Model Specification:

Applying the primary model (i.e. treatment, centre, age, corresponding baseline score, and other covariates which attained statistical significance), normal, linear models will be fitted to each continuous secondary variable specified in [Section 8.2.1](#), except for the EuroQol VAS and CGI-Severity of Illness responses. As described in [Section 9.2.4](#) a separate model building procedure will be undertaken for the EuroQol VAS. Since the analysis of change from baseline in the CGI-Severity of Illness score from earlier SB paroxetine clinical trials has shown this measure to be skewed in distribution the WRST will be used for the comparison of treatment groups for this response.

Diagnostics:

As for the primary analysis, the fitted models will be evaluated by graphical diagnostics (see Section 9.2.2.3). If for a given model the assumptions are strongly violated then the WRST will be used instead.

Presentation of Results: The adjusted mean change and differences in means (95% CI and P-values) between each dose level of paroxetine and placebo will be tabulated and displayed graphically.

If non-parametric analyses were performed because the assumptions of the normal model were strongly violated the results from both types of analyses will be presented. In this situation inference will be based on the non-parametric results.

Summaries of the absolute values at each timepoint (including baseline) will be provided.

Binary Variables*Model Specification:*

Applying the primary model (i.e. treatment, centre, age, corresponding baseline score, and other statistically significant covariates) logistic regression models will be fitted to the four binary secondary endpoints.

Diagnostics:

Standardised deviance residuals will be plotted against continuous covariates to check for linearity of the relationship on the logistic scale. A half normal plot of the standardised residuals with a 95% simulated envelope will be used to identify large residuals. Observations with large residuals or which are strongly influencing the fit of the model to the data will also be investigated by examining the change in deviance on exclusion of these observations. However, influential outliers will be included in the final model.

Presentation of Results:

Adjusted odds ratios (i.e. the odds of a patient being a responder on a paroxetine arm relative to the odds of a patient being a responder on placebo) and the associated 95% confidence intervals and P-values will be tabulated. The point estimates and 95% CIs will also be displayed graphically.

Summaries showing counts and the proportions in each response category by visit and treatment group will be presented.

9.2.4 Pharmacoeconomic Analysis

The EuroQol has 2 components: the health state classification (EQ-5D) and the visual analogue scale.

EuroQol-5D health profiles: The EQ-5D describes health status in 5 dimensions: mobility, self-care, usual activity, pain/ discomfort and anxiety / depression. Patients rate their health status on 3 levels for each dimension: no problem, moderate problems and extreme problems (scored as 1,2 and 3 respectively). The answers to each question are used to define the patient's health state as a sequence of five digits ranging from 11111 to 33333. These health states will be converted to a 'utility' value (EQ-5D_{utility}), ranging from '0' for death to '1' for perfect health, using the EuroQoL tariff (provided in [Appendix A3](#)).

The number and percentage of patients in each category for each of the five questions will be tabulated by treatment group and visit. Histograms of the EQ-5D responses will be presented at baseline and treatment cycle 3, with each of the five questions representing one bar on the histogram for each response category. For each EQ-5D response summary statistics will also be provided by treatment group at baseline and treatment cycle 3. In addition, summary statistics will be tabulated by treatment group for baseline and change from baseline to treatment cycle 3 in the EQ-5D_{utility} score.

EuroQol VAS: Summary statistics will be presented for the EuroQol VAS score by treatment group and visit.

Since the covariates considered to be important for the VAS efficacy data may not be important to the EuroQol, a separate covariate selection procedure will be applied to the EuroQol VAS response. Following the same strategy used for the primary analysis, the final model will include terms for treatment group, centre, age and baseline EuroQol VAS score. The same candidate covariates (i.e. duration of PMDD, baseline functionality assessments and the number of previous pregnancies), and additionally employment status at entry (currently employed or unemployed from the WPAI), will be entered separately into the model. Those that achieve statistical significance at the 5% level will all be included in the final model. As a supplementary analysis, interactions between the selected covariates and treatment will be explored. Model diagnostics will be carried out as described in Section 9.2.2.3.

International Standard Classification of Occupations (ISCO-88): The number and percentage of patients in each category will be tabulated by treatment group.

Work Productivity and Activity Improvement Instrument (WPAI): The number and percentage of patients employed and unemployed will be tabulated by treatment group at each timepoint. Summary statistics will be tabulated by visit and treatment group for the number of hours missed from work because of health problems, number of hours missed from work for other reasons and total number of hours worked during the past seven days.

9.2.5 Interim Analyses

There are no planned interim analyses.

9.3 Safety Analyses

In this study the ITT population will be used for all safety summaries.

9.3.1 Adverse Experiences

Adverse experiences (AEs) will be coded using the WHO coding system which will then be mapped to the ADECS (COSTART based) classification to give a body system and preferred term for each experience

Definition of Treatment Emergent Adverse Events

Following the ICH E9 guidelines, a *treatment emergent* AE will be defined as:

'An event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state.'

However, this study is divided into 3 phases, 'Pre-treatment', 'Treatment' and 'Post-treatment'. Only the fourteen day follow-up period of the post-treatment phase will be included in tabulations.

An AE will be assigned as treatment or follow-up emergent if the onset date is during the treatment or follow-up phase, respectively and was absent in the pre-treatment phase or worsened relative to the pre-treatment phase.

Examples showing how emergent AEs are categorised are given in [Appendix A4](#).

All AEs will be listed by treatment group. Unless otherwise specified, the following tables will be produced separately for the on-treatment and follow-up periods by treatment group:

- 1) Adverse Experiences (Pre-treatment, Treatment and Follow-up)
- 2) Serious Adverse Experiences (Treatment and Follow-up Phases Combined)
- 3) Adverse Experiences by Intensity/Severity ('Mild', 'Moderate' or 'Severe')
- 4) Related or Possibly Related Adverse Experiences
- 5) AEs leading to Withdrawal during the Treatment Phase only
- 6) Number (%) of Patients with AEs by Maximum Severity by Body System. Deaths will only be listed by patient and treatment group.

In addition, tables displaying AEs and Serious AEs occurring in 1% or more of the placebo or paroxetine groups will be presented by preferred term only. These will be sorted in descending order of frequency for paroxetine CR 25mg.

Discontinuation Symptoms

Since randomised study medication is taken intermittently during the luteal phase (i.e. approximately the last 14 days) of the menstrual cycle, discontinuation symptoms may occur after temporarily stopping the active study drug at the end of a menstrual cycle or after permanent discontinuation of study drug. In this study investigators are not being asked to identify and report discontinuation symptoms any differently from the routine reporting of AEs. Instead, discontinuation symptoms will be identified as follows:

All adverse events with onset date within 14 days of stopping randomised study medication or before restarting drug (which ever was earliest) will be identified.

A blinded listing of patients with the adverse event absent pre-treatment, or which had worsened, will be sent to the Central Safety team to review and document any discontinuation symptoms.

Note, the discontinuation symptoms occurring in the 14 days after permanent study drug discontinuation will also be included in the routine AE follow-up tables. The number and proportion of discontinuation symptoms will be tabulated by body system and preferred term by cycle, and overall. In addition, similar

tables will be produced for the subset of AEs with onset date within 7 days of study drug discontinuation.

9.3.2 Clinical Laboratories

Summary statistics will be presented for the laboratory data (haematology and blood chemistry) by visit and for change from baseline. Each patient's baseline measurement for a given parameter will be classified into one of five categories: within the normal range, above or below the normal range (F1), or as a low or high value from a pre-determined clinically important range (F3). Available values from the last on treatment assessment and follow-up visit (within 14 days of the last study dose) will be classified using the same procedures. The proportion in each category at each timepoint, and transition from baseline will be examined by cross-tabulating the assigned post-baseline levels against the baseline categories.

9.3.3 Vital Signs

Summary statistics for change from baseline will be presented by treatment group for blood pressure, heart rate, weight and body mass index. Summary statistics for the absolute values at entry, including height, will be presented. Additionally, for blood pressure, heart rate and weight the number of patients in each treatment group with values outside pre-determined clinically important ranges and/or with changes from baseline of clinical importance will be tabulated (see [Appendix A2](#)).

10 References

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11 Appendices

Appendix A1 Laboratory Normal Ranges and Predetermined Values of Clinical Concern

F1 Lab Normal Ranges

		Age	F1 Low	F1 High	Units
HGB	Hemoglobin	18-46	120.04	156.30	G/L
HCT	Hematocrit	18-46	35	46	%
RBC	Red blood cell count	18-46	3.9	5.2	10 ¹² /L
WBC	White blood cell count	18-46	3.8	10.8	10 ⁹ /L
NEUTB	Neutrophil bands	18-46			%
NEUTS	Segmented neutrophils	18-46	40	75	%
LYMPH	Lymphocytes	18-46	16	46	%
MONO	Monocytes	18-46	0	12	%
EOSIN	Eosinophils	18-46	0	7	%
BASO	Basophils	18-46	0	2	%
PLATE	Platelets	18-46	130	400	10 ⁹ /L
BILTOT	Total Bilirubin	18-46	0	22	UMOL/L
ASAT	Aspartate aminotransferase	18-46	0	42	IU/L
ALAT	Alanine aminotransferase	18-46	0	48	IU/L
ALKPH	Alkaline Phosphatase	18-19	30	165	IU/L
		20-46	20	125	IU/L
CREAT	Creatinine	18-46	44	124	UMOL/L
BUN	Blood Urea Nitrogen	18-46	2.5	9	MMOL/L
TSH	Thyroid stim. hormone	18-46	0.4	5.5	MU/L
FT3	Thyroid total T3	18-46	3.5	6.5	PMOL/L
FT4	Thyroid total T4	18-46	10.3	23.2	PMOL/L

F3 Lab Clinical Concern Ranges

		F3 Low	F3 High	F3 Units
HGB	Hemoglobin (HGB)	≤95		G/L
HCT	Hematocrit (HCT)	≤32		%
RBC	Red blood cell count (RBC)		≥10	10 ¹² /L
WBC	White blood cell count (WBC)	≤2.8	≥16	10 ⁹ /L
NEUTB	Neutrophil bands (NEUTB)		≥10	%
NEUTS	Segmented neutrophils (NEUTS)	≤15		%
LYMPH	Lymphocytes (LYMPH)		≥75	%
MONO	Monocytes (MONO)		≥15	%
EOSIN	Eosinophils (EOSIN)		≥10	%
BASO	Basophils (BASO)		≥10	%
PLATE	Platelets (PLATE)	≤75	≥700	10 ⁹ /L
BILTOT	Total Bilirubin (BILTOT)		≥34.2	UMOL/L
ASAT	Aspartate aminotransferase (ASAT)		≥150	IU/L
ALAT	Alanine aminotransferase (ALAT)		≥165	IU/L
ALKPH	Alkaline Phosphatase (ALKPH)		≥390	IU/L
CREAT	Creatinine (CREAT)		≥176.8	UMOL/L
BUN	Blood Urea Nitrogen (BUN)		≥10.71	MMOL/L
TSH	Thyroid stim. hormone (TSH)		≥10	MU/L
FT3	Thyroid total T3 (FT3)	≤1.75	≥13.00	PMOL/L
FT4	Thyroid total T4 (FT4)	≤5.15	≥46.40	PMOL/L

Notes on Laboratory Flagging

Before laboratory values are flagged as above/below the ranges of clinical concern, they are converted to SB preferred units. The normal ranges are also converted to SB preferred units before any multiplier is applied to obtain the clinical concern range.

Differentials, however, are converted as follows: the laboratory value is a percentage (e.g. lymph = 30%) and is converted to the SB preferred units by taking the percentage of the White Blood Cell Count (e.g. if WBC = 9.3 10⁹/L, then LYMPH = 30% of 9.3 = 2.79 10⁹/L). The normal ranges cannot be converted in this way (because the WBC value itself may be abnormal), so a

default normal range is used. The multipliers for clinical concern ranges are then applied to this default normal range.

Default Normal Range for Differentials

	Normal Low	Normal High
Basophils $10^9/L$	0	0.1
Eosinophils $10^9/L$	0	0.4
Lymphocytes $10^9/L$	1.5	5.0
Monocytes $10^9/L$	0	0.8
Neutrophils	1.5	10.0

Appendix A2 Limits for the Vital Signs data

Systolic Blood Pressure (mmHg)

Normal Range 90-180 mmHg

Significant Increase Increase of ≥ 40 mmHg from baseline

Significant Decrease Decrease of ≥ 30 mmHg from baseline

Diastolic Blood Pressure (mmHg)

Normal Range 50-105 mmHg

Significant Increase Increase of ≥ 30 mmHg from baseline

Significant Decrease Decrease of ≥ 20 mmHg from baseline

Heart Rate (bpm)

Normal Range 50-120 bpm

Significant Increase Increase of ≥ 30 bpm from baseline

Significant Decrease Decrease of ≥ 30 bpm from baseline

Weight (lb)

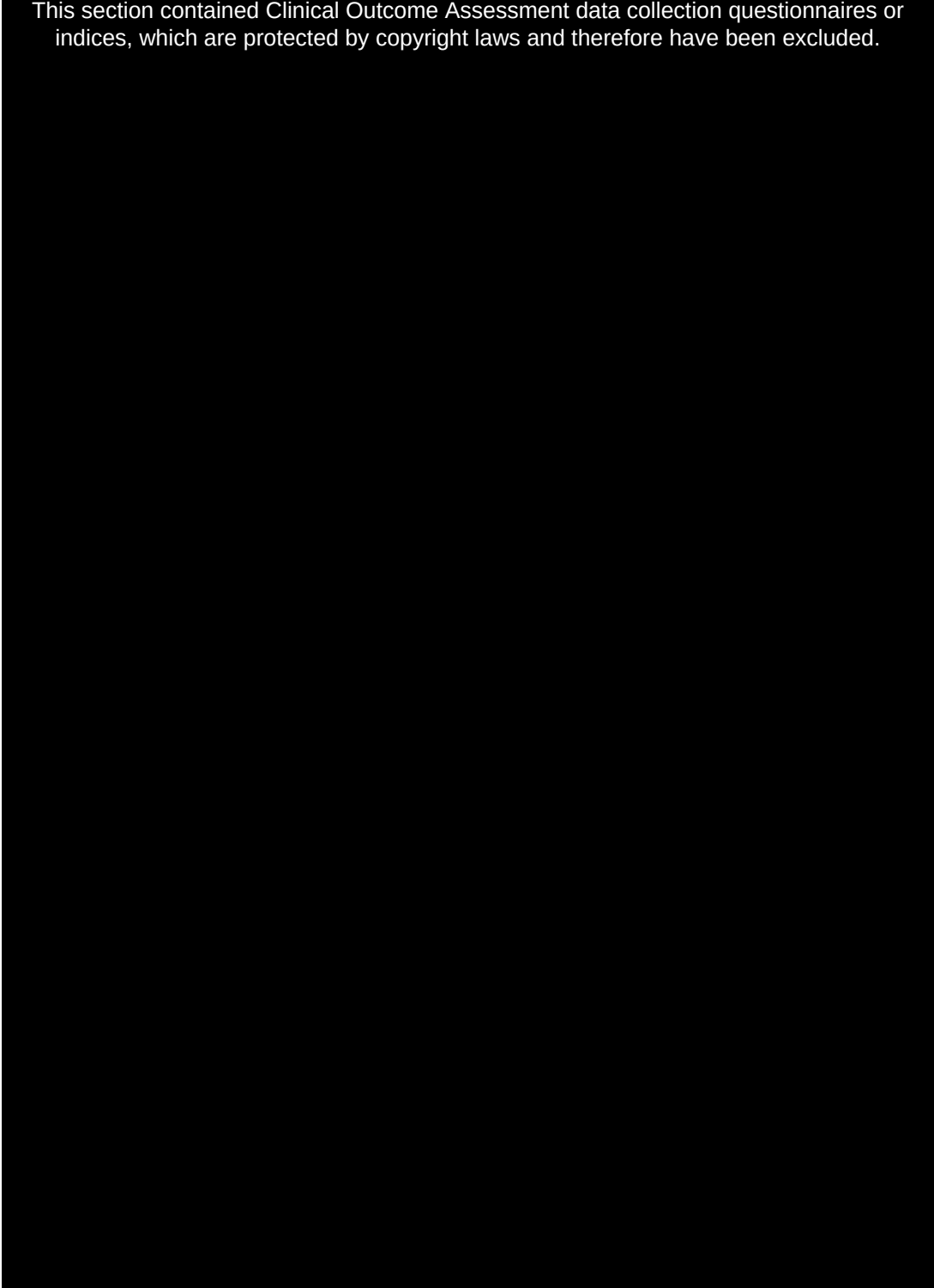
Normal Range Within 7% of baseline weight

Significant Increase Increase of $\geq 7\%$ from baseline

Significant Decrease Decrease of $\geq 7\%$ from baseline

Appendix A3 EuroQol Tarrifs

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



Appendix A4 Examples of emergent Adverse Events

The criteria for defining treatment or follow-up emergent adverse experiences (AEs) are illustrated in the following examples:

1. Treatment and Follow-up phase Emergent

A given AE, not present during the Pre-treatment period, is incident during the Treatment Phase and recurs during the Follow-up phase. Because these are both new occurrences, not present prior to Treatment, this is considered as an 'emergent' AE for both the Treatment and Follow-up phase.

Phase: ← Pre-treatment → ← Treatment → ← Follow-up →

AE: S---E S---E

where S = start of AE

E = end of AE

This AE will be classed as emergent in both the Treatment Phase and the Follow-up Phase.

2. Ongoing at the same intensity

A given AE is first reported during the Treatment Phase and continues into the Follow-up phase. This is an 'emergent' AE for the Treatment phase only because it was not present prior to Treatment, with no new occurrence in the Follow-up phase.

Phase: ← Pre-treatment → ← Treatment → ← Follow-up →

AE: S-----E

where S = start of AE

E = end of AE

This AE will be classed as emergent in the Treatment Phase only.

3. Present Pre-treatment with recurrences at later phases

A given AE is reported during the pre-treatment phase with at least one recurrence during the treatment or Follow-up phase. If the intensity has not

increased (i.e. worsened) during the treatment or Follow-up phase relative to Pre-treatment then the AE will only be included in the Pre-treatment AE table. Two illustrative examples are shown below:

Phase:	← Pre-treatment →	← Treatment →	← Follow-up →
AE:	S---E	S----E	S—E
Intensity:	Severe	Mild	Mild

Phase:	← Pre-treatment →	← Treatment →	← Follow-up →
AE:	S---E	S----E	S—E
Intensity:	Severe	Mild	Severe

where S = start of AE

E = end of AE

In both examples the AE will NOT be classed as emergent during the Treatment or Follow-up phase.

4. Increase in intensity

The same AE is reported during all phases, however the AE during Treatment and the Follow-up Phase is of a higher severity than at Pre-treatment:

Phase:	← Pre-treatment →	← Treatment →	← Follow-up →
AE:	S---E	S----E	S—E
Intensity:	Mild	Severe	Severe

where S = start of AE

E = end of AE

The AE will be included in tables for the Pre-treatment Phase at the severity at which it occurs. The AE will be classed as emergent in both the Treatment and Follow-up phase as the AE worsens relative to the Pre-treatment state.

5. Different intensity levels within a phase

The same AE is reported twice at pre-treatment with different intensities, then also later in the study:

Phase:	← Pre-treatment →	← Treatment →	← Follow-up →
AE:	S-E S—E	S----E	S—E
Intensity:	Moderate Mild	Mild	Mild

where S = start of AE

E = end of AE

The AE will be counted once at the maximum intensity during the Pre-treatment Phase. The AE will not be classed as emergent in the Treatment or Follow-up Phase as the intensity is lower than the maximum pre-treatment intensity.

Modular Appendices

Protocol and Protocol Amendments

Confidential

29060

**A double-blind, placebo-controlled, 3-arm fixed dose study of paroxetine CR
intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder**

717

[REDACTED]
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*Neuroscience TU, **Biometrics

SB Document Number: BRL-029060/RSD-101DLF/3

Issue Date: 5th March 2001

Amendment 1: 13th July 2001; Amendment 2: 11th September 2002

Endorsements



Clinical Unit: Neurosciences Therapeutic Unit

Document No.: BRL-029060/RSD-101DLF/3

Drug Name: Paroxetine CR

Compound No: 29060

Protocol Title: A double-blind, placebo-controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder

CPMS Number: 717

SB Site Monitor:

Contact Information:

I, the undersigned, have reviewed this protocol, including Appendices, and I will conduct the clinical study as described and will adhere to the Ethical and Regulatory Considerations stated.

Yes I have read and understood the contents of the Investigator Brochure.

<Name>, Investigator
<Address>

<Date>

Table of Contents

	Page
Abbreviations	894
Definitions	895
Synopsis	896
1 Introduction	899
2 Objectives	903
3 Study Design Overview	904
3.1 Study Design	904
3.2 Schedule of Assessments	905
3.3 Method of Randomization	905
4 Study Population	907
4.1 Planned Number of Patients	907
4.2 Inclusion Criteria	908
4.3 Exclusion Criteria	909
5 Conduct of the Study	911
5.1 Ethical and Regulatory Considerations	911
5.1.1 Ethics Review Committee (ERC)/ Institutional Review Board (IRB)	911
5.1.2 Informed Consent	911
5.2 Outline of Study Procedures	912
5.3 Detailed Description of Study Stages/ Visits	916
5.4 Laboratory Parameters	933
6 Study Medication and Administration	934
6.1 Study Medication	934
6.2 Dosage and Administration	934
6.3 Blinding	934
6.3.1 Code Breaking For supplies to North American sites:	935
6.4 Packaging	935
6.4.1 Reference Cycle 2	936
6.4.2 Treatment Cycles (Treatment Cycle 1 ,2, 3)	936
6.5 Labelling and Preparation	936
6.6 Storage	939
6.7 Drug Accountability	939
6.8 Assessment of Compliance	939
6.9 Treatment of Study Medication Overdose	939
6.10 Occupational Safety	940
6.11 Concomitant Medication/ Treatment	940
7 Outcomes Research and Pharmacoeconomics	941
7.1 Outcomes Measurement and Analysis	941
7.2 Economic Data Collection and Analysis	941

8 Adverse Events.	942
8.1 Eliciting and Documenting Adverse Events	942
8.1.1 Adverse Event Definition	942
8.1.2 Serious Adverse Event Definition	943
8.2 Recording of Adverse Events	945
8.2.1 Soliciting of Adverse Events	946
8.2.2 Evaluating the Adverse Event	946
8.3 Reporting and Recording of Serious Adverse Events.	947
8.3.1 Regulatory Responsibilities	947
8.3.2 Recording of Serious Adverse Events	947
8.3.3 Reporting Serious Adverse Events to SmithKline Beecham. . .	948
8.3.4 Follow- up of Serious Adverse Events	949
8.4 Overdose	950
8.4.1 Reporting of Overdose	950
8.4.2 Further Information on Overdose	950
8.5 Treatment Failures	951
8.6 Post- Study Events	951
8.7 Pregnancy	951
8.7.1 Reporting of Pregnancy.	952
8.7.2 Follow- up of Pregnancies.	952
8.7.3 Action Taken As A Result of Pregnancy	952
8.8 Unblinding Treatment Code	952
8.9 Investigator Letters	953
9 Patient Completion and Withdrawal	954
9.1 Definitions	954
9.2 Procedures for Handling Withdrawals.	954
9.3 Reasons for Withdrawal	955
10 Statistical Issues: Design and Analysis	956
10.1 Objectives	956
10.1.1 Primary Objective	956
10.1.2 Secondary Objectives	956
10.2 Hypotheses	956
10.3 Definition of Variables	956
10.3.1 Primary Variable(s).	956
10.3.2 Secondary Variable(s)	957
10.3.3 Other Variable(s)	958
10.4 Comparisons of Interest	959
10.4.1 Primary Comparisons of Interest.	959
10.4.2 Other Comparisons of Interest	959
10.5 Interim Analysis	959
10.6 Target Sample Size.	959
10.6.1 Sample Size Assumptions	959
10.6.2 Sample Size Sensitivity	960
10.6.3 Sample Size Re- estimation	960

10.7 Methods of Analysis	961
10.7.1 Populations of Interest.	961
10.7.2 Statistical Methods	962
10.7.3 Safety	964
11 Administrative Matters	966
12 References	967
13 Appendices	970

Abbreviations

AE	Adverse Experience
AUC	Area Under the Curve
BMI	Body Mass Index
CGI	Clinical global impression
CR	Controlled Release
CRF	Case Record Forms
DSM-IV	Diagnostic and Statistic Manual (version 4)
eCRF	Electronic Case Record Form
ERC	Ethics Review Committee
FDA	Food and Drug Administration (US)
GCP	Good Clinical Practice
5-HT	Serotonin (5-hydroxytryptamine)
IR	Immediate Release
IRB	Institutional Review Board
ISCO	International Standard Classification of Occupation
ITT	Intention to Treat
LOCF	Last Observation Carried Forward
MADRS	Montgomery Asberg Depression Rating Scale
MINI	Mini International Neuropsychiatric Interview
MSDS	Material Safety Data Sheet
NSAID	Non-Steroidal Anti Inflammatory Drug
OC	Observed Cases
PESM	Patient's evaluation of study medicine
PGE	Patient Global Evaluation
PID	Patient identification number
PMDD	Premenstrual dysphoric disorder
PMS	Premenstrual Syndrome
PMTS	Premenstrual tension scale
PP	Per Protocol
RDM	Remote Data Management
SAE	Serious adverse experience
SB RAMOS	SB Randomisation and Medication Order System
SDS	Sheehan Disability Scale
SSRI	Selective Serotonin Reuptake Inhibitor
VAS	Visual Analogue Scale
WPAI	Work Productivity and Activities Index

Definitions

Luteal Phase: is defined as the 14 days prior to the onset of continuous menstrual bleeding (*For the eligibility calculations and for efficacy assessment luteal phase = mean VAS symptom severity score for the last 5 days of the cycle*).

Follicular Phase: is defined as all days from day 1 of the cycle prior to the luteal phase (*For the eligibility calculations and for efficacy assessment follicular phase = mean VAS symptom severity score for days 6-10 of the cycle*).

First day of continuous menses/bleeding (not spotting) is defined as day 1 of the menstrual cycle.

Prior and Concomitant Medications include all medications, whether prescribed, non-prescribed or herbal.

Synopsis

Compound/Protocol No.

29060/717

Protocol Title

A double-blind, placebo-controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder.

Rationale

On the basis of the putative involvement of the neurotransmitter serotonin in the regulation of irritability/aggression, mood, and carbohydrate craving, there is reason to believe that antidepressant drugs facilitating serotonergic neurotransmission in the brain could be effective in reducing premenstrual complaints. This hypothesis has recently been confirmed in a considerable number of trials with the serotonin reuptake inhibitors clomipramine, paroxetine, fluoxetine, sertraline and citalopram. These compounds have all been shown to be superior to placebo in reducing premenstrual complaints.

The efficacy of paroxetine IR in reducing the symptoms of PMDD gains support from the results of three trials which have been published to date.

In most trials investigating the effect of serotonin reuptake inhibition in PMDD, the SSRI has been administered continuously throughout the menstrual cycle. Studies investigating the effect of continuous dosing with paroxetine CR in the treatment of PMDD are currently ongoing. However, several recent trials suggest that PMDD may also be effectively treated by administration of an SSRI intermittently, during luteal phases only. Thus, the objectives of the present trial are to compare the efficacy, safety and tolerability of intermittent dosing with paroxetine CR with those of placebo in the treatment of PMDD.

Objective(s)

Primary: To compare the efficacy of intermittent dosing with paroxetine CR (12.5mg and 25mg) with that of placebo for the treatment of PMDD. The

hypothesis to be tested is that paroxetine treatment results in a greater improvement in symptoms of PMDD compared with placebo treatment.

Secondary: To evaluate the safety and tolerability of intermittent dosing with paroxetine CR (12.5mg and 25mg) for the treatment of PMDD.

Study Population

Women fulfilling DSM-IV criteria A-C for PMDD at a screening visit will be asked to perform daily symptom rating for up to three consecutive menstrual cycles (reference cycles). Those who are confirmed as having PMDD according to DSM-IV (on the basis of their daily VAS ratings) during these reference cycles will be randomised into the double-blind treatment phase of the study. During this double-blind phase they will receive intermittent treatment for up to three menstrual cycles.

The study is designed to randomise 324 patients to start double-blind treatment in order to obtain at least 86 patients per group who will complete at least one treatment cycle. It is estimated that as few as 1:20 women who undergo an initial pre-screen will actually be randomised into the treatment cycles. Many of the patients who are initially contacted about the study or who perhaps have a telephone pre-screen will be clearly ineligible for the study (e.g. due to prohibited medications, concurrent illnesses). It is estimated that only 1:5 women who do have initial contact about the study will actually attend a screening visit and proceed to enter into the reference cycle phase of the study. Of these patients it is estimated that only 1:4 will actually be randomised into the double-blind treatment phase of the study.

Study Design

This is a double-blind, placebo-controlled, 3-arm parallel group study comparing intermittent dosing with paroxetine CR 12.5mg and paroxetine CR 25mg with placebo. The study duration will be up to three reference cycles (during the last of which single-blind placebo medication is administered) followed by three double-blind treatment cycles for each patient.

Safety Parameters

Vital Signs

Adverse Experiences

Laboratory Evaluation

Pregnancy Testing

Physical Examination & Medical/Surgical History

Indication

Premenstrual Dysphoric Disorder (PMDD)

Efficacy Parameters

Visual Analogue Scales (assessing the 11 PMDD symptoms from DSM-IV)

Clinical Global Impression (Global Improvement and Severity of Illness)

Premenstrual Tension Scale

Patient Global Evaluation

Patient Evaluation of Study Medication

Sheehan Disability Scale

Pharmacoeconomic Parameters

ISCO 88 classification of occupation

EuroQol

Work Productivity and Activities Index (WPAI)

Data Capture

This study will employ a remote data management system on a laptop computer to collect all of the information which the investigator would normally capture in a paper CRF. The system which will be used in this study is the SmithKline Beecham Research and Development Remote Data Management System (Version 1.1). The patient diary data will however be captured using paper diaries.

1 Introduction

PMDD is characterised by cyclically recurring premenstrual (luteal) phase mood, behavioural and somatic symptoms. These symptoms are not limited to the relatively mild and primarily physical symptoms such as bloating, breast tenderness, headache as well as minor mood changes seen in PMS, but include symptoms such as irritability, tension, dysphoria and affective lability which seriously interfere with the sufferer's social and occupational functioning. It has been noted that, in order to meet the DSM-IV definition of PMDD, the symptoms must be primarily psychological, cognitive or affective in nature (thus the predominant symptoms are depression, anxiety or irritability as opposed to breast swelling or tenderness, abnormal bloating, weight gain etc.)[5].

These symptoms typically occur during the last week of the luteal phase and begin to remit within a few days of the onset of menses. However, in severe cases, symptoms may begin around ovulation and continue for 2 weeks through the first few days of menses. It has been noted that, the symptoms are typically of comparable severity (though not duration) to those of a major depressive episode [4]. In order to meet the DSM-IV diagnosis the symptoms must cause an obvious and marked impairment in the ability to function socially or occupationally in the week prior to menses [4].

It is estimated that at least 75% of women report minor or isolated premenstrual changes [4]. While limited studies suggest an occurrence of "premenstrual syndrome" (variably defined) of 20-50% [4], only some 3-8% of women experience symptoms which may meet the criteria for Premenstrual Dysphoric disorder [5].

On the basis of the putative involvement of the neurotransmitter serotonin in the regulation of irritability/aggression, mood, and carbohydrate craving, there is reason to believe that antidepressant drugs facilitating serotonergic neurotransmission in the brain could be effective in reducing premenstrual complaints. This hypothesis has recently been confirmed in a considerable number of trials; thus, clomipramine [7] and the serotonin reuptake inhibitors (SSRIs) paroxetine [1], fluoxetine [6], sertraline [8], and citalopram [9] have all been shown superior to placebo in reducing premenstrual complaints. In contrast, antidepressant drugs with a noradrenergic profile appear considerably less effective [1]. That paroxetine IR reduces the symptoms of PMDD gains support from three studies published to date [1] [2] [3].

Paroxetine IR is a potent and selective SSRI that is currently registered worldwide for the treatment of depression, panic disorder, obsessive compulsive disorder and social anxiety disorder. To date there have been more than 70 million patient treatments with paroxetine IR worldwide.

The side effects of paroxetine IR are similar to those caused by the other SSRIs; most commonly reported are, nausea, headache, sweating, diarrhoea, somnolence, insomnia, dry mouth, nervousness and sexual dysfunction. Most of these side effects are mild; the symptoms are self limiting and usually require no medical intervention. Nevertheless, adverse events may result in reduced treatment compliance or discontinuation of therapy. Clinical trials in major depression have shown an incidence of withdrawal due to adverse events on paroxetine IR of 20% (1199/6145). The most common event associated with withdrawal on paroxetine IR was nausea (3.2%), whereas 1.1% of patients on placebo withdrew due to nausea.

The duodenum is known to have a high density of 5-HT₃ receptors and it is hypothesised that the nausea caused by paroxetine is due to an increase in 5-HT in peripheral duodenal synapses – the stimulation of 5-HT₃ receptors initiates transmission in a neural pathway leading to nausea. The nausea may then wane following a decline in the initial very high synaptic concentrations of 5-HT and down-regulation of 5-HT₃ receptors. Alteration to the absorption profile of paroxetine may result in improved tolerability, including a reduced incidence of nausea. Therefore a controlled release formulation of paroxetine (paroxetine CR) having both slow-release and delayed release characteristics was developed to reduce the frequency of adverse events associated with paroxetine IR.

Paroxetine CR was recently approved in the US for the treatment of Major Depressive Disorder. FDA approval for the treatment of Panic Disorder is pending. Studies investigating the effect of continuous dosing with paroxetine CR in the treatment of PMDD are currently ongoing.

The paroxetine CR doses chosen for the study in this protocol were based on a number of considerations. Previous studies with the SSRIs indicated that the effective dose for the treatment of PMDD appeared to be at the lower end of the effective dose range for depression. This finding was noted for paroxetine IR [3], fluoxetine [6] and clomipramine [7]. In addition, there appeared to be little rationale to study higher doses, Steiner et al [6] found that a study of fluoxetine 20mg, 60mg and placebo failed to demonstrate significant superiority for the 60mg dose over the 20mg dose. The higher dosage was however associated with a significantly higher incidence of side-effects (withdrawals due to side-effects

were 8/105, 11/102 and 35/106 for placebo, 20mg and 60mg respectively). Finally, the results of three paroxetine IR flexible dose studies have been published to date. While all allowed a flexible dose regimen (10-30mg/day), in all cases the results indicated that a relatively low dose was effective. The results from two of the studies showed that the mean paroxetine IR dose at study endpoint was 22mg/day [2] and 17.3mg/day [3], while the results from the third study showed that the majority of patients titrated to a 20mg/day dose [1].

In most trials investigating the effect of serotonin reuptake inhibition in PMDD, the SSRI has been administered continuously throughout the menstrual cycle. However several recent trials suggest that PMDD may be effectively treated by administration of an SSRI intermittently, during luteal phases only [9] [11] [12] [13] [14] [16] [21] [22] [SB data on file]. Thus, the onset of action of SSRIs appears to be much shorter when used for PMDD than when used for depression, panic disorder or obsessive compulsive disorder [19. PPD Development. December 2000. A placebo-controlled study to investigate the efficacy of intermittent and continuous treatment with paroxetine in patients with premenstrual dysphoric disorder (PMDD): Report of additional analyses 20].

The objectives of the present trial are to evaluate the efficacy and safety of intermittent treatment with paroxetine CR (12.5mg and 25mg) compared with that of placebo for the treatment of Premenstrual Dysphoric Disorder.

As described above, PMDD symptoms typically occur during the last week of the luteal phase and begin to remit within a few days of the onset of menses [4]. In some cases, symptoms may begin around ovulation and continue for 2 weeks through the first few days of menses. The intermittent dosing regime needs to take into account the relatively rapid onset of efficacy seen in PMDD [19. PPD Development. December 2000. A placebo-controlled study to investigate the efficacy of intermittent and continuous treatment with paroxetine in patients with premenstrual dysphoric disorder (PMDD): Report of additional analyses

20] and the duration over which PMDD symptoms may be experienced. Therefore patients will be instructed to start study medication when they estimate themselves to be 14 days prior to the onset of their next menstrual cycle (following discussion with the Investigator) and they will be instructed to stop study medication on the first day of menses. This methodology for intermittent dosing during the luteal phase only is consistent with other studies in this disease area [9] [11] [12] [13] [14] [16] [SB data on file].

Patient receiving intermittent treatment with sertraline did not report a high frequency of initial side effects each time they started medication; nor did they experience any marked discontinuation symptoms when stopping medication after the onset of menses [21] [22]. A similar pattern was also seen in a recent study of intermittent dosing with paroxetine IR in patients with PMDD [SB data on file].

Please refer to the Investigator Brochure for a review of the pre-clinical and clinical studies of paroxetine CR.

2 Objectives

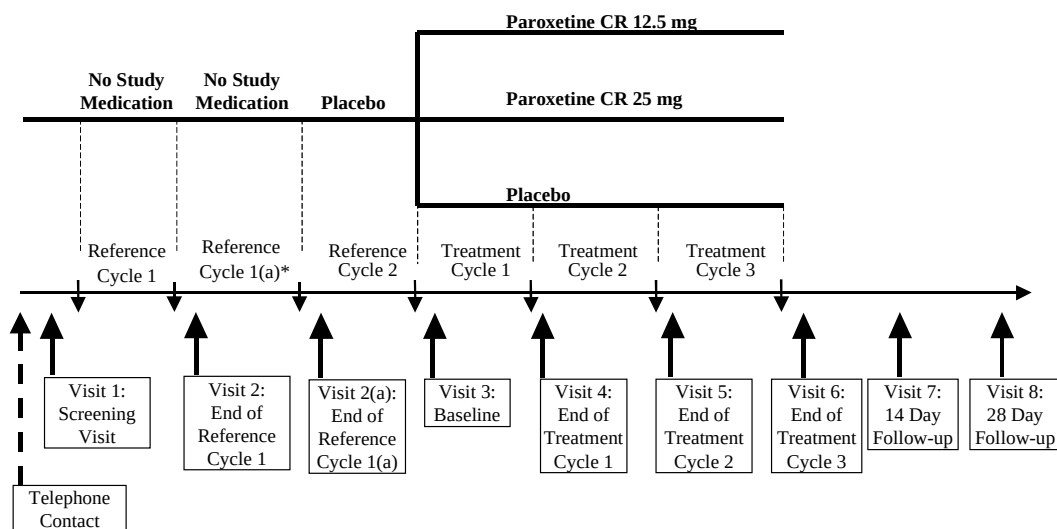
The primary objective of this study is to compare the efficacy of intermittent dosing with paroxetine CR (12.5mg and 25mg) with that of placebo for the treatment of PMDD. The hypothesis to be tested is that paroxetine treatment results in a greater improvement in symptoms of PMDD compared with placebo treatment.

The secondary objective of this study is to evaluate the safety and tolerability of intermittent dosing with paroxetine CR (12.5mg and 25mg) for the treatment of PMDD.

3 Study Design Overview

3.1 Study Design

Figure 1 Study Design



* = Patients who did not qualify for inclusion in the study on the basis of their reference cycle 1 diary scores may, at the discretion of the investigator, enter an optional reference cycle 1(a) rather than being withdrawn from the study.

Experimental Design: Double-blind, randomised, 3-arm, parallel group study.

Indication: Premenstrual Dysphoric Disorder

Blinding: The placebo medication taken during the final reference cycle (reference cycle 2) will be single-blind. The medication for the three treatment cycles of the study will be double-blind.

Control: Placebo Controlled.

Treatment Allocation: Randomised.

Randomisation: Equal Fixed Randomisation (1:1:1)(paroxetine CR 12.5mg: paroxetine CR 25mg: Placebo)

Duration of Washout and Active Treatment Phases: Patients are required to prospectively record their symptoms for up to three complete menstrual cycles in order to confirm the DSM-IV diagnosis of PMDD. During the last of these three

cycles patients will receive single-blind placebo medication. Patients who are randomised will then receive double-blind medication for a total of three "treatment cycles".

Dosage Instruction: Patients will be instructed to take one capsule each morning during the luteal phase (i.e. the last 14 days) of their menstrual cycle, i.e. study medication will start following ovulation (approximately 14 days prior to the expected time of next menses) and will continue until the first day of menses. Investigators are responsible for reviewing the details of each of their patients reference cycles and from this review they should provide their patients with clear instructions describing when they should start and stop taking their study medication. For example, a patient with an average cycle length of 30 days will be instructed to start their study medication on day 17 of their cycle and to stop taking study medication on the first day of menses. In addition, patients will receive written instructions on how and when to take the study medication.

Duration of Study: The anticipated study duration is 20 months in total from study start to last patient last visit.

Data Capture: This study will employ a remote data management system on a laptop computer to collect all of the information which the investigator would normally capture in a paper CRF. The system which will be used in this study is the SmithKline Beecham Research and Development Remote Data Management System (Version 1.1). The patient diary data will however be captured using paper diaries.

3.2 Schedule of Assessments

A full chart of study procedures at each clinic visit is included in [section 5.2](#).

3.3 Method of Randomization

The SB Randomisation and Medication Order System (SB RAMOS) will be used to allocate study medication to patients. After a patient has satisfied the inclusion and exclusion criteria, the investigator will access SB RAMOS by telephone to receive the patient's randomisation and study medication container number. Patients will be randomized to one of three treatments on a 1:1:1 ratio: paroxetine CR 12.5mg, paroxetine CR 25mg, placebo. To ensure balance with respect to the number of patients assigned to each treatment group, the allocation schedule will be generated in blocks using the SB Coding Memo System. All trial medications

will be packaged to be indistinguishable irrespective of treatment. All patients in the study will be tracked using a unique patient identification number (PID) which will be assigned at the start of the study. In addition, all randomised patients will have a distinct randomisation number which will remain the same throughout the study.

The master randomisation list will be held by the Sponsor.

4 Study Population

4.1 Planned Number of Patients

The statistical design for the protocol calls for 86 patients per treatment group evaluable for the primary VAS-MOOD response. Allowing for a 20% attrition rate after randomisation, 108 patients per treatment group are required to be randomised, a total of 324 patients overall. Enrolment will be stopped when the required number of patients have been randomised into the treatment cycles of the study.

It is anticipated that the study will be carried out in approximately 40 centres, and that each centre will randomise 1 patient/month into the study. Each centre should aim to randomise up to 18 patients into the treatment cycles of the study.

A high screening dropout rate is expected in the study. It is estimated that as few as 1:20 women who undergo an initial pre-screen will actually be randomised into the treatment cycles. Many of the patients who are initially contacted about the study or who perhaps have a telephone pre-screen will be clearly ineligible for the study (e.g. due to prohibited medications, concurrent illnesses). It is estimated that only 1:5 women who do have initial contact about the study will actually attend a screening visit and proceed to enter into the reference cycle phase of the study. Of these patients it is estimated that only 1:4 will actually be randomised into the double-blind treatment phase of the study.

All data including copies of the patient diaries will be collected for patients withdrawn prior to randomisation. Relevant data which is entered onto the RDM system (including the reason for withdrawal) will be collected, cleaned and databased by SB. Copies of the patient diaries will be collected by SB for patients withdrawn prior to randomisation, **but the original copies of these diaries must be retained as source documents in the investigator's files.**

A telephone screening log must be maintained to document all patients who made the telephone screening contact, regardless of whether they came to the clinic for further assessment or were excluded at that point. The following data needs to be captured in the telephone screening log as a minimum; Initials, Screening Date, whether or not they were included (i.e. scheduled to come to the clinic for visit 1) and the reason for exclusion (if appropriate). **Please remember to complete the details in this log for those patients who attend clinic visit 1**

but withdraw prior to giving informed consent and conducting any study related procedures.

4.2 Inclusion Criteria

- Female outpatients who must be between 18–45 years of age.
- Patients must have regular menstrual cycles (duration between 22-35 days).
- Patients must meet DSM-IV criteria for PMDD (Criteria A-C to be fulfilled at visit 1 screening interview and criterion D in the two reference cycles).
- The condition should have been present for at least the past year during which symptoms were present in at least 9 out of 12 menstrual cycles (checked at visit 1).
- During two consecutive reference cycles the patient must rate at least 200% higher (i.e. worse) on one, or at least 100% higher on two or more, of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ([\text{mean luteal score} - \text{mean follicular score}] / \text{mean follicular score})$). For these items the mean follicular phase score must be ≤ 20 mm and the mean luteal phase score must be ≥ 40 mm. Patients do not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores should also be low and SB must be consulted prior to inclusion of a patient if these scores are not ≤ 25 mm.
- The patient must have a baseline (Visit 3) Clinical Global Impression severity of illness score of ≥ 3 .
- The patient must, in the investigator's opinion, be using an adequate **non-hormonal** form of contraception. Thus, methods such as IUD, tubal ligation and double-barrier contraception (any two of diaphragm / spermicidal foam / condom) are acceptable while the use of oral contraceptives or systemic contraception are not.
- The patient must have given written informed consent to participate in the study.

4.3 Exclusion Criteria

- Patients who fulfil DSM-IV criteria for any Axis 1 disorder (other than PMDD or specific phobias) in the 6 months prior to screening.
- Patients with severe, clinically significant, co-existing conditions which, in the investigator's opinion, would render the patient unsuitable for the study.
- Patients with diagnosed and clinically significant gynaecological disease (e.g. clinically significant uterine fibroids, ovarian / uterine / cervical carcinoma, or endometriosis).
- Patients with a screening MADRS score of ≥ 10 **during the follicular phase** of the menstrual cycle at Visit 1.
- Patients for whom there is a significant risk of suicide.
- Any ongoing medication (including herbal medication and **any** use of sedatives/hypnotics) which in the opinion of the investigator could affect the patient's PMDD symptomatology (within one month prior to the screening visit and for the duration of the study period) except the following permitted treatments. Permitted medications include the occasional use of fibrinolysis inhibitors for abundant menstrual bleeding. Also permitted are the **occasional** use of paracetamol (acetaminophen), acetylsalicylic acid or other NSAIDs to treat menstrual cramps or headaches (their use **must** be documented in the concomitant medication section).
- Any previous adequate treatment with an SSRI for premenstrual symptoms (defined as continuous or intermittent treatment for at least 3 consecutive menstrual cycles on an adequate dose equivalent to Prozac 20mg).
- History of hypersensitivity or adverse reaction to paroxetine or other SSRIs.
- Any previous participation in a psychiatric drug trial (including PMDD trials) in the past 6 months.
- Patients who are breast-feeding, pregnant or planning to become pregnant during the study period.
- Patients with any clinically significant abnormality in screening laboratory tests.

- Use of an investigational drug within 30 days or 5 half-lives (whichever is longer) prior to the screening visit (visit 1).
- Patient characteristics which, in the opinion of the investigator, are likely to reduce compliance with the protocol (e.g. poor medication compliance, poor diary card compliance).

5 Conduct of the Study

5.1 Ethical and Regulatory Considerations

The study will be conducted according to Good Clinical Practice guidelines and the Declaration of Helsinki, as amended (Protocol [Appendix A](#)) and US 21 CFR Part 50-Protection of Human Subjects, and Part 56 - Institutional Review Boards.

5.1.1 Ethics Review Committee (ERC)/Institutional Review Board (IRB)

ERCs/IRBs must be constituted according to the local laws/customs of each participating country.

This protocol will be submitted to an appropriate Committee or Board and their written unconditional approval obtained and submitted to the sponsor before commencement of the study. SB will supply relevant data for the investigator to submit to the hospital/university/independent ERC/IRB for the protocol's review and approval. Verification of the ERC/IRB's unconditional approval of the protocol and either the written informed consent statement or oral witnessed consent form with written information to be given to the patients will be transmitted to the SB Study Monitor prior to shipment of drug supplies and CRFs to the site. This approval must refer to the study by exact protocol title and number, identify the documents reviewed and state the date of review.

The ERC/IRB must be informed by the investigator of all subsequent protocol amendments and of serious or unexpected adverse experiences occurring during the study which are likely to affect the safety of the patients or the conduct of the study. Approval for such changes must be transmitted in writing to the SB Study Monitor via the investigator.

5.1.2 Informed Consent

The principles of informed consent in the current edition of the Declaration of Helsinki (Protocol [Appendix A](#)) should be implemented in each clinical study before protocol-specified procedures are carried out.

Informed consent will be obtained in accordance with 21 CFR 50.25.

Information should be given in both oral and written form whenever possible and deemed appropriate by the ERC/IRB. Patients, their relatives, guardians or, if

necessary, legal representatives must be given ample opportunity to enquire about details of the study.

The consent form generated by the investigator with the assistance of SB, must be approved (along with the protocol) by the ERC/IRB and be acceptable to SB. Consent forms must be in a language fully comprehensible to the prospective patient. Informed consent shall be documented by the use of a written consent form approved by the ERC/IRB and signed by the patient or the patient's legally authorised representative.

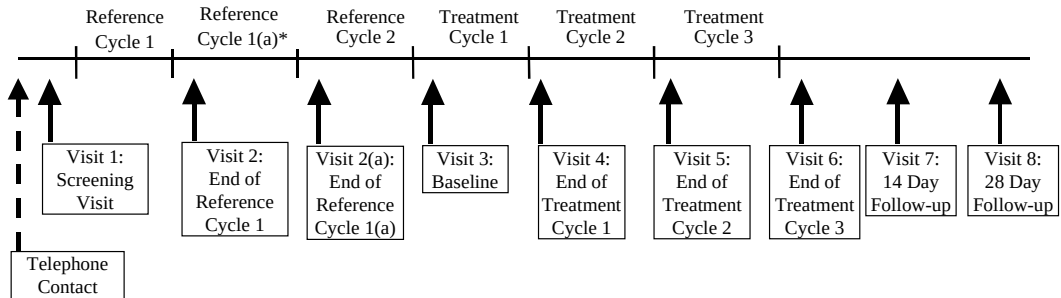
The written consent document will embody the elements of informed consent as described in the Declaration of Helsinki and will also comply with local regulations. This form may be read to the patient or the patient's legally authorised representative, but, in any event, the investigator shall give either the patient or the representative adequate opportunity to read it before it is signed.

Consent must be documented either by the dated signature of the patient or the patient's legally authorised representative. The signature confirms that the consent is based on information that has been understood. Each patient's signed informed consent form must be kept on file by the investigator for possible inspection by Regulatory Authorities and/or SB professional and Regulatory Compliance persons.

A sample patient information sheet and informed consent form for this study can be found in Protocol [Appendix C](#).

5.2 Outline of Study Procedures

An outline of the study visits and of the specific procedures to be carried out at each visit is provided in the following figure and table. Full details of the procedures to be carried out at each visit are provided in the following section (see [5.3 Detailed Description of Study Stages/Visits](#)).

Figure 2 Study Schematic

* = Patients who did not qualify for inclusion in the study on the basis of their reference cycle 1 diary scores may, at the discretion of the investigator, enter an optional reference cycle 1(a) rather than being withdrawn from the study.

	Screening	\$ End of Reference Cycle 1	End of Reference Cycle 1(A)	Baseline
	(Visit 1)	(Visit 2)	(Visit 2(A))	(Visit 3)
Informed Consent	✓			
Demographic Data	✓			
Vital Signs	✓	✓	✓	✓
Prior & Con. Med	✓	✓	✓	✓
Med. Surg. History	✓			
Physical Exam.	✓			
DSM-IV Criteria	✓**	✓**	✓**	✓**
MADRS	✓			
Incl / Excl Criteria	✓			✓
Dispense Diaries***	✓	✓*	✓	✓
Collect Diaries		✓	✓	✓
Con. Med.				
Adverse Experiences		✓	✓	✓
Obs/Gyne History			✓	
PMDD History			✓	
PMDD TXT History			✓	
Psychiatric History			✓	
Pregnancy Test			✓	
Lab. Evaluation			✓	
Dispense Medication			✓	✓
Collect Medication				✓
CGI				✓
PGE (Prompt)				✓
SDS (Prompt)				✓
PMTS-O				✓
PESM				
ISCO 88				✓
EuroQol (Prompt)				✓
WPAI (Prompt)				✓
Study Conclusion				

	End of Treatment Cycle 1 (Visit 4)	End of Treatment Cycle 2 (Visit 5)	End of Treatment Cycle 3 (Visit 6)	14 Day Follow- Up ### (Visit 7)	28 Day Follow- Up ### (Visit 8)	Early Withdrawal Visit ###
Informed Consent						
Demographic Data						
Vital Signs	✓	✓	✓	✓	✓	✓
Prior & Con. Med						
Med. Surg. History						
Physical Exam.			✓			✓
DSM-IV Criteria						
MADRS						
Incl / Excl Criteria						
Dispense Diaries***	✓					
Collect Diaries	✓	✓	✓			✓
Con. Med.	✓	✓	✓	✓	✓	✓
Adverse Experiences	✓	✓	✓	✓	✓	✓
Obs/Gyne History						
PMDD History						
PMDD TXT History						
Psychiatric History						
Pregnancy Test			✓			✓
Lab. Evaluation			✓	✓##		✓
Dispense Medication						
Collect Medication	✓	✓	✓			✓
CGI	✓	✓	✓			✓
PGE (Prompt)	✓	✓	✓			✓
SDS (Prompt)	✓	✓	✓			
PMTS-O	✓	✓	✓			
PESM			✓			✓
ISCO 88						
EuroQol (Prompt)	✓	✓	✓			✓
WPAI (Prompt)	✓	✓	✓			
Study Conclusion				✓#	✓#	

* Only if additional reference cycle required.

** Provisional diagnosis of PMDD (On Criteria A-C) will be checked at screening (Visit 1).

Confirmation of "on-offness" according to the VAS scores will be checked during the reference cycles and confirmation of the diagnosis will be made at Baseline.

*** The nomenclature used for the patient diaries will be as follows: Study Cycle 1, Study Cycle 1a, Study Cycle 2, Study Cycle 3, Study Cycle 4 & Study Cycle 5. This will prevent the patients deducing whether a particular diary is for a "reference cycle" or for a "treatment cycle".

(see [Appendix E](#)).

Study conclusion should be completed at 14 day follow-up, except for patients who required repeat labs or had ongoing AEs for whom it should be completed at 28 Day Follow-up.

Only where repeat labs are required.

For randomised patients only.

\$ Patients who are eligible on the basis of their reference cycle 1 VAS scores do not need to complete reference cycle 1(a). Thus they will not complete the Visit 2 assessments at the end of reference cycle 1 but will instead go on to complete the Visit 2(a) assessments.

5.3 Detailed Description of Study Stages/Visits

The DSM-IV diagnosis of PMDD requires that prospective daily rating of the patient's symptoms must be carried out over at least two consecutive symptomatic cycles in order to confirm the diagnosis. The need for these "reference cycles" in order to confirm the diagnosis means that the patient is not randomised into the "treatment cycles" of the study until daily symptom ratings have been carried out for two to three* (*an optional third reference cycle may be allowed, see details below) complete menstrual cycles.

The VAS entry criteria stipulate that during two consecutive reference cycles the patient must rate at least 200% higher (i.e. worse) on one, or at least 100% higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score ($\% \text{ worsening} = 100 \times ([\text{mean luteal score} - \text{mean follicular score}] / \text{mean follicular score})$). For these items the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$. Patients do not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores should also be low and SB must be consulted prior to inclusion of a patient if these scores are not $\leq 25\text{mm}$.

To assist with the assessment of the VAS entry criteria for the study, patient eligibility calculation worksheets will be provided (see [Appendix D](#)).

In this study, patients who fail to meet the VAS entry criteria during the first reference cycle (reference cycle 1) may, at the investigator's discretion, enter an additional reference cycle 1(a) rather than being excluded from the study at this point. This would apply where the investigator felt that the patient should probably qualify on the VAS scores although they failed to do so in the first reference cycle (e.g. scores just outside the entry criteria or unusual circumstances which caused an elevated follicular phase score). The DSM-IV criteria for PMDD stipulate that the patients must qualify on **two consecutive symptomatic cycles**. Various scenarios to clarify when a patient would be eligible for the study or excluded are provided in the following table.

Table 1 Patient eligibility for inclusion in the study based on reference cycle VAS scores

Reference Cycle 1	Reference Cycle 1(a)	Reference Cycle 2	Decision
Eligible	-	Eligible	Randomise
Eligible	-	Not Eligible	Exclude
Not Eligible	Eligible	Eligible	Randomise
Not Eligible	Eligible	Not Eligible	Exclude
Not Eligible	Not Eligible	-	Exclude

Single-blind placebo medication shall be administered to all patients during reference cycle 2.

A high screening dropout rate is expected in the study. It is estimated that as few as 1:20 women who undergo an initial pre-screen will actually be randomised into the treatment cycles. Many of the patients who are initially contacted about the study or who perhaps have a telephone pre-screen will be clearly ineligible for the study. It is estimated that only 1:5 women who do have initial contact about the study will actually attend a screening visit and proceed to enter into the reference cycle phase of the study. Of these patients it is estimated that only 1:4 will actually be randomised into the double-blind treatment phase of the study.

Although an initial telephone pre-screening contact should eliminate many patients who are not eligible due to basic exclusions (e.g. prohibited medications, concurrent illnesses) and more who attend the first clinic visit are expected not to continue into the study, further patients will be excluded during the reference cycles. As it is anticipated that a significant number of patients will be excluded on the basis of non-eligibility on the VAS scores, most of the screening assessments are thus carried out only after patients have been shown to qualify on the VAS scores for one complete reference cycle.

Full details of the visit specific study procedures are provided on the following pages.

Advertising/Telephone Pre-screening

In order to recruit the required number of patients at each centre, many more will need to be screened. Thus, the use of advertisement and telephone pre-screening of patients should be considered where possible. SB can make available suggested advertising text to any centres who require this. Also a standard telephone pre-screening questionnaire for use in the study is available. Please note that both advertising material and telephone screening forms need IRB approval.

NB. A telephone screening log must be maintained to document all patients who made the telephone screening contact, regardless of whether they came to the clinic for further assessment or were excluded at that point. The following data needs to be captured in the telephone screening log as a minimum; Initials, Screening Date, Whether or not they were included (i.e. scheduled to come to the clinic for visit 1) and the reason for exclusion (if appropriate). **Please remember to complete the details in this log for those patients who attend clinic visit 1 but withdraw prior to giving informed consent and conducting any study related procedures.**

Visit 1 : Screening

Visit 1 should be scheduled **in the follicular phase** prior to Reference Cycle 1 (When the patient begins to prospectively record her PMDD symptoms). It should be scheduled to occur at least 7 days after premenstrual symptoms from the previous cycle have ended. It is recognised that in some women with short menstrual cycles this may mean scheduling this visit at the start of the luteal phase. **The critical point to ensure is that this visit must occur when the patient is free of PMDD symptoms.**

The following assessments will be performed at the screening visit and recorded in the eCRF. Written informed consent will be obtained for all patients before any study specific procedures are carried out.

- Informed Consent
- Demographic data
- Vital Signs (height, weight, sitting blood pressure and pulse)
- Prior and Concomitant medication (includes any medication which the patient has taken in the past month) (N.B. All concomitant medication, including prescribed medication, non-prescribed medication and herbal medication must be recorded).
- Medical/Surgical History
- Physical Examination
- Check DSM-IV criteria A-C for PMDD
- Montgomery Asberg Depression Rating Scale (MADRS interview) [**Note:** the Screening Visit must be scheduled so that this MADRS interview is conducted at a time when the patient is expected to be free of PMDD symptoms].
- Screening inclusion/exclusion criteria
- Dispense patient diaries for Reference Cycles 1 & 2 (if patient eligible). Note that these patient diaries will refer to Study Cycle 1 and Study Cycle 2 – this nomenclature prevents the patient deducing that these diaries are for "reference cycles". Instruct the patient that **RATING SCALES SHOULD BE**

COMPLETED EACH EVENING BEFORE GOING TO BED. Patients will be assigned a patient number when they are given their diaries.

PATIENTS WILL BE INSTRUCTED TO START RECORDING THEIR SYMPTOMS ON THE VISUAL ANALOGUE SCALES (VAS) (FOR REFERENCE CYCLE 1) ON THE FIRST DAY OF CONTINUOUS MENSES/BLEEDING (NOT SPOTTING) IN THEIR FORTHCOMING MENSTRUAL CYCLE.

Patients will be asked to switch to the second diary at the first day of continuous menses/bleeding (not spotting) during the next menstrual cycle (Reference Cycle 1(a) or 2).

An appointment will be made with the patient to return for their next clinic visit between days 1-3 of the next menstrual cycle (Reference Cycle 1(a) or 2). The completed Reference Cycle 1 diary card will be taken to the clinic at this visit and reviewed with the investigator.

Patients who are not eligible at Visit 1 will be informed that they cannot participate in the trial and advised as to where to turn to in order to get further help.

Visit 2: End of Reference Cycle 1

When the patient returns for their next clinic appointment, the completed reference cycle 1 diary will be reviewed with the investigator. The patient may or may not qualify for inclusion in the study on the basis of their reference cycle 1 VAS scores (see [Table 1](#) Patient eligibility for inclusion in the study based on reference cycle VAS scores).

For patients who are eligible for inclusion in the study on the basis of their reference cycle 1 VAS scores, follow the procedures under visit 2(a) overleaf.

- For patients who are not eligible for inclusion in the study on the basis of their reference cycle 1 VAS scores, the following procedures must be carried out.
 - Vital Signs (sitting blood pressure and pulse)
 - Prior and Concomitant medication
 - Baseline Adverse Experiences

In addition, there are two options for ineligible patients.

- a) These patients may be excluded from the study and asked to return their diary cards; they will be advised as to where to turn in order to get help for their premenstrual complaints.
- b) At the discretion of the investigator, the patient may be asked to complete an additional reference cycle (Reference cycle 1(a)). An additional reference diary is dispensed to the patient and an appointment made to return for their next clinic visit (Visit 2(a)) between days 1-3 of the next menstrual cycle.). Note that this patient diary will refer to Study Cycle 1a – this nomenclature prevents the patient deducing that this diary is for a "reference cycle".

Visit 2(a): End of Reference Cycle 1(a)

Visit 2(a) will take place in the follicular phase (between Days 1-3) of reference cycle 2. The following assessments will be performed at this visit and recorded in the eCRF.

- Review reference cycle 1 (or reference cycle 1(a)) diary for eligibility, the patient may either be excluded from the study on the basis of these data or proceed into reference cycle 2. (see [Table 1](#) Patient eligibility for inclusion in the study based on reference cycle VAS scores).
- Vital Signs (sitting blood pressure and pulse) (regardless of patient eligibility)
- Prior and Concomitant medication (regardless of patient eligibility)
- Baseline Adverse Experiences (regardless of patient eligibility)
- Obstetrics/Gynaecological history
- History of PMDD
- Previous treatment for PMDD
- Full Psychiatric History (including MINI interview)
- Serum pregnancy test
- Laboratory Evaluation (haematology, clinical chemistry)
- Dispense placebo medication for reference cycle 2. The patient will receive oral and written instructions on how to take the medication
- Dispense patient diary for Treatment Cycle 1. Note that this patient diary will refer to Study Cycle 3 – this nomenclature prevents the patient deducing that this diary is for a "treatment cycle".
- An appointment will be made with the patient to return for their next clinic visit between days 1-3 of the next menstrual cycle (Treatment Cycle 1). The completed Reference Cycle 2 diary card will be taken to the clinic at this visit and reviewed with the investigator.

Patients who are not eligible for the study will be informed that they cannot participate in the trial and advised as to where to turn to in order to get further help.

Visit 3 : Baseline

Visit 3 will take place in the follicular phase (between Days 1-3) of treatment cycle 1.

- Review reference cycle 2 diary for eligibility, the patient may either be excluded from the study on the basis of these data or proceed into treatment cycle 1. (see [Table 1](#) Patient eligibility for inclusion in the study based on reference cycle VAS scores).
- Collect any unused placebo run-in medication; check medication compliance and complete study medication record page.
- Vital Signs (sitting blood pressure and pulse)(regardless of patient eligibility)
- Body Weight
- Prior and concomitant medications (regardless of patient eligibility)
- Baseline Adverse Experiences (regardless of patient eligibility)
- Check results from laboratory assessments (regardless of patient eligibility)
- Clinical Global Impression (Severity of Illness) (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Premenstrual Tension Scale (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Patient Global Evaluation (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Sheehan Disability Scale (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for EuroQol (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for WPAI (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Complete ISCO 88

- Baseline Inclusion/Exclusion criteria
- Trial medication for treatment cycles 1-3 will be dispensed and the patient will receive oral and written instructions on how to take the medication.
- Dispense patient diary for Treatment Cycle 2. Note that this patient diary will refer to Study Cycle 4 – this nomenclature prevents the patient deducing that this diary is for a "treatment cycle".
- An appointment will be made with the patient to return for their next clinic visit between days 1-3 of the next menstrual cycle (Treatment Cycle 2). The patient will be reminded to bring the completed diary for treatment cycle 1 to the clinic at this visit.

Visit 4 : End of treatment cycle 1

Visit 4 will take place in the **follicular phase (between Days 1-3)** of treatment cycle 2.

- Collect and review treatment cycle 1 diary.
- Collect any unused treatment cycle 1 medication, check medication compliance and complete study medication record page.
- Vital Signs (sitting blood pressure and pulse)
- Concomitant medications
- Adverse Experiences
- Clinical Global Impression (Global Improvement and Severity of Illness) (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Premenstrual Tension Scale (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Patient Global Evaluation (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Sheehan Disability Scale (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for EuroQol (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for WPAI (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Dispense patient diary for Treatment Cycle 3. Note that this patient diary will refer to Study Cycle 5 – this nomenclature prevents the patient deducing that this diary is for a "treatment cycle".
- An appointment will be made with the patient to return for their next clinic visit between days 1-3 of the next menstrual cycle (Treatment Cycle 3). The patient will be reminded to bring the completed diary for treatment cycle 2 to the clinic at this visit.

Visit 5: End of treatment cycle 2

Visit 5 will take place in the follicular phase (between Days 1-3) of treatment cycle 3.

- Collect and review treatment cycle 2 diary.
- Collect any unused treatment cycle 2 medication, check medication compliance and complete study medication record page.
- Vital Signs (sitting blood pressure and pulse)
- Concomitant medications
- Adverse Experiences
- Clinical Global Impression (Global Improvement and Severity of Illness) (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Premenstrual Tension Scale (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Patient Global Evaluation (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Sheehan Disability Scale (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for EuroQol (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for WPAI (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- An appointment will be made with the patient to return for their next clinic visit between days 1-3 of the next menstrual cycle. The patient will be reminded to bring the completed diary for treatment cycle 3 to the clinic at this visit.

Visit 6 : End of treatment cycle 3

The end of treatment visit will take place in the follicular phase (between Days 1-3) of the next menstrual cycle immediately following treatment cycle 3.

- Collect and review treatment cycle 3 diary.
- Collect any unused treatment cycle 3 medication, check medication compliance and complete study medication record page.
- Vital Signs (sitting blood pressure and pulse)
- Body Weight
- Concomitant medications
- Adverse Experiences
- Clinical Global Impression (Global Improvement and Severity of Illness) (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Premenstrual Tension Scale (Observer rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Patient Global Evaluation (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for Sheehan Disability Scale (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for EuroQol (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Prompt for WPAI (Patient Rated) [**Note:** this rating refers to the symptomatic luteal phase which has just ended]
- Patient Evaluation of Study Medication (Observer rated)
- Serum pregnancy test
- Laboratory Evaluation (haematology, clinical chemistry)

- Physical Examination
- Make an appointment for a follow-up visit within the next 14 days

Visit 7: 14-day follow-up (randomised patients only)

This follow up visit should take place within 14 days of stopping randomised study medication.

- Vital Signs (sitting blood pressure and pulse)
- Adverse Experiences
- Concomitant medication
- Check results from laboratory assessments (repeat if necessary)
- A further 28-day follow up visit should be arranged for any patients who still have ongoing Adverse Experiences or unresolved laboratory values at this visit.
- Study Conclusion page (if not attending 28-day follow-up visit)

The patient will be advised as to where to turn to in order to get further help.

Visit 8: 28-day follow-up (randomised patients only)

This follow up visit should take place within 28 days of stopping study medication.

- Vital Signs (sitting blood pressure and pulse)
- Adverse Experiences
- Concomitant medication
- Check results from laboratory assessments (if repeat labs were carried out at 14-day follow-up)
- Study Conclusion page

The patient will be advised as to where to turn to in order to get further help.

Early Withdrawal visit (randomised patients only):

In the event of an early withdrawal (randomised patients only), a clinic visit will be scheduled as soon as possible and the following procedures will be carried out.

- Collect and review any outstanding patient diaries.
- Collect any unused medication and check compliance.
- Vital Signs (sitting blood pressure and pulse)
- Body Weight
- Concomitant medications
- Adverse Experiences
- Clinical Global Impression (Global Improvement and Severity of Illness) (Observer rated) [**Note:** this rating refers to the most recently ended symptomatic luteal phase]
- Patient Global Evaluation (Patient Rated) [**Note:** this rating refers to the most recently ended symptomatic luteal phase]
- Patient evaluation of study medication (Observer Rated) [**Note:** this rating refers to the most recently ended symptomatic luteal phase]
- Prompt for EuroQol (Patient Rated) [**Note:** this rating refers to the most recently ended symptomatic luteal phase]
- Serum pregnancy test
- Laboratory Evaluation (haematology, clinical chemistry)
- Physical Examination
- Make an appointment for a follow-up visit within the next 14 days.

5.4 Laboratory Parameters

All laboratory assessments will be carried out centrally by Quest Diagnostics Ltd.. The following haematological and clinical chemistry parameters will be assessed at visit 2(a) (End of Reference Cycle 1(a)), and at visit 6 (End of Treatment Cycle 3) or at the early withdrawal visit if a patient is withdrawn early from the study. Serum pregnancy tests will also be conducted at these timepoints.

- Haematology - Haemoglobin, Haematocrit (PCV), RBCs, total and differential white blood cell counts, platelets.
- Clinical Chemistry-Urea, creatinine, total bilirubin, alkaline phosphatase, SGPT (ALT), SGOT (AST), total protein, globulin and albumin.
- Serum Pregnancy Test
- Thyroid function tests (TSH, FT3, FT4) will also be conducted at visit 2(a) (End of Reference Cycle 1(a)) only.

Laboratory assessments should be repeated if clinically significant abnormalities are detected and followed up until resolved or stabilised. However, for any patient with a positive pregnancy test, the patient should be withdrawn from the study immediately (this does not apply if the pregnancy test was at visit 6 or early withdrawal in which case the patient would already have stopped taking study medication) and the test should not be repeated.

Clinically significant abnormalities in laboratory parameters should be recorded as adverse experiences. Positive pregnancy tests should be reported as serious adverse experiences (see [Sections 8.1.2](#) and [Section 8.7](#)).

6 Study Medication and Administration

6.1 Study Medication

Matched placebo will be identical in external appearance to medication containing over-encapsulated enteric-coated controlled release tablets containing paroxetine 12.5mg and 25 mg. Both active and placebo paroxetine CR will be provided as Supro B capsules comprising an opaque Swedish orange body and cap.

6.2 Dosage and Administration

Patients will be instructed to take one capsule each morning during the luteal phase (i.e. last 14 days) of their menstrual cycle. Thus, study medication will start approximately 14 days prior to the expected time of next menses and will continue until the first day of menses. During the rest of the menstrual cycle the patients will not take study medication.

During the final reference cycle (Reference Cycle 2) patients will receive single blind placebo medication during the luteal phase (i.e. last 14 days) of their menstrual cycle.

Investigators are responsible for reviewing the details of each of their patients reference cycles and from this review they should provide their patients with clear instructions describing when they should start and stop taking their study medication. For example, a patient with an average cycle length of 30 days will be instructed to start their study medication on day 17 of their cycle and to stop taking study medication on the first day of menses. In addition, patients will receive written instructions on how and when to take the study medication.

The medication during the three treatment cycles (Treatment Cycles 1, 2 and 3) will be double-blind. Each patient will be randomised to receive either 12.5mg paroxetine CR or 25mg paroxetine CR or placebo throughout the three treatment cycles.

6.3 Blinding

Active paroxetine CR and placebo capsules will be identical in appearance and all packaging will maintain the double-blind nature of the study for the treatment cycles.

All centres will be supplied with an initial supply of the single-blind medication for Reference Cycle 2.

Each patient will be randomised to one of the three treatment arms by the SB Randomisation and Medication Ordering System (SB RAMOS). The investigator will phone into this system to register the patient at the start of single-blind medication. A randomisation number and a container number will be issued when the patient is randomised at the start of the double-blind phase of the study, which will determine which patient pack will be dispensed. The blinded status of the SB monitors, investigators, and patient shall be maintained at all times. Complete details will be supplied at the time of study initiation.

6.3.1 Code Breaking

For supplies to North American sites:

Each of the three individual bottles for the double-blind supply will have a three panel label attached to the outside of the bottle, of which one of the three panels has the disclosure panel. In order to unblind a patient treatment an alcohol wipe is needed to remove the black protective ink. SmithKline Beecham must be notified of any case of code-breaking.

For supplies to non-North American sites:

Individual patient code breaks will be provided to the investigator and the study monitor. These will contain the container number and the treatment allocation. In order to unblind a patient treatment the disclosure panel must be scratched with a coin. SmithKline Beecham Clinical Research and Product Development will hold a copy of the master randomisation code. These are provided for use in emergency situations only. All opened and unopened envelopes must be returned to SmithKline Beecham at the end of the study. SmithKline Beecham must be notified of any case of code-breaking.

6.4 Packaging

All study medication will be provided in 60cc white opaque high density polyethylene (HDPE) bottles with 33mm white, opaque, plastic, child-resistant caps with coated polyester film bonded aluminium foil inner seal.

6.4.1 Reference Cycle 2

The single-blind medication for the final reference cycle (Reference Cycle 2) will be supplied as one bottle containing 24 days medication. This bottle will be packed separately from the double-blind treatment.

6.4.2 Treatment Cycles (Treatment Cycle 1 ,2, 3)

The double-blind medication for each of the three treatment cycles (Treatment Cycle 1, 2 and 3) will be supplied in bottles each containing 24 days medication.

Each patient will receive three bottles contained in a carton which will comprise the double-blind patient pack

Patients will be instructed to return the carton containing all three bottles at each visit.

6.5 Labelling and Preparation

For supplies to North American sites:

The individual bottle which comprises the single-blind treatment (Reference Cycle 2) will be labelled with a two panel tear-off label.

Each of the three individual bottles which comprise double-blind treatment (Treatment Cycle 1, 2, 3) will be labelled with a three panel tear-off label. The left panel is permanently affixed to each bottle and will contain the following information:

- Protocol Number
- Job Number (only the single-blind medication).
- Container Number (except for the single-blind placebo medication)
- Contents i.e.: i.e. quantity and description of dose form
- Treatment period (i.e. Study Cycle:)
- Dosage Directions
- Storage instructions

- "Keep out of reach of children"
- Investigational drug statement
- Sponsor address
- Any other information required by the regulatory authorities in the participating countries

The second and third panels make up the tear-off portion of the label. The second panel contains the blinded disclosure and the third panel contains the container number, protocol number, and fill count along with instructions for the investigator to remove and keep this portion of the label. The tear-off portion should be affixed to the workbook at the time the medication is dispensed.

The three bottles will be presented in a carton which will be labelled with a single-panel label. The label text will contain the following information:

- Protocol Number
- Container Number
- Contents, i.e. number of bottles and fill count
- Storage instructions
- "Keep out of reach of children"
- Investigational drug statement
- Sponsor address
- Any other information required by the regulatory authorities in the participating countries

For supplies to non-North American sites:

The individual bottle which comprises the single-blind treatment for the final reference cycle (Reference Cycle 2) will be labelled with two labels i.e. a tear-off label and a multi-language re-closable booklet label which will be affixed to the opposite face of the bottle.

Each of the three individual bottles which comprise the double-blind treatment (Treatment Cycle 1, 2, 3) will be labelled with two labels i.e. a with a plain white label and a multi-language re-closable booklet label which will be affixed to the opposite face of each bottle.

The three bottles will be presented in a carton which will also be labelled with two labels i.e. a tear-off label and a multi-language re-closable booklet label which will be affixed to the opposite face of each carton.

The label text will contain the following information:

- Protocol Number
- Job Number
- Container Number (except for single-blind placebo medication)
- Contents i.e.: i.e. quantity and description of dose form
- Treatment period (i.e. Study Cycle:)
- Dosage Directions
- Storage instructions
- "Keep out of reach of children"
- "FOR CLINICAL TRIAL USE ONLY"
- Sponsor address
- Any other information required by the regulatory authorities in the participating countries

NB (For All Sites): The investigator will be required to write the study cycle number (i.e. 3, 4, and 5) in the space provided on the main label applied to each

of the three bottles of study medication i.e. SC: 3, SC: 4, SC: 5) prior to dispensing the carton containing the three bottles to the patient.

6.6 Storage

The study medication should be stored at room temperature (between 20° to 25° C) under secure conditions.

6.7 Drug Accountability

The investigators agree not to supply trial products to any person except to the patients enrolled in the trial or to those named as co-investigators. Unused trial medication and empty or partly used containers will be returned to the sponsor after the trial has been completed.

6.8 Assessment of Compliance

Every effort should be made to encourage patient compliance with the dosage regimen as per protocol. All patients should be instructed to return their medication pack, with any unused drug, to the investigator at the end of the study. A record of the supplies dispensed, taken and returned will be made in the eCRF at the appropriate visits.

If there are any significant irregularities in compliance, in the opinion of the investigator, the patient should be withdrawn from the study. This includes patients who do not take the study medication during the correct stage of their menstrual cycles (i.e. during the last 14 days). Please note that if a patient misses more than three consecutive days medication, SB should be contacted to confirm whether the patient must be withdrawn from the study.

6.9 Treatment of Study Medication Overdose

Symptoms of overdose with paroxetine include nausea, vomiting, tremor, dilated pupils, dry mouth and irritability. No specific antidote is known. Treatment should consist of those general measures employed in the management of overdose of any antidepressant. Early administration of activated charcoal may delay the adsorption of paroxetine.

Any overdose should be reported to SmithKline Beecham within 24 hours as a serious adverse experience (see [Section 8.4](#) Overdose).

6.10 Occupational Safety

Study medications are not expected to pose significant occupational safety risks to investigational staff under normal conditions of use and administration. A Material Safety Data Sheet (MSDS) describing occupational hazards and recommended handling precautions is available upon request by contacting your SB Site Monitor.

6.11 Concomitant Medication/Treatment

All concomitant medication taken during the study must be recorded in the case report form with indication, daily dose and dates of administration. Please note the exclusion criteria below;

- Any ongoing medication (including herbal medication and **any** use of sedatives/hypnotics) which in the opinion of the investigator could affect the patient's PMDD symptomatology (within one month prior to the screening visit and for the duration of the study period) except the following permitted treatments. Permitted medications include the occasional use of fibrinolysis inhibitors for abundant menstrual bleeding. Also permitted are the **occasional** use of paracetamol (acetaminophen), acetylsalicylic acid or other NSAIDs to treat menstrual cramps or headaches (their use **must** be documented in the concomitant medication section).

7 Outcomes Research and Pharmacoeconomics

7.1 Outcomes Measurement and Analysis

The EuroQol is a validated, standardised instrument designed to measure health outcomes across a wide range of health conditions and treatments. It provides a descriptive profile and a single index value that can be used as part of a pharmaco-economic evaluation. The EuroQol has 2 components: the health state classification (EQ-5D) and the visual analogue scale. The EQ-5D describes health status in 5 dimensions: mobility, self-care, usual activity, pain/ discomfort and anxiety / depression. Patients rate their health status on 3 levels for each dimension: no problem, moderate problems and extreme problems. The data, i.e. the sequence of five digits, form a descriptive picture of health states, can be combined into numeric scores, and additionally converted into health status utilities using validated tariffs. The scale for the calculated health state utilities ranges from '0' for death to '1' for perfect health. The visual analogue scale provides an overall summary rating of patients current health related quality of life on a scale of 0 to 100. The EuroQol will be collected at baseline (visit 3) and the end of each treatment cycle (and at early withdrawal if applicable).

7.2 Economic Data Collection and Analysis

The Work Productivity and Activity Impairment instrument (WPAI) is a valid and reproducible measurement of the benefit and costs of pharmaceutical interventions [10]. The scale consists of 6 items which capture information on the effect of health problems on both the patient's work and regular daily activities. It may be either interviewer rated or self rated by the patient, in this study the questionnaire will be included in the patient diary for self-rating. The WPAI will be assessed at baseline (visit 3) and at the end of each treatment cycle.

8 Adverse Events

The recording of adverse experiences is an important aspect of study documentation. Detailed guidelines are set out below.

8.1 Eliciting and Documenting Adverse Events

It is the responsibility of the investigator to detect and document all adverse events (AEs) which occur during the study and which fulfil the definitions and criteria outlined in this protocol.

8.1.1 Adverse Event Definition

An adverse event (AE) is defined as:

“Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product”

An AE includes:

- An exacerbation, or an unexpected increase in frequency or intensity of a pre-existing condition (other than condition under investigation), including intermittent or episodic conditions.
- Significant or unexpected worsening or exacerbation of the condition/indication under investigation
- A suspected drug interaction.
- An intercurrent illness
- Any clinically significant laboratory abnormality

An AE does not include:

- Anticipated day-to-day fluctuations of any pre-existing conditions, including the disease under study.
- Signs and symptoms of the disease under study that do not represent a significant worsening or exacerbation.
- Expected progression of the disease under investigation.

8.1.2 Serious Adverse Event Definition

A serious adverse event must be reported to SB within 24 hours (see [section 8.3.3 Reporting Serious Adverse Events to SmithKline Beecham](#))

A serious adverse event (AE) is any untoward medical occurrence which fulfils the definition for an AE (as defined in [section 8.1.1 Adverse Event Definition](#)) AND in addition, is:

- **Fatal**
- **Life threatening**
- **Disabling/incapacitating**
- **Results in hospitalisation or prolongs a hospital stay**
- **A congenital abnormality**
- **Any important medical occurrence which the investigator regards as serious based on appropriate medical judgement**

In addition, SmithKline Beecham policy dictates that the following events must be notified within 24 hours and must be documented and reported as for serious AEs, on the Serious AE Form :

- **Cancer**
- **Overdose**
- **Pregnancy**

To assist with the above definitions the following information is provided for clarification/interpretation

Life Threatening:

The patient was at immediate risk of death from the event. This term does not refer to an event which hypothetically might have caused death if it were more severe.

Disabling/Incapacitating:

The event results in a substantial and/or permanent disruption of the patient's ability to carry out normal life functions.

The investigator must use clinical judgement in this assessment. The definition is not intended to include experiences which may be of relatively minor medical significance e.g. headache, nausea, influenza or accidental trauma e.g. sprained ankle which may temporarily prevent everyday life functions unless a substantial disruption is recorded.

Hospitalisation:

Hospitalisation signifies that the patient has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or received treatment that would not have been appropriate in the physician's office or in an out-patient setting.

A Serious AE does **not** include hospitalisation for:

- Elective surgery or routine treatment/procedures related to a pre-existing condition that did not worsen. Instead, these must be recorded in the medical/surgical procedures section of the eCRF. If anything untoward (i.e. complications) are reported during the procedure, these must be reported as an AE, either 'serious' or 'non-serious' according to the usual criteria.
- A routine clinical procedure as stipulated by the protocol.
- Non-medical reasons (i.e. social admissions, hospitalisations for social, convenience or respite care).

Cancer:

The patient must have developed a new cancer or recurrence. The expected progression of a pre-existing cancer (which is documented as pre-existing cancer in the eCRF) is not a SERIOUS AE.

Overdose:

See [section 8.4](#) Overdose for reporting of overdose

Pregnancy:

See [section 8.7](#) Pregnancy for reporting of pregnancy.

Other Medically Important Events:

Medical and scientific judgement should be exercised to ensure that other important medical events are promptly reported to SmithKline Beecham. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions or development of drug dependency.

8.2 Recording of Adverse Events

Any pre-existing conditions or signs and/or symptoms present in a patient prior to the start of the study (i.e. before informed consent) should be recorded on the "Significant Medical/Surgical History and Physical Examination" panel within the eCRF.

Adverse experiences which occur after informed consent is obtained, but prior to starting single-blind placebo run-in medication during Reference Cycle 2 will be documented in the "Significant Medical/Surgical History and Physical Examination" record as instructed by the SB clinical study monitor.

All adverse experiences occurring during administration of single-blind placebo run-in medication in Reference Cycle 2 will be reported in the Baseline Adverse Experience form in the patient's eCRF.

All adverse experiences occurring after first administration of single-blind placebo run-in medication in Reference Cycle 2 but prior to administration of the first dose of randomised study medication will be reported in the Baseline Adverse Experience form in the patient's eCRF.

All adverse experiences occurring after administration of the first dose of randomised study medication (i.e., active drug, placebo) must be reported on the Adverse Experience form in the patient's eCRF.

All adverse experiences must be reported regardless of whether or not they are considered drug related.

At each visit/assessment in the period defined above AEs will be evaluated by the investigator and recorded in the appropriate AE/Serious AE section of the eCRF.

Any AEs already documented at a previous assessment and designated as ongoing, should be reviewed at subsequent visits as necessary. If these have resolved, the documentation in the eCRF should be completed. If an AE changes in intensity/frequency then this should be recorded as a separate event (i.e. a new record started)

8.2.1 Soliciting of Adverse Events

As a consistent method of soliciting AEs, the patient should be asked a non-leading question such as “Have you felt different in any way since starting the new treatment/or since the last visit?”

8.2.2 Evaluating the Adverse Event

8.2.2.1 Assessment of Intensity/Severity

The assessment of intensity/severity must be based on the investigator’s clinical judgement. Maximum intensity/severity should be assigned to one of the following categories:

Mild: An AE which is easily tolerated by the patient, causing minimal discomfort and not interfering with everyday activities.

Moderate: An AE which is sufficiently discomforting to interfere with normal everyday activities.

Severe: An AE which prevents normal everyday activities.

NB - An AE which is assessed as severe should not be confused with a serious AE. Refer to [section 8.1.2](#) for serious AE definition.

8.2.2.2 Assessment of Causality

Investigators are obligated to explain each adverse event and assess its relationship, if any, to study medication

The investigator must use clinical judgement to determine the degree of certainty with which an AE is attributed to drug treatment. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors and the temporal relationship of the event to study medication must be considered and investigated.

The investigator may also consult the investigator brochure to consider his/her assessment in relation to the pharmacology of the drug, similar reactions with the class of drug, and any existing literature.

Causality should be assessed using the following categories:

Unrelated: The adverse experience is definitely not related to the test drug.

Probably unrelated: Cause and effect relationship between the drug and the adverse experience has not been demonstrated, is improbable but not impossible.

Possibly related: A direct cause and effect relationship between the drug and the adverse experience has not been demonstrated but is possible or likely.

Related: There is a direct cause and effect relationship between the adverse experience and the study drug.

8.3 Reporting and Recording of Serious Adverse Events

8.3.1 Regulatory Responsibilities

SmithKline Beecham (SB) has a legal responsibility to notify both the local regulatory agencies, i.e. where the study is ongoing, and other regulatory agencies worldwide about the safety of a drug under investigation. Prompt notification (within 24 hours) of Serious AEs by the investigator to SB is essential so that legal and ethical responsibilities related to patient safety are fulfilled (see [8.3.3 Reporting Serious Adverse Events to SmithKline Beecham](#)).

8.3.2 Recording of Serious Adverse Events

All serious AEs which occur after administration of the first dose of randomised study medication must be recorded. This includes events occurring up to and including 30 days from receiving the last dose of study medication.

All serious AEs will be recorded in the AE panel of the eCRF, with the "Serious" box answered as "Yes", and replication of the data back to SB must be carried out

within 24 hours. All serious AEs will also be recorded on the Serious AE paper form and faxed to SB within 24 hours.

Any serious AEs which occur after 30 days and which are brought to the attention of the investigator need to be recorded and forwarded to SB if assessed as possibly drug related.

Serious AEs which relate to pre-existing conditions and which occur prior to the start of the study (i.e. before consent has been signed) must be reported on the "Significant Medical/Surgical History and Physical Examination" record in the eCRF and not as serious AEs.

However, any serious AEs considered by the investigator as related to study design, study conduct and/or study defined procedures which occur at any point in the study (this includes serious AEs which occur after informed consent has been obtained but prior to administration of the first dose of randomised study medication) must be recorded and reported to SB to fulfil regulatory requirements. In this case, the event must be recorded on the Serious AE paper form and in the AE panel of the eCRF, and reported back to SB in the same timescale as for other serious AEs.

8.3.3 Reporting Serious Adverse Events to SmithKline Beecham

All serious AEs will be reported to SB **within 24 hours**. Facsimile transmission is always the preferred method of reporting (including non-working hours).

SB study contact :

Telephone number :

Facsimile number: :

Alternate SB contact :

Telephone number :

Facsimile number: :

**Emergency 24 hour
medical contact :**

Telephone number :

Investigators must not wait to receive all information before notifying SB of a serious AE on the Serious AE Form.

The Serious AE Form in the eCRF must always be completed as fully as possible. The SB Serious AE worksheet must also be completed in the same manner, signed by the investigator and faxed to the SB contact. Telephone reporting is not encouraged. It may be used for the initial notification but **does not replace the need for the investigator to complete and sign the serious AE Form within 24 hours.**

As many details of the serious AE as possible must be reported. The investigator must always provide an assessment of causality at the time of the initial report (see 8.2.2.2 Assessment of Causality) .

For each serious AE the Serious AE Form (two pages) must always be sent to SmithKline Beecham in the initial report.

In parallel with the above, the following panels in the eCRF must be completed as fully as possible and the data must be replicated back to SB within 24 hours:

- Demography
- Significant medical/surgical history and physical examination
- Study medication record
- Concomitant medication
- Adverse experiences / Baseline adverse experiences
- Form D (if applicable)

8.3.4 Follow-up of Serious Adverse Events

After the initial serious AE report the investigator is required to proactively provide further information regarding the patient's condition.

Investigators must follow-up all patients with serious AEs until the event has subsided (or disappeared), the condition has stabilised, the event is otherwise explained, or the patient is lost to follow-up.

All follow-up information must be forwarded to the SB contact (as specified in [8.3.3 Reporting Serious Adverse Events to SmithKline Beecham](#) above) **within 24 hours** of receipt.

To fulfil ethical and regulatory obligations, SB may request additional follow-up information on any serious AE and the investigator is obligated to assist. When requested by SB, information from relevant hospital reports, pathology and autopsy reports must also be forwarded, if available.

8.4 Overdose

An overdose is defined as an excessive dose taken by a patient, either accidentally or intentionally, irrespective of whether it involves study medication or non-study medication. Overdose may be suspected or confirmed and may or may not be associated with clinical signs and symptoms.

It would definitely include, but not be limited to those events which based on the investigators clinical judgement were considered to be of medical concern and/or require clinical observation and/or medical intervention.

As a guide, an overdose would include any dose greater than the highest daily dose included in the protocol or prescribing information (for marketed products).

Minor deviations to study drug administration (i.e. resulting from poor patient compliance) must be recorded in the study medication compliance section of the eCRF and not as Serious AEs.

8.4.1 Reporting of Overdose

For all overdoses the Serious AE Form must be completed and reported within 24 hours as for any other Serious AE (see [section 8.3.3 Reporting Serious Adverse Events to SmithKline Beecham](#)). The documentation must include details of any associated signs/symptoms or if the overdose is asymptomatic this must be stated.

8.4.2 Further Information on Overdose

Symptoms of overdose with paroxetine include nausea, vomiting, tremor, dilated pupils, dry mouth and irritability. No specific antidote is known.

The treatment should consist of those general measures employed in the management of overdose with any antidepressant.

The stomach should be emptied either by the induction of emesis, lavage or both. Following evacuation, 20 to 30 grams of activated charcoal may be administered every 4 to 6 hours during the first 24 hours after ingestion. Supportive care with frequent monitoring of vital signs and careful observation is indicated.

8.5 Treatment Failures

Re-emergence of underlying disease which has resulted from the possible ineffectiveness of study medication (treatment failure) does not need to be reported as an AE or serious AE unless the resulting event is more frequent than at baseline. Expected progression of the underlying disease does not need to be reported as a AE or serious AE unless the event is atypical in nature.

Details of treatment failures must be captured elsewhere in the eCRF under specific efficacy assessments.

8.6 Post-Study Events

A post study event is any event that occurs outside the protocol defined period. This includes after completion of the study (i.e. beyond the post-treatment follow-up period/30 days), or following premature withdrawal .

All serious AEs (including deaths) if brought to the attention of the investigator at any time post-study and considered by the investigator to be possibly related to study medication, must be reported to SmithKline Beecham (see [section 8.3.3](#) Reporting Serious Adverse Events to SmithKline Beecham).

8.7 Pregnancy

Details of all pregnancies in patients that occur during the treatment and the follow-up period must be documented and reported to SmithKline Beecham. In addition any pregnancies brought to the attention of the investigator after this period , and where it is known that study medication was taken at the time of conception, must also be reported.

Pregnancies in patients that occur during the screening phase and prior to the first dose of single-blind placebo medication should be recorded in the 'Significant Medical/Surgical History and Physical Examination Record' in the eCRF. Pregnancies in patients that occur after the first dose of single-blind placebo medication but before the patient has been administered the first dose of

randomised study medication should be recorded in the 'Baseline Adverse Experience Record' in the eCRF as a non-serious event.

In the rare event that a pregnancy occurring at any time prior to administration of the first dose of randomised study medication is considered to be related to study design, it should also be reported to SB using the Serious AE form (see Section 8.7.1 Reporting of Pregnancy).

8.7.1 Reporting of Pregnancy

All pregnancies will be reported to SB promptly. Although pregnancies are not generally serious AEs (and there is no serious criteria fulfilled) the Serious AE Form must be completed and forwarded to the SB contact specified in [section 8.3.3 Reporting Serious Adverse Events to SmithKline Beecham](#) within 24 hours. This will provide a record of the initial notification of the pregnancy.

8.7.2 Follow-up of Pregnancies

All pregnancies will require the completion of a pregnancy form which will be provided after initial notification on the Serious AE Form. All pregnancies will be followed to term. A special form will be provided at the expected time of delivery. Any premature terminations, including elective abortions must be reported. The status of the mother and child must be forwarded to SmithKline Beecham after delivery.

8.7.3 Action Taken As A Result of Pregnancy

Patients who become pregnant during the study should be withdrawn from the study immediately.

8.8 Unblinding Treatment Code

Only in the event of a medical emergency which the investigator feels cannot be adequately treated without knowing the identity of the study medication, may the treatment code be unblinded for a particular patient. Only if the situation is a medical emergency may the investigator unblind the treatment code.

Wherever possible, the investigator must make every effort to contact the SB medical contact (see [section 8.3.3 Reporting Serious Adverse Events to SmithKline Beecham](#)) prior to unblinding. If this is not possible and the access to individual treatment codes is available (direct, or via a third party) at the

investigational site the Investigator may unblind and inform the SB medical contact as soon as possible thereafter.

The investigator must complete a Serious AE Form and forward it to the SB contact designated in [section 8.3.3](#) Reporting Serious Adverse Events to SmithKline Beecham within 24 hours.

8.9 Investigator Letters

Investigator letters are prepared according to SB policy and are forwarded to investigators as necessary. The purpose of these letters is to communicate significant emerging safety issues and/or to fulfil specific regulatory requirements, regarding the drug under investigation.

An investigator who receives an investigator letter describing an SERIOUS AE or other specific safety information from SB must file it with the Investigator Brochure and must notify the Ethics Committee/IRB, if appropriate, according to local requirements.

9 Patient Completion and Withdrawal

9.1 Definitions

A patient will be considered to have completed the study if they progress through the study up to and including the End of Treatment Cycle 3 visit.

A withdrawal is any patient who enters the study, i.e. gives informed consent, and does not complete the study up to and including Visit 6 (whether or not the patient receives treatment).

9.2 Procedures for Handling Withdrawals

For all patients who are withdrawn early during the treatment cycles of the study, an early withdrawal visit should be conducted as soon as possible. The detailed schedule of assessments to be carried out at the early withdrawal visit have been described in full earlier in the protocol (see [5.3](#) Detailed Description of Study Stages/Visits).

For patients who withdraw from the study prior to receiving single-blind placebo medication in Reference Cycle 2 the following data must be recorded in the eCRF:

- Patient demography (Date of Birth, Race)
- Reason for withdrawal (from the Patient Continuation/Withdrawal panel)
- Eligibility based on the reference cycle VAS scores

Furthermore, for any patients who had SAEs related to study design or procedures during this period, the additional information (medical history, baseline AEs, prior/concomitant medications) must be captured as for patients withdrawing following administration of any single-blind placebo medication during Reference Cycle 2 (see following paragraph).

For patients who withdraw from the study after administration of any single-blind placebo medication during Reference Cycle 2 the following data must be recorded in the eCRF:

- Patient demography (Date of Birth, Race)
- Reason for withdrawal (from the Patient Continuation/Withdrawal panel)
- Medical History
- Baseline AEs
- Prior/Concomitant Medications
- Eligibility based on the reference cycle VAS scores

9.3 Reasons for Withdrawal

A patient may withdraw (or be withdrawn) from the study prematurely for the following reasons:

1. Adverse experience (Adverse Experience section must be completed)
2. Lack of efficacy
3. Protocol deviation (including non compliance)
4. Lost to follow-up
5. Other

The reason for termination will be recorded in the Study Conclusion section of the eCRF.

10 Statistical Issues: Design and Analysis

10.1 Objectives

10.1.1 Primary Objective

To compare the efficacy of intermittent dosing with paroxetine CR (12.5mg and 25mg) with that of placebo for the treatment of PMDD. The hypothesis to be tested is that paroxetine treatment results in a greater improvement in symptoms of PMDD compared with placebo treatment.

10.1.2 Secondary Objectives

To evaluate the safety and tolerability of intermittent dosing with paroxetine CR (12.5mg and 25mg) for the treatment of PMDD.

10.2 Hypotheses

The null hypothesis is that there is no difference between each dose level of paroxetine CR (12.5mg and 25mg) and placebo in the change from baseline in the VAS – MOOD score at the treatment cycle 3 LOCF endpoint in the intent-to-treat (ITT) population. The alternative hypothesis is that there is a difference between either dose level of paroxetine and placebo. The null hypothesis will be rejected, and the study judged a success, if there is sufficient evidence for either of the alternative hypotheses. The study has been powered to detect a difference of 16.3mm between either dose level of paroxetine and placebo.

10.3 Definition of Variables

10.3.1 Primary Variable(s)

The primary efficacy variable is the change from baseline in luteal phase VAS – MOOD score at the treatment cycle 3 endpoint. For each patient, VAS –MOOD score is the mean of luteal phase VAS scores for the four core PMDD symptoms: irritability, tension, depressed mood and affective lability. Each symptom score is the mean of the last five days of their menstrual cycle. For this analysis, baseline measures are the luteal phase scores during the final reference cycle (reference cycle 2).

Change in VAS – MOOD score has been selected as the primary variable because this composite measure captures the four core psychological symptoms of PMDD.

10.3.2 Secondary Variable(s)

The main secondary efficacy variable, based on a high relative clinical importance, is:

Change from baseline in the mean luteal phase VAS Physical Symptoms score at the treatment cycle 3 endpoint. Mean luteal phase score is the mean of the last 5 days of the menstrual cycle, calculated for each patient.

The other secondary variables are as follows:

Proportion of responders defined by a 50% reduction in their baseline luteal phase VAS - MOOD score at the treatment cycle 3 endpoint where

$$\% \text{ Change} = \frac{(VAS - MOOD_{\text{endpoint}} - VAS - MOOD_{\text{baseline}})}{VAS - MOOD_{\text{baseline}}} \times 100$$

Proportion of responders defined by a mean luteal phase VAS - MOOD score at the treatment cycle 3 endpoint of less than or equal to their baseline mean follicular phase VAS - MOOD score.

Change from baseline in area under the curve (AUC) for treatment cycles 1 – 3 in the daily luteal phase VAS - MOOD scores, adjusting for the total number of luteal days.

Change from baseline in the individual items of the Sheehan Disability Scale (SDS; work, social life and family life) at the treatment cycle 3 endpoint.

Change from baseline in the Sheehan Disability Scale (SDS) total score at the treatment cycle 3 endpoint

Change from baseline in the observer rated Premenstrual Tension Scale total score at the treatment cycle 3 endpoint.

Change from baseline in the CGI - Severity of Illness score at the treatment cycle 3 endpoint.

Proportion of patients who scored 1 or 2 (very much improved or much improved) on the CGI – Global Improvement item at the treatment cycle 3 endpoint.

Proportion of patients who scored a 1 or 2 (very much improved or much improved) on the Patient Global Evaluation (self-rated) at the treatment cycle 3 endpoint.

Change from baseline in the EuroQol VAS score at treatment cycle 3 endpoint.

These secondary efficacy endpoints utilise a number of measurements including disease-specific measures, global clinician and patient evaluations, the Sheehan Disability Scale and a number of health economic measures; together these measurements provide a more complete description of the disease.

10.3.3 Other Variable(s)

The following will be summarised by descriptive statistics with no formal statistical analysis performed:

Change from baseline in each individual VAS item score, excluding the Physical Symptoms item, at the treatment cycle 3 endpoint.

Patient evaluation of Study Medication (observer-rated) at treatment cycle 3 endpoint or early withdrawal.

Overall work productivity score from the Work Productivity and Activity Improvement Instrument.

International Standard Classification of Occupations at baseline (visit 3).

EQ-5D health profiles at baseline and treatment cycle 3.

Change from baseline in the weighted EQ-5D health profile score based on the EuroQol tariff (EQ-5D utility).

10.4 Comparisons of Interest

10.4.1 Primary Comparisons of Interest

The paroxetine arms versus placebo comparisons of change from baseline in the luteal phase VAS-MOOD score at the treatment cycle 3 LOCF endpoint in the ITT population are the primary comparisons of interest in this study.

For this study to be considered a success a clinically and statistically significant difference must be observed (after adjustment for multiple comparisons) between the placebo arm and either of the paroxetine arms.

10.4.2 Other Comparisons of Interest

Other comparisons of interest include an LOCF analysis of the secondary endpoints at the treatment cycle 3 visit. In addition, an analysis of the primary and secondary efficacy variables based on the 70% LOCF dataset and the observed cases (OC) dataset at the treatment cycle 3 visit will be performed. A per protocol (PP) analysis of the primary endpoint only will be performed.

The difference between the two paroxetine arms is not of central scientific interest and this comparison will not be considered when adjusting for multiple comparisons. This comparison will be presented for the primary variable alone for information only.

10.5 Interim Analysis

There are no planned interim analyses.

10.6 Target Sample Size

10.6.1 Sample Size Assumptions

This study is powered to demonstrate a difference of 16.3mm between paroxetine CR (12.5mg and 25mg) and placebo, in mean change from baseline to treatment cycle 3 in VAS - MOOD score. The mean difference of 16.3 mm was recommended to GSK as a target difference by an opinion leader in the PMDD research area based on the results of a single previous study [17]. Based on data presented from an earlier study of fluoxetine continuous dosing [6] [17] and from a paroxetine study [19] a common standard deviation of 30mm was assumed for the change in VAS - MOOD score at the treatment cycle 3 LOCF endpoint. A

total of 86 evaluable patients in each of the three study arms will provide 90% power to detect a difference of 16.3mm. To adjust for the two treatment comparisons a two-sided alpha level of 0.025 has been used. Assuming a 20% attrition rate, the total number of patients randomised to each treatment group is increased to 108, a total of 324 patients overall.

10.6.2 Sample Size Sensitivity

The robustness and sensitivity of the sample size calculation has been considered in order to assess the impact on the power of the study should the observed standard deviation be higher or lower than expected.

Given a fixed sample size and a difference of 16.3mm the size of the standard deviation will affect the power of the study to detect this difference between the treatment groups, as shown in the following table:

Standard Deviation	Power (%) with 86 evaluable patients per group	Evaluable patients required per group for 90% Power
SD maximum 40	65	151
35	78	116
SD best 30	90	86
25	97	60
SD minimum 20	>99	39

The minimum standard deviation value of 20 was chosen based on data from the placebo and intermittent paroxetine dosing arms from a recent study [19], and the maximum value was chosen in order to be symmetric about the assumed value.

10.6.3 Sample Size Re-estimation

There is no plan to re-estimate the target sample size during the course of the study.

10.7 Methods of Analysis

10.7.1 Populations of Interest

10.7.1.1 Patient Populations

Two patient populations will be evaluated; primary inference for efficacy and safety will be based on the intent-to-treat population.

Intent-to-Treat (ITT): The modified ITT population, referred to as the ITT population, consists of all randomised patients who received at least one dose of study medication and have at least one post-baseline assessment.

Per protocol (PP): This population comprises the subset of the ITT population who meet all the following criteria:

- Have no major protocol violation with regard to inclusion or exclusion criteria.
- Have no major protocol violation between randomisation and completion of the active treatment phase of the study (treatment cycles 1-3).
- Have no break in study medication for more than 3 consecutive days or compliance outside 80-120% during the active treatment phase of the study (treatment cycles 1-3).
- Have been exposed to randomised study medication for at least one luteal phase (i.e. last 14 days) of a menstrual cycle.

Only the primary efficacy variable (i.e. no secondary efficacy measures) will be analysed using the PP population. The PP population will not be analysed if it comprises more than 95%, or less than 50%, of the patients in the ITT population. Patients to be excluded from the PP efficacy analysis will be identified prior to unblinding of the study.

10.7.1.2 Datasets

Three dataset definitions apply for this study:

Last Observation Carried Forward (LOCF)	On treatment observations are carried forward to estimate subsequent missing data points for a patient.
70% Last Observation Carried Forward (70%)	This comprises the LOCF dataset at the latest timepoint where at least 70% of the patients in each

LOCF)	treatment group remain in the study.
Observed Cases (OC)	In this dataset data are evaluated only at the time-point at which they were collected with no missing values filled in with estimates.

These datasets will be used for both the ITT and PP populations. For the OC dataset any efficacy assessment performed more than seven days after the last dose of double-blind study medication will be excluded from the analyses, but will be presented in data listings. The LOCF dataset will be constructed from the OC dataset.

10.7.2 Statistical Methods

10.7.2.1 Efficacy Analyses

Analysis Methods

Since PMDD is a relatively new area of research there is limited information on the variables which affect response. For this reason, the statistical model on which the primary inference will be based will include terms for treatment group, centre, baseline VAS - MOOD score and age (in years) at entry to the study. If the number of patients at one or more centres is small, centres will be grouped by centre type as described in the Statistical Analysis Plan for this study.

To assess the robustness of the primary model, interactions between treatment and each of the other main effects included in the primary model will be investigated in turn, assessing the statistical significance of these terms at the 10% level. All significant treatment interactions will be tabulated. Statistically significant treatment interactions with either of the continuous covariates (i.e., baseline VAS-MOOD and age) will be plotted and also presented for the following pre-defined categories:

- VAS-MOOD score at baseline: quartiles of the observed values
- Age: 18-25, 26-35, ≥ 36

In the event that more than one interaction term is found to be statistically significant, the significant interactions will be modelled together to assess their joint significance. Note, investigation of interaction terms will be confined to the primary variable using the treatment cycle 3 LOCF dataset for the ITT population.

The final model for the primary variable (i.e., adjusting for treatment, centre, age and where applicable corresponding baseline score) will be applied to all the secondary efficacy variables. For the EuroQol VAS endpoint employment status (as captured on the WPAI) will be included as an additional covariate.

All confidence intervals and hypothesis tests will be two-sided. For the primary variable the treatment effect will be considered statistically significant at the overall 5% level, with an adjustment for two treatment comparisons using Hochberg's modification to the Bonferroni inequality [15]; adjusted 95% confidence intervals will be presented. For the purpose of applying Hochberg's method to the calculation of adjusted confidence intervals, comparisons will be ordered on the basis of the corresponding p-value. For secondary variables no multiplicity adjustment will be applied; the treatment effect will be considered statistically significant at the 5% level and confidence intervals will be presented at the 95% level.

All efficacy measures over the course of the study will be presented and summarised in graphs and tables. Categorical data will be summarised by counts and the proportions in each response category and continuous data will be summarised by means, standard deviations, medians, maxima, minima.

For continuous endpoints the data will be analysed using a normal, linear model. The assumptions of normality and homogeneity of variance will be assessed by inspection of normal probability plots, plots of standardised residuals versus predicted, and standardised residuals versus continuous covariates. If these assumptions are not met, non-parametric methods adjusting for the pre-specified covariates (i.e., treatment, centre, age and corresponding baseline score) will also be used [18].

Binary endpoints will be analysed using logistic regression. Plots of standardised deviance residuals against continuous covariates will be examined to check for linearity of the relationship on the logistic scale.

Handling Missing Data

For each subject, a mean luteal or follicular phase score for each of the four core VAS mood items (depressed mood, tension, irritability and affective lability as captured from the Visual Analogue Scales) for a given menstrual cycle, will only be calculated if scores are available for four or five of the designated 'luteal' or 'follicular phase' days within that cycle.

If data are missing for no more than 1 day within the last 5 days of the menstrual cycle (representing the luteal phase), and no more than 1 day's data are missing between days 6 and 10 (representing the follicular phase), then the mean will be calculated on the remaining non-missing daily scores (mean = (sum of non-missing scores)/(number of days with non-missing data)).

A VAS-Mood total score for the luteal or follicular phase will only be calculated if mean scores are available for three or four of the individual items (depressed mood, tension, irritability and affective lability) within that phase.

In using the LOCF approach the practice of using all available efficacy data regardless of missed clinic visits in evaluating a patient's response to treatment is followed. In order to address the issue of potential bias which may result from missing VAS data, the percentage of missing VAS - MOOD responses will be tabulated by visit and treatment group using the OC dataset. The percentage of missing data for the individual VAS – MOOD items will also be tabulated by visit and treatment.

Handling of missing data for secondary endpoints is detailed in the Statistical Analysis Plan. For the change from baseline endpoints subjects will be excluded from an analysis if they lack either a baseline or post-baseline response measure.

10.7.3 Safety

All safety reporting will be based on the ITT population.

Adverse experiences will be coded using the WHO coding system for each patient with reference to body system and preferred terms. The number and percent of patients in each treatment group with treatment emergent adverse experiences will be compared, subjectively, for overall incidence and also by body system and preferred term. Counts of adverse experiences will be made for the entire treatment phase (i.e. treatment cycles 1-3). Counts will also be presented for patients with serious adverse experiences, adverse experiences leading to withdrawal, adverse experiences by severity, and adverse experiences by relationship to study drug. In addition, study drug discontinuation symptoms over each menstrual cycle will be examined.

The number and percentage of withdrawals due to adverse experiences and withdrawal for other reasons will be presented.

Summary statistics for absolute values and changes from baseline will be presented by treatment group for blood pressure, heart rate, weight, height and

body mass index. Additionally, for blood pressure, heart rate and weight the number of patients in each treatment group with values outside pre-determined clinically important ranges and/or with changes from baseline of clinical importance will be tabulated.

Summary statistics will be presented for the laboratory data (haematology and blood chemistry) by visit and for change from baseline. Each patient's baseline measurement for a given parameter will be classified into one of five categories: within the normal range, above or below the normal range, or as a low or high value from a pre-determined clinically important range. Available values from the last on treatment assessment and follow-up visit (within 14 days of the last study dose) will be classified using the same procedures. The proportion in each category at each timepoint, and transition from baseline will be examined by cross-tabulating the assigned post-baseline levels against the baseline categories.

11 Administrative Matters

To comply with Good Clinical Practice Guidelines, important administrative obligations relating to investigator responsibilities, monitoring, archiving data, audits, confidentiality and publications must be fulfilled (see [Appendix B](#) Administrative Matters, page 80).

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13 Appendices

Appendix A Declaration of Helsinki

World Medical Association

DECLARATION OF HELSINKI

Recommendations Guiding Physicians

in Biomedical Research Involving Human Subjects

Adopted by the 18th World Medical Assembly

Helsinki, Finland, June 1964

and amended by the

29th World Medical Assembly

Tokyo, Japan, October 1975

35th World Medical Assembly

Venice, Italy, October 1983

41st World Medical Assembly

Hong Kong, September 1989

and the

48th General Assembly

Somerset West, Republic of South Africa, October 1996.

INTRODUCTION

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfilment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in

the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the etiology and pathogenesis of disease.

In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

I. BASIC PRINCIPLES

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee

independent of the investigator and the sponsor provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.

3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interest of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or

she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely-given informed consent, preferably in writing.

10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity make it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replace that of the subject in accordance with national legislation.

Whenever the minor child is in fact able to give a consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.

12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE (Clinical Research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgement it offers hope of saving life, re-establishing health or alleviating suffering.
2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient - including those of a control group, if any - should be assured of the best proven diagnostic and therapeutic method. This does not exclude the use of inert placebo in studies

where no proven diagnostic or therapeutic method exists.

4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission the independent committee (see [1,2](#)).
6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (Non-Clinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers -- either healthy persons or patients for whom the experimental design is not related to the patient's illness.
3. The investigator of the investigation team should discontinue the research if in his/her or their judgement it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

Appendix B Administrative Matters

I Responsibilities Of The Investigator Conducting a Study Using the SB Remote Data Management System (RDM)

To ensure that he/she has sufficient time to conduct and complete the study and has adequate staff and appropriate facilities which are available for the duration of the study and to ensure that other studies do not divert essential patients or facilities away from the study at hand.

To submit an up-to-date curriculum vitae and other credentials (e.g. medical license number in the United States) to the sponsor and - where required - to relevant authorities.

To acquire the normal ranges for laboratory tests performed locally and, if required by local regulations, obtain the Laboratory Licence or Certification.

To prepare and maintain adequate case histories designed to record observations and other data pertinent to the study.

II Protocol Amendments

No changes to the study protocol will be allowed unless discussed in detail with the SmithKline Beecham (SB) Medical Monitor and filed as an amendment/modification to this protocol.

Any amendment/modification to the protocol will be adhered to by the participating centre (or all participating centres) and will apply to all patients following approval as appropriate by the Ethical Review Committee or Institutional Review Board.

III Sponsor's Termination Of Study

SB reserves the right to discontinue the clinical study at any time for medical or administrative reasons. When feasible, a 30-day written notification will be tendered. The investigator will return all RDM equipment to SB at an agreed upon time following termination of the study.

IV Case Report Form Instructions

This study will use a Remote Data Management system for data capture. Electronic CRFs (eCRFs) (and patient diary cards, if applicable), will be supplied

by SB for recording all data. Prior to screening the first potential participant, the investigator will provide a list showing the signature of all individuals authorised to make or change entries in the eCRFs. If the authorised individuals should change during the study, the investigator is to inform SB.

It is the responsibility of the investigator or co-investigator to ensure that the eCRFs (and patient diary cards) are fully completed.. The investigator, co-investigator, or authorised study co-ordinator will enter the patient's identification (2-3 alphabetic letters representing the patient's initials or first 2-3 letter of patient's first or last name), the patient identification (ID) and the visit date, in the eCRF as required.

When a patient completes a visit, it is anticipated that relevant sections of the eCRF will be completed by the investigator (or designated staff) within 24 hours of the last data becoming available, but in no case later than 5 days. Similarly, when a patient completes a study, it is anticipated that all relevant eCRF data entries will be completed within 24 hours of the last data becoming available, but in no case later than 5 days. This also applies to forms for potential study participants who were not randomised to a treatment group.

An eCRF must be completed and replicated to SB for all patients who have undergone protocol specific procedures, whether or not the patient completed the study.

While completed eCRFs will be reviewed and source document-verified by an SB professional monitor at the study site, errors detected by subsequent in-house eCRF review may necessitate requests for clarification or correction of errors (SB reviewer queries). The clarifications and/or corrections and documentation at the site must be reviewed approved by the investigator.

Any questions or comments related to the protocol should be directed to the assigned study monitor. Any RDM technical questions or comments should be directed to RDM Help Desk.

V Monitoring By SmithKline Beecham (i.e. the Sponsor)

Monitoring visits by a professional representative of the sponsor will be scheduled to take place before entry of the first patient, during the study at appropriate intervals and after the last patient is completed.

These visits are for the purpose of confirming that SB sponsored studies are being conducted in compliance with the relevant Good Clinical Practice

regulations/guidelines, verifying adherence to the protocol and the completeness and exactness of data entered in the eCRF and Drug Inventory Forms. The monitor will verify eCRF entries by comparing them with the hospital/clinic/office records which will be made available for this purpose. The monitor will ensure that the sending of the eCRF data to SB has been timely and successful. Adequate time and space for the monitoring visits must be made available by the investigator.

Investigator must ensure provision of reasonable space and adequate qualified personnel for monitoring visits.

VI Archiving Of Data

The investigator must retain patient records and eCRFs as well as drug disposition records in an easily retrievable form/location until such time as has been agreed in writing with SB. The investigator must have a 'key' linking the patient's identification code (i.e. treatment number) to the patient's clinical file. If the investigator moves or retires, he/she must nominate someone in writing to be responsible for record keeping. Archived data may be held on microfiche or electronic record, provided that a back-up exists and a hard copy can be obtained from it if required.

SB agrees to retain a copy of the protocol, documentation, approvals and all other documents related to the study, including certificates that satisfactory audit and inspection procedures have been carried out.

VII Audits

For the purpose of compliance with Good Clinical Practice and Regulatory Agency Guidelines it may be necessary for SB or a Drug Regulatory Agency to conduct a site audit. This may occur at any time from start to after conclusion of the study.

When an investigator signs the protocol, he agrees to allow the Drug Regulatory Agency and SB auditors to inspect his/her study records. Furthermore, if an investigator refuses an inspection, his data will not be accepted in support of a New Drug Registration and/or Application.

SB has a substantial investment in clinical studies. Having the highest quality data and studies are essential aspects of drug development. SB has a Regulatory Compliance staff who audit investigational sites. Regulatory Compliance assesses the quality of data with regard to accuracy, adequacy and consistency. In

addition, Regulatory Compliance assures that SB sponsored studies are in accordance with the relevant Good Clinical Practices regulations/guidelines are being followed.

To accomplish these functions, Regulatory Compliance selects investigational sites to audit. These audits usually take 1 to 2 days. The SB audits entail review of source documents supporting the adequacy and accuracy of the eCRFs, review of documentation required to be maintained, and checks on drug accountability. The SB audit therefore helps prepare an investigator for a possible regulatory agency inspection as well as assuring SB of the validity of the database across investigational sites.

The Inspector will be especially interested in the following items:

Log of visits from the sponsor's representatives

ERC/IRB approval

Test article accountability

Approved study protocol and amendments

Informed consent of the patients (written or witnessed oral consent)

Medical records supportive of all eCRF data entries

Reports to the ERC/IRB and the sponsor

Record retention

SB will gladly help investigators prepare for an inspection.

VIII Confidentiality And Publication

You agree that all information communicated to you by SB is the exclusive property of SB and you will ensure that the same shall be kept strictly confidential by you or any other person connected with the work and shall not be disclosed by you or such person to any third party without the prior written consent of SB. You shall communicate the results of the work promptly to SB.

We agree that you shall have the right to publish or permit the publication of any information or material relating to or arising out of the work after prior submission to us provided that if we shall so request you will delay publication

for a maximum of six months to enable us to protect our rights in such information or material. Any proposed publication or presentation (e.g. manuscript, abstract or poster) for submission to a journal or scientific meeting, should be sent to the study monitor prior to submission. SB will undertake to comment on such documents within four weeks.

All rights and interests worldwide in any inventions, know-how or other intellectual or industrial property rights which arise during the course of and/or as a result of the clinical study which is the subject of this Protocol or which otherwise arise from the information or materials supplied under this Agreement, shall be assigned to, vest in and remain the property of SmithKline Beecham plc.

In drafting this section, additional stipulations can be included in accordance with local custom and practice but the above aspects must also be retained.

Appendix C Sample Informed Consent

Study Title: A double-blind, placebo-controlled, 3-arm fixed dose study of paroxetine CR intermittent dosing (12.5mg and 25mg) for Premenstrual Dysphoric Disorder.

Protocol Number: 29060/717

1. Description and Purpose of the Study

This is a medical research study. The purpose of the study is to investigate the efficacy and safety of intermittent dosing with controlled-release paroxetine (paroxetine-CR) in the treatment of Premenstrual Dysphoric Disorder (PMDD). The study doctor and/or institution is being paid to conduct this study [US only].

Following an initial visit to the clinic you will be asked to record your symptoms on each day in a patient diary beginning from the start of your next menstrual cycle. You will be asked to continue recording your symptoms on the diary for five or six complete menstrual cycles. In the first one or two cycles, you simply record symptoms on the diary in order to help your doctor to confirm whether you have a diagnosis of PMDD. For the remaining 4 menstrual cycles you will receive study medication to be taken once daily for the two weeks prior to the date you are due to start your next menstrual cycle. You will be asked to attend the clinic for a follow up visit 14 days after taking your last dose of study medication.

A total of 324 patients will be treated in this study.

Paroxetine is currently marketed for treating depression and anxiety disorders. Clinical trials have shown that paroxetine and similar drugs are effective in treating PMDD. Studies of the efficacy of continuous dosing of a new controlled-release formulation of paroxetine (paroxetine CR) in the treatment of PMDD are currently ongoing. In this study intermittent dosing with paroxetine CR will be studied in the treatment of PMDD. Although paroxetine CR is not currently commercially available, it has been recently approved in the United States for the treatment of depression.

2. Procedures

At each clinic visit, your doctor will record details of your vital signs (pulse and blood pressure), of any adverse experiences (side effects), and of any changes in medications which you are taking. All medications which you are taking, whether on prescription from your doctor, non-prescription ("over the counter") or herbal medication, must be recorded. All adverse experiences which you have during the course of the study must be reported to your investigator at the clinic visits.

In addition, during your initial visits your doctor will record details of your medical and surgical history, your obstetrics and gynaecological history, your history of PMDD, and of any treatments which you have previously taken for PMDD. Your doctor will also interview you to determine whether you have any psychiatric disorders and to determine whether you meet the criteria for a diagnosis of PMDD.

Your doctor will conduct a physical examination at your first clinic visit and at certain visits blood samples will be taken for routine laboratory evaluation and for pregnancy testing.

During the study, you will be asked to use a patient diary to make a daily record of your PMDD symptoms for a total of five or six menstrual cycles. For the first one or two menstrual cycles you simply record your symptoms on the diary each day, this helps your doctor to confirm whether you have a diagnosis of PMDD. For the remaining 4 menstrual cycles you will receive study medication to be taken once daily for the two weeks prior to the date you are due to start your next menstrual cycle. After your initial clinic visit, and after you begin to record your symptoms in the diary, you will be asked to attend for a clinic visit once at the start of each subsequent menstrual cycle for the duration of the study. You will also be asked to attend the clinic for a follow up visit 14 days after taking your last dose of study medication (in addition, you may be asked to attend for a further visit 28 days after taking your last dose of study medication if for example you have any ongoing adverse experience at the 14 day visit). During all of the clinic visits when you are taking study medication your doctor will ask you to complete some additional forms in the back of your patient diary, these help to more fully understand the effects of the medication.

Once your doctor has confirmed that you meet the criteria for PMDD and are eligible to participate in the study you will be randomly assigned to receive either controlled release paroxetine (at one of 2 possible doses) or an inactive placebo substitute. The chance of receiving controlled release paroxetine and not placebo

is 2:3, or 66%; the chance of receiving placebo and not controlled release paroxetine is 1:3 or 33%. During some part of the study all patients will receive placebo medication.

Neither you nor your doctor will know which treatment you are receiving during the study. You will not find out which treatment you have received until the analysis of the study results is completed. However, in the event of an emergency your doctor can break the study blind in order to find out which medication you are receiving.

You will incur no costs for your participation in the study. No visit in connection with your participation in the study will be billed to you or your insurance carrier.

3. Discomforts and Risks

All drugs may cause side-effects in some patients. In clinical trials with paroxetine CR, the following common side-effects ($\geq 5\%$ incidence) have been reported with a frequency of approximately twice that of placebo:

somnolence, dizziness, tremor, decreased libido, nausea, diarrhea, constipation, trauma, abnormal ejaculation, female genital disorders (e.g. anorgasmia), impotence and sweating

You may experience discomfort when having blood drawn; this may be a source of mild pain, and some mild swelling may occur at the site of the blood draw. Although it is uncommon, this may also cause you to feel faint, to bleed slightly, or to develop an infection at the site of the blood draw.

4. Risks if you become pregnant

Because the effects of paroxetine CR on the unborn baby are uncertain, you will not be allowed to enter this study if you are pregnant. If you do enter this study and there is any chance you could become pregnant, you must use one of the allowed contraceptive methods while you are in the study and for at least one month afterwards. Your doctor will explain these methods to you and help you decide which might be best for you. Your doctor can also suggest where you can get more information and advice. (N.B. Oral contraceptives ("the pill") and implanted contraceptives may affect the symptoms of your PMDD and for this reason these hormonal methods of contraception are not permitted during the study).

Even when you use one of the allowed contraceptive methods, there is a small risk you could become pregnant anyway. Because of this, you will be tested during the study to see if you might have become pregnant. These tests **do not prevent** you from becoming pregnant and you will only find this out a week or two **after** you are already pregnant. Even if you stop taking paroxetine CR as soon as your pregnancy is discovered, you cannot be sure your baby has suffered no harm. So, if you should suspect that you are pregnant or are concerned that you may have become pregnant, you should advise your doctor immediately. If you should become pregnant during the study, your doctor will help to make sure you get proper advice.

5. Benefits

You and other patients in the future may benefit from any medical research. Such benefits include the possibility that your condition may improve and that this study may help develop a new therapy for others with similar conditions.

6. Alternative Therapies

Premenstrual symptoms have been treated with a variety of medications, including non-steroidal anti-inflammatory drugs, diuretics, oral contraceptives and other hormonal agents, and vitamins, minerals and herbal remedies.

[If applicable – only insert this statement if applicable for your country: Sarafem (fluoxetine) is the only prescription medication approved for the treatment of PMDD].

If you do not participate in this study or withdraw from the study, alternative treatment options may be discussed with your doctor.

7. Confidentiality and Source Document Review

For Non-US patients:

You understand and consent to the following:

It will be necessary for representatives of SmithKline Beecham or possibly health authorities/drug regulatory agencies to access your medical records. Your participation in the study will be treated as confidential, that is, any personally identifiable information will be held and processed under secure conditions at SmithKline Beecham (or an agent of SmithKline Beecham) with access limited to appropriate SmithKline Beecham staff or other authorised agents having a

requirement to maintain the confidentiality of the information. You will not be referred to by name in any report of the study. Your identity will not be disclosed to any person, except for the purposes described above and in the event of a medical emergency or if required by law.

Your personal data will be processed electronically to determine the outcome of this study, and to provide it to health authorities/drug regulatory agencies. Your data may be transferred to other countries (such as USA). For these purposes SmithKline Beecham complies with internal procedures to protect personal information even in countries whose data privacy laws are less strict than those of this country. The data may also be used for other medical or scientific research purposes. If your data is used for any other purpose it will first be de-identified, that is all personally identifiable information will be removed, and will only be processed in a de-identifiable form.

You may be entitled under law to access your personal data and to have any justifiable corrections made. If you wish to do so, you should request this from the doctor conducting the study.

For US patients:

You understand and consent to the following:

It will be necessary for representatives of SmithKline Beecham or possibly drug or health regulatory agencies to access your medical records. Your participation in the study will be treated as confidential, that is, any personally identifiable information will be held and processed under secure conditions at SmithKline Beecham (or an agent of SmithKline Beecham) with access limited to appropriate SmithKline Beecham staff or other authorised agents having a requirement to maintain the confidentiality of the information. You will not be referred to by name in any report of the study. Your identity will not be disclosed to any person, except for the purposes described above and in the event of a medical emergency or if required by law.

Your personal data will be processed electronically to determine the outcome of this study, and to provide it to drug or health regulatory agencies. Your data may be transferred to other countries for these purposes.

SmithKline Beecham complies with internal procedures to protect personal information even in countries whose data privacy laws are less strict than those of this country. The data may also be used for other medical research purposes.

You may be entitled under law to access your personal data and to have any justifiable corrections made. If you wish to do so, you should request this from the doctor conducting the study.

8. Risk of Injury

The investigators do not expect any unusual risks (other than those noted in [sections 2 and 3](#) above) as a direct result of participation in this project. However, should any unforeseen physical injury occur, appropriate medical care will be provided, but no financial compensation will be given.

9. Right to ask questions and/or withdraw from the study

You have the right to ask any questions concerning the potential and/or known hazards of this study at any time.

You will be informed of any significant new information pertaining to your safety.

If you have any questions concerning this study, please contact.

Name Tel.No

You have the right to withdraw from the study at any time. Participation in this study is voluntary and refusal to participate at any time will involve no penalty of loss of benefits to which you are otherwise entitled, nor will it have any negative consequences or effect on medical care being provided.

Your doctor may withdraw you from the study at any time he/she feels it is in your best interest. For example, at the start of the study you are asked to complete the daily diary in order to confirm your symptoms. When your doctor reviews your diary, your symptom scores may indicate that you are not eligible to enter the study as you do not have PMDD, in which case you would be withdrawn from the study.

If you should withdraw voluntarily from the study or are asked by the doctor to leave the study, you must return all unused study medications. You will be asked questions about your experience with the study drug. You also may be asked to co-operate in having whatever laboratory tests and physical examinations the doctor considers necessary.

10. Compensation

If you become ill or injured as a result of participation in this clinical study, medical treatment will be provided, and the reasonable cost of such treatment will be paid by SmithKline Beecham. If you have any questions concerning the availability of compensation/medical care or if you think you have experienced a drug-related illness or injury you should contact

(name) (tel.)

You will be given a copy of this form to keep.

I ACKNOWLEDGE THAT I HAVE READ AND FULLY UNDERSTAND THE ABOVE EXPLANATION OF THE PROJECT, THAT ALL MY QUESTIONS HAVE BEEN SATISFACTORILY ANSWERED. I AGREE TO PARTICIPATE IN THIS RESEARCH PROJECT.

Signature of Participant Date

I CERTIFY THAT I HAVE EXPLAINED FULLY TO THE ABOVE PATIENT THE NATURE AND PURPOSE, PROCEDURES, POSSIBLE RISKS AND POTENTIAL BENEFITS OF THIS RESEARCH PROJECT.

Signature of Person Who Conducted Informed Date

Consent Discussion

Signature of Investigator (if different from Date
Person Who Performed Consent Discussion)

Appendix D Patient Eligibility Calculation Worksheet

29060 / 717

PATIENT ELIGIBILITY CALCULATION WORKSHEET

1 Record the centre number, patient number, patient initials and the reference cycle number in the boxes below.

29060 / 717 / /

Centre Patient Initials

Reference Cycle (01 / 1A / 02)

2 Measure the scores on the patient's VAS diary for the 4 core PMDD symptoms (depressed mood, tension, affective lability and irritability) and complete the table below for days 6 - 10 and the last 5 days of the cycle (no more than one day's data should be missing for each of these calculations).

FOLLICULAR PHASE
(DAYS 6 - 10 OF CYCLE)

	Day	6	7	8	9	10	Mean Score (Days 6-10)
Depressed Mood							
Tension							
Affective Lability							
Irritability							

LUTEAL PHASE
(LAST 5 DAYS OF CYCLE)

	Day	-5	-4	-3	-2	-1	Mean Score (Last 5 days)
Depressed Mood							
Tension							
Affective Lability							
Irritability							

3 Now calculate the mean score for each of the 4 core symptoms over days 6 - 10 and the last 5 days of the cycle and complete the boxes indicated (shaded area). No more than one day's data should be missing for each of these calculations.

4 Remember that in order to be eligible, a patient must rate at least 200 % higher (ie. worse) on one, or at least 100% higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times \frac{(\text{mean luteal score} - \text{mean follicular score})}{\text{mean follicular score}}$) - (For these items, the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$). Patients do not need to qualify on the same symptom(s) in both reference cycles. Please use the table provided to help you check the patient's eligibility.

* The follicular phase score of $\leq 20\text{mm}$ applies only to the "qualifying items" (those core symptoms showing the 100% or 200% change). For the "non-qualifying symptoms" (ie. the remainder of the four core symptoms other than the qualifying symptoms) the mean follicular phase score should also be low and SB must be consulted prior to randomising a patient if these scores are not $\leq 25\text{mm}$.

5 Please note if the patient was eligible based on these scores.

☐ No

☐ Yes → If "Yes", please tick the box to indicate on which item(s) the patient qualified.

	200%	100%
Depressed Mood	☐	☐
Tension	☐	☐
Affective Lability	☐	☐
Irritability	☐	☐

Appendix E Table of Study Cycle Nomenclature

Treatment / Reference Cycle Names	Study Cycle Names
Reference Cycle 1	Study Cycle 1
Reference Cycle 1a	Study Cycle 1a
Reference Cycle 2	Study Cycle 2
Treatment Cycle 1	Study Cycle 3
Treatment Cycle 2	Study Cycle 4
Treatment Cycle 3	Study Cycle 5

Sample Case Report Form

CONFIDENTIAL

STUDY DATA COLLECTION FORMS																	
Center Number	<table border="1"><tr><td></td><td></td><td></td></tr></table>				Patient Number	<table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						Patient Initials	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>				

PROTOCOL 29060/717

BOOK 1

SCREENING AND BASELINE

**A DOUBLE-BLIND, PLACEBO-CONTROLLED, 3-ARM FIXED DOSE STUDY
OF PAROXETINE CR INTERMITTENT DOSING (12.5MG AND 25MG)
FOR PREMENSTRUAL DYSPHORIC DISORDER.**

CONFIDENTIAL

STUDY DATA COLLECTION FORMS																	
Center Number	<table border="1"><tr><td></td><td></td><td></td></tr></table>				Patient Number	<table border="1"><tr><td></td><td></td><td></td><td></td><td></td></tr></table>						Patient Initials	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>				

PROTOCOL 29060/717

BOOK 2

TREATMENT PHASE

**A DOUBLE-BLIND, PLACEBO-CONTROLLED, 3-ARM FIXED DOSE STUDY
OF PAROXETINE CR INTERMITTENT DOSING (12.5MG AND 25MG)
FOR PREMENSTRUAL DYSPHORIC DISORDER.**

Page 2

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 1 Visit 4	Date of Visit	/	/	
				Day	Month	Year

PATIENT CONTINUATION

Is the patient continuing in the study?

- ☐ No → If "No", please complete all assessments in the Early Withdrawal section
- ☐ Yes → If "Yes", please complete all assessments for this visit

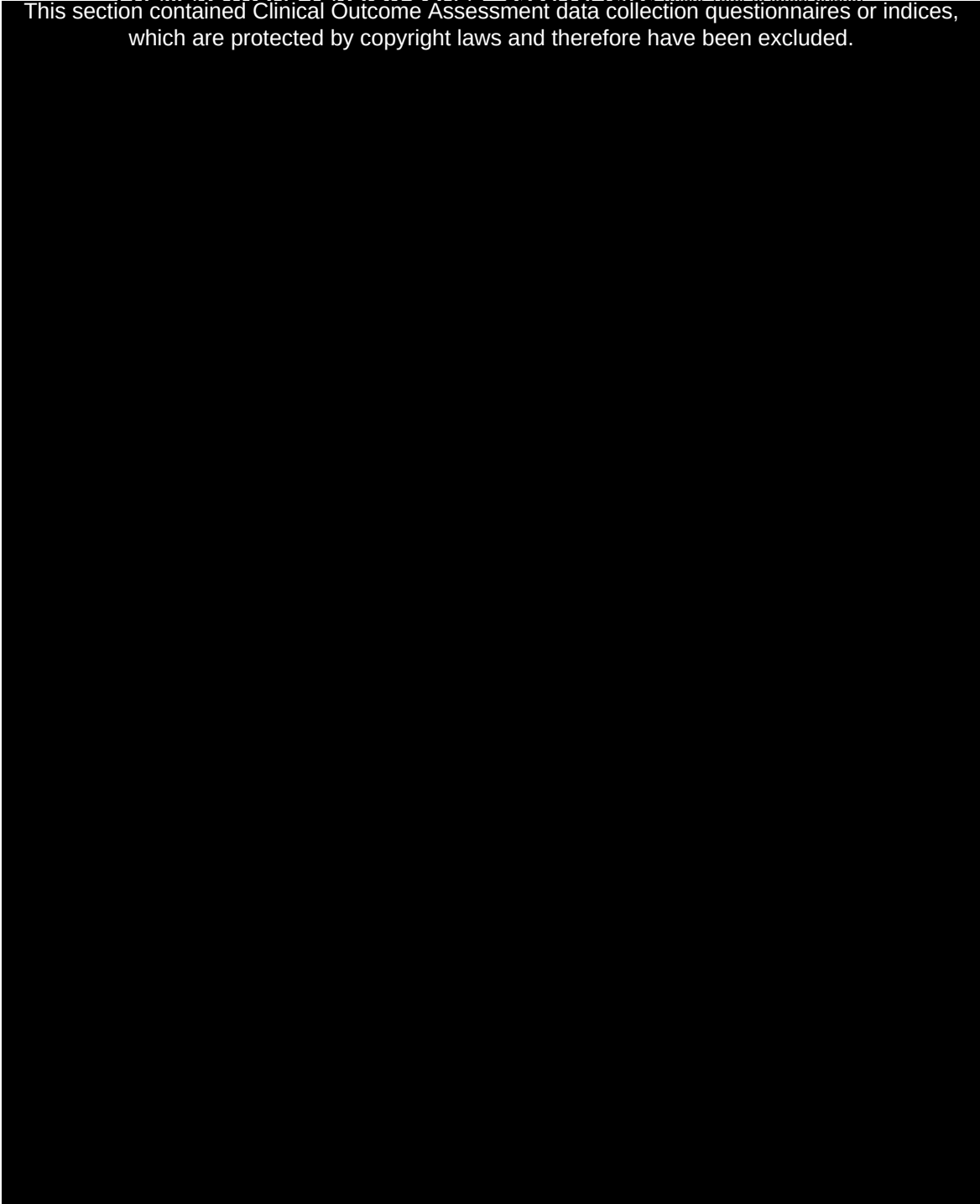
CLINICAL GLOBAL IMPRESSION*This rating refers to the symptomatic luteal phase which has just ended*

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 1 Visit 4

PREMENSTRUAL TENSION SCALE - observer rated (must refer to luteal phase)

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 1 Visit 4

PREMENSTRUAL TENSION SCALE - observer rated cont. (must refer to luteal phase)

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

VITAL SIGNS

Pulse: _____ beats/min

Sitting B.P: _____ / _____ mmHg
(systolic / diastolic)
(after sitting for 3 mins)

Page	5

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 2 (Visit 5)	Date of Visit	/	/	
				Day	Month	Year

PATIENT CONTINUATION

Is the patient continuing in the study?

- ☐ No → If "No", please complete all assessments in the Early Withdrawal section
- ☐ Yes → If "Yes", please complete all assessments for this visit

CLINICAL GLOBAL IMPRESSION

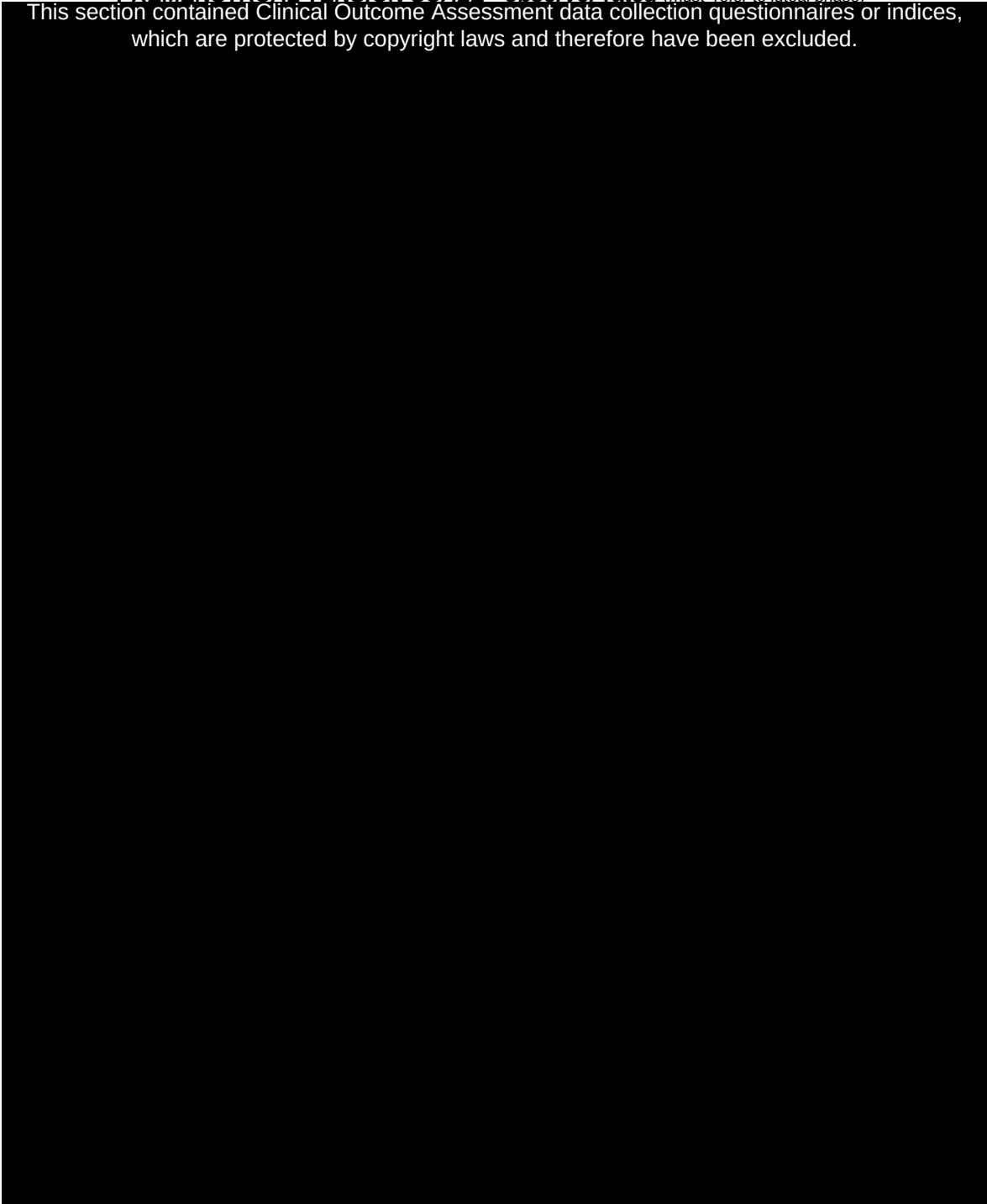
This rating refers to the symptomatic luteal phase which has just ended.

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 2 (Visit 5)

~~PREMENSTRUAL TENSION SCALE - observer rated~~ *(must refer to luteal phase)*

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 2 (Visit 5)

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

VITAL SIGNS

Pulse: _____ beats/min	Sitting B.P: _____ / _____ mmHg (systolic / diastolic) (after sitting for 3 mins)

Page 8

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 3 (Visit 6)	Date of Visit	/	/	
				Day	Month	Year

PATIENT CONTINUATION

Is the patient continuing in the study?

- ☐ No → If "No", please complete all assessments in the Early Withdrawal section
- ☐ Yes → If "Yes", please complete all assessments for this visit

CLINICAL GLOBAL IMPRESSION*This rating refers to the symptomatic luteal phase which has just ended.*

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

WEIGHT

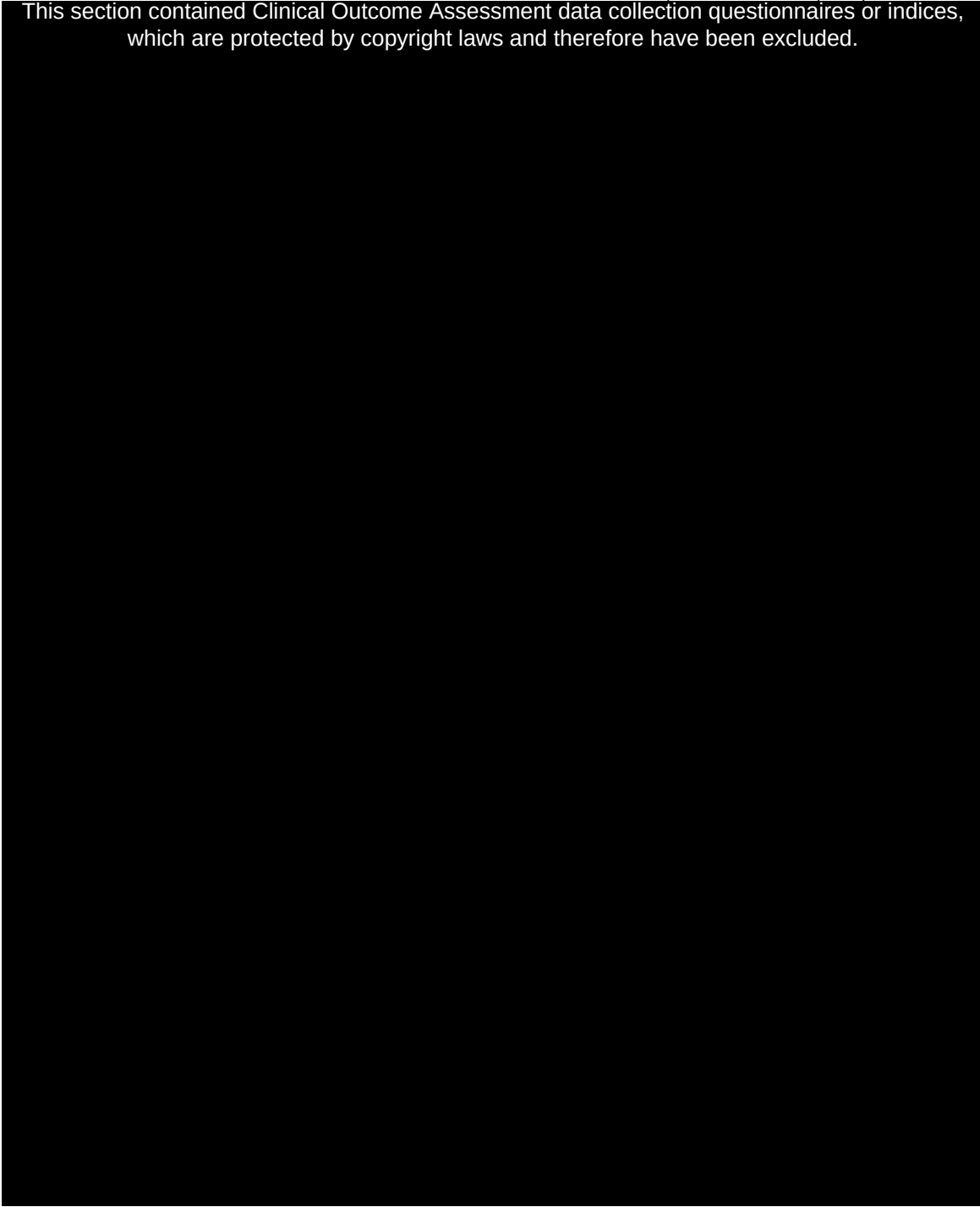
Weight:

☐ lbs☐ kg

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 3 (Visit 6)

PREMENSTRUAL TENSION SCALE - observer rated *(must refer to luteal phase)*

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 3 (Visit 6)

PREMENSTRUAL TENSION SCALE - observer rated cont. (must refer to luteal phase)

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

PATIENT EVALUATION OF STUDY MEDICATION

Please ask the patient the following question and then mark the one box below that most appropriately describes their response :

"Did you find the medication sufficiently beneficial to ask for it again ?"

☐ Yes

☐ No

☐ Not sure

☐

→ If "No" or "Not sure", please ask the patient to volunteer a reason for her response.

N.B. This reason should not be prompted, but should be interpreted by the Investigator into the single most appropriate category below

☐ Lack of efficacy

☐ Side effects (please ensure that this is consistent with the adverse experiences recorded during the study)

☐ Anti-medication (ie. dislike of taking tablets)

☐ Other, please specify : _____

PROGRESS NOTES	PROTOCOL 29060/717	End of Treatment Cycle 3 (Visit 6)

VITAL SIGNS

Pulse: _____ beats/min

 Sitting B.P: _____ / _____ mmHg
 (systolic / diastolic)
 (after sitting for 3 mins)
PREGNANCY TEST*Please take a blood sample for serum pregnancy test.*
 Sample Date: _____ / _____ / _____
 (Day / Month / Year)

Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly (please ensure to include the sample for laboratory evaluation).
To be completed when the laboratory results are available

Was the serum pregnancy test positive ?

☐ No☐ Yes → If "Yes", please report within 24 hours using the SAE form.**LABORATORY EVALUATION***Please take a blood sample for routine analysis.*
 Sample Date: _____ / _____ / _____
 (Day / Month / Year)

Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly (please ensure to include the sample for the pregnancy test).
To be completed when the laboratory results are available

Were any clinically significant abnormalities detected at Visit 6?

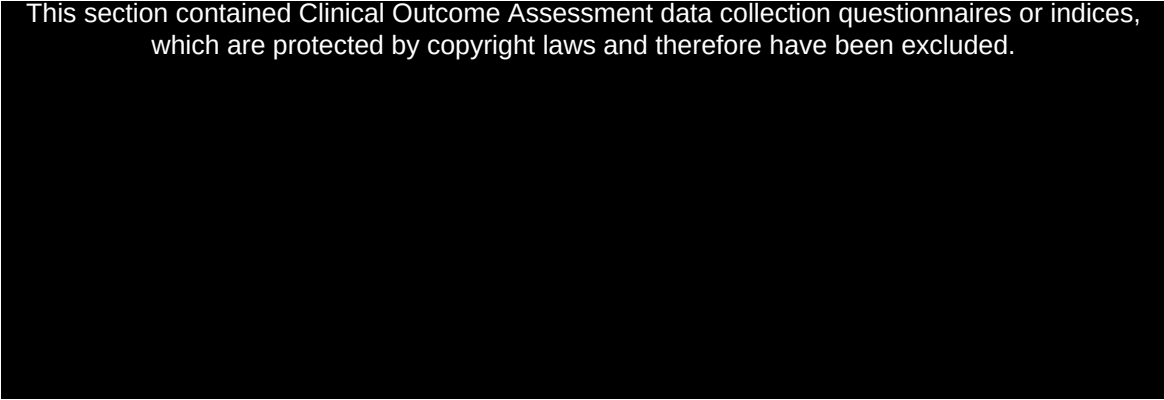
☐ No
☐ Yes → If "Yes", please record details in the Adverse Experiences section (Page 20) and repeat laboratory assessments at the 14 Day Follow-up.
Attach the Quest Diagnostics laboratory report in the plastic wallet at the end of this workbook.**Please record the laboratory numbers below or affix the laboratory label in the box provided**ACCT REQ

Attach label here

PROGRESS NOTES	PROTOCOL 29060/717	Early Withdrawal	Date of Visit	/	/	
				Day	Month	Year

CLINICAL GLOBAL IMPRESSION

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



PROGRESS
NOTESPROTOCOL
29060/717

Early Withdrawal

PATIENT EVALUATION OF STUDY MEDICATION

Please ask the patient the following question and then mark the one box below that most appropriately describes their response :

"Did you find the medication sufficiently beneficial to ask for it again ?"

☐ Yes

☐ No

☐ Not sure

☐


If "No" or "Not sure", please ask the patient to volunteer a reason for her response.

N.B. This reason should not be prompted, but should be interpreted by the Investigator into the single most appropriate category below

☐ Lack of efficacy

☐ Side effects (please ensure that this is consistent with the adverse experiences recorded during the study)

☐ Anti-medication (ie. dislike of taking tablets)

☐

Other, please specify : _____

VITAL SIGNS

Pulse: _____ beats/min

Sitting B.P: _____ / _____ mmHg
(systolic / diastolic)
(after sitting for 3 mins)

WEIGHT

Weight:

☐ lbs

☐ kg

PROGRESS
NOTESPROTOCOL
29060/717

Early Withdrawal

PREGNANCY TEST*Please take a blood sample for serum pregnancy test.*Sample Date: / /
(Day / Month / Year)***Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly (please ensure to include the sample for laboratory evaluation).******To be completed when the laboratory results are available***

Was the serum pregnancy test positive ?

☐ No☐ Yes → *If "Yes", please report within 24 hours using the SAE form***LABORATORY EVALUATION***Please take a blood sample for routine analysis.*Sample Date: / /
(Day / Month / Year)***Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly (please ensure to include the sample for the pregnancy test).******To be completed when the laboratory results are available***

Were any clinically significant abnormalities detected at the Early Withdrawal Visit?

☐ No☐ Yes → *If "Yes", please record details in the Adverse Experiences section (Page 20) and repeat laboratory assessments at the next visit****Attach the Quest Diagnostics laboratory report in the plastic wallet at the end of this workbook.******Please record the laboratory numbers below or affix the laboratory label in the box provided***ACCT REQ

Attach label here

PROGRESS NOTES	PROTOCOL 29060/717	Study Conclusion	Date of Visit	/	/	
				Day	Month	Year

STUDY CONCLUSION

Did the patient complete the study as planned?

☐ Yes → (A patient will be considered to have completed the study if they progress through the study up to and including the End of Treatment Cycle 3 visit)

☐ No → If 'No', please mark the one most appropriate reason below (mark one box only).

- ☐ Adverse Experience (please complete AE page)
- ☐ Lack of efficacy
- ☐ Protocol Deviation (including non-compliance/protocol violation)
- ☐ Lost to follow-up
- ☐ Other - specify: _____

Which was the last visit the patient attended: ☐ Baseline

☐ End of Treatment Cycle 1 Visit

☐ End of Treatment Cycle 2 Visit

Date of Final Dose of double-blind study medication : / /
(Day / Month / Year)

Please complete the Investigator Signature page

PROGRESS NOTES	PROTOCOL 29060/717	14 Day Follow-Up (Visit 7)	Date of Visit		
			Day	Month	Year

VITAL SIGNS

Pulse: _____ beats/min

 Sitting B.P: _____ / _____ mmHg
 (systolic / diastolic)
 (after sitting for 3 mins)
LABORATORY EVALUATION

Please take a blood sample for routine analysis if an abnormality was detected at Visit 6 or Early Withdrawal.

 Sample Date: ____/____/____ or ☐ Not required
 (Day / Month / Year)

Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly

To be completed when the laboratory results are available

Were any clinically significant abnormalities detected at this visit ?

☐ No

☐ Yes → If "Yes", please record details in the Adverse Experiences section (Page 20).

Attach the Quest Diagnostics laboratory report in the plastic wallet at the end of this workbook.

Please record the laboratory numbers below or affix the laboratory label in the box provided

ACCT REQ

Attach label here

Page	17

PROGRESS NOTES	PROTOCOL 29060/717	28 Day Follow-Up Visit (Visit 8)	Date of Visit			
				Day	Month	Year

VITAL SIGNS

Pulse: _____ beats/min	Sitting B.P.: _____ / _____ mmHg (systolic / diastolic) (after sitting for 3 mins)

CONCOMITANT MEDICATION***ROUTE KEY***

PO = by mouth
IV = intravenous
IM = intramuscular
IAR = intra-arterial
TO = topical
SL = sublingual
IT = intrathecal
VA = vaginal
NA = nasal
IA = intra-articular injection
TD = transdermal
IH = inhaled
SC = subcutaneous
PR = rectal
ID = intradermal

PROGRESS
NOTESPROTOCOL
29060/717**CONCOMITANT MEDICATION**

Please mark appropriate box below or complete page with concomitant medication details.

☐ No concomitant medication

Any new medical illness/diagnosis or symptoms in the absence of a diagnosis should be recorded on the Adverse Experience form using the same terminology.

If a medication was marked 'Continuing' at the last visit, but has since had a dosage change or has been stopped, it must be recorded as a change with the start and end date.

Drug Name (Trade Name Preferred)	Total Daily Dose (eg 500mg)	Route*	Medical Illness/ Diagnosis (or symptom in absence of diagnosis)	Start Date (be as precise as possible)			End Date (or if continuing mark box)			☐
				Day	Mth	Yr	Day	Mth	Yr	
				/	/		/	/		☐
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* For Route, see route key for acceptable abbreviations

PROGRESS NOTES	PROTOCOL 29060/717	

CONCOMITANT MEDICATION (CONTINUED)

Any new medical illness/diagnosis or symptoms in the absence of a diagnosis should be recorded on the Adverse Experience form using the same terminology.

If a medication was marked 'Continuing' at the last visit, but has since had a dosage change or has been stopped, it must be recorded as a change with the start and end date

[illegible]

* For Route, see route key for acceptable abbreviations

ADVERSE EXPERIENCES**DEFINITIONS****INTENSITY (Maximum)**

MILD	Adverse experience which is easily tolerated
MODERATE	Adverse experience sufficiently discomforting to interfere with daily activities
SEVERE	Adverse experience which prevents normal everyday activities

RELATIONSHIP TO INVESTIGATIONAL DRUG

RELATED	There is a direct cause and effect relationship between the adverse experience and the study drug.
POSSIBLY RELATED	A direct cause and effect relationship between the drug and the adverse experience has not been demonstrated but is possible or likely
PROBABLY UNRELATED	Cause and effect relationship between the drug and the adverse experience has not been demonstrated, is improbable but not impossible.
UNRELATED	The adverse experience is definitely not related to the test drug.

SERIOUS ADVERSE EXPERIENCE

A serious adverse experience is any experience which is :

- fatal
- life threatening
- permanently or temporarily disabling
- incapacitating
- results in hospitalisation (excluding elective surgery or routine clinical procedures)
- prolongs a hospital stay
- associated with congenital abnormality, carcinoma or overdose

In addition any event which the investigator regards as serious or which would suggest any significant hazard, contraindication, side effect or precaution that may be associated with the study procedures should be reported as a serious experience

**PLEASE REMEMBER ALL QUESTIONS ON THE ADVERSE EXPERIENCES FORM
MUST BE COMPLETED**

Use each form for a maximum of three events. If additional events are noted please use a separate form

PROGRESS NOTES	PROTOCOL 29060/717	

ADVERSE EXPERIENCES

RECORD ANY ADVERSE EXPERIENCE OBSERVED OR ELICITED BY THE FOLLOWING DIRECT QUESTION TO PATIENT:
Do you feel different in any way since starting the treatment or since the last visit?

Please record one experience per column or mark this box to indicate no adverse experiences ☐

EXPERIENCE				
Date Started		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Date Stopped		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Duration if less than 24 hours		<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins
Experience continuing at end of study		☐	☐	☐
Course	Continuous	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	If NO, no of episodes	<u> </u> <u> </u>	<u> </u> <u> </u>	<u> </u> <u> </u>
Intensity	1. Mild	☐	☐	☐
	2. Moderate	☐	☐	☐
	3. Severe	☐	☐	☐
Action taken on Study Medication	1. None	☐	☐	☐
	2. Dose decreased	☐	☐	☐
	3. Dose increased	☐	☐	☐
	4. Drug stopped	☐	☐	☐
Suspected Relationship	1. Related	☐	☐	☐
	2. Possibly related	☐	☐	☐
	3. Probably unrelated	☐	☐	☐
	4. Unrelated	☐	☐	☐
Corrective Therapy	If 'YES' record on Medication form	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Do you consider this a serious adverse experience by the definitions on the tab?		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
		AE Number <u> </u>	AE Number <u> </u>	AE Number <u> </u>

If "YES", report to SB by telephone within 24 hours

If patient died, complete Form D

PROGRESS NOTES	PROTOCOL 29060/717	

ADVERSE EXPERIENCES

RECORD ANY ADVERSE EXPERIENCE OBSERVED OR ELICITED BY THE FOLLOWING DIRECT QUESTION TO PATIENT: <i>Do you feel different in any way since starting the treatment or since the last visit?</i>				
Please record one experience per column or mark this box to indicate no adverse experiences ☐				
EXPERIENCE				
Date Started		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Date Stopped		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Duration if less than 24 hours		<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins
Experience continuing at end of study		☐	☐	☐
Course	Continuous	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	If NO, no of episodes	<u> </u> <u> </u>	<u> </u> <u> </u>	<u> </u> <u> </u>
Intensity	1. Mild	☐	☐	☐
	2. Moderate	☐	☐	☐
	3. Severe	☐	☐	☐
Action taken on Study Medication	1. None	☐	☐	☐
	2. Dose decreased	☐	☐	☐
	3. Dose increased	☐	☐	☐
	4. Drug stopped	☐	☐	☐
Suspected Relationship	1. Related	☐	☐	☐
	2. Possibly related	☐	☐	☐
	3. Probably unrelated	☐	☐	☐
	4. Unrelated	☐	☐	☐
Corrective Therapy	If 'YES' record on Medication form	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Do you consider this a serious adverse experience by the definitions on the tab?		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
		AE Number <u> </u>	AE Number <u> </u>	AE Number <u> </u>
If "YES", report to SB by telephone within 24 hours				

If patient died, complete Form D

PROGRESS NOTES	PROTOCOL 29060/717	

ADVERSE EXPERIENCES

RECORD ANY ADVERSE EXPERIENCE OBSERVED OR ELICITED BY THE FOLLOWING DIRECT QUESTION TO PATIENT: <i>Do you feel different in any way since starting the treatment or since the last visit?</i>				
Please record one experience per column or mark this box to indicate no adverse experiences ☐				
EXPERIENCE				
Date Started		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Date Stopped		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Duration if less than 24 hours		<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins
Experience continuing at end of study		☐	☐	☐
Course	Continuous	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	If NO, no of episodes	<u> </u> <u> </u>	<u> </u> <u> </u>	<u> </u> <u> </u>
Intensity	1. Mild	☐	☐	☐
	2. Moderate	☐	☐	☐
	3. Severe	☐	☐	☐
Action taken on Study Medication	1. None	☐	☐	☐
	2. Dose decreased	☐	☐	☐
	3. Dose increased	☐	☐	☐
	4. Drug stopped	☐	☐	☐
Suspected Relationship	1. Related	☐	☐	☐
	2. Possibly related	☐	☐	☐
	3. Probably unrelated	☐	☐	☐
	4. Unrelated	☐	☐	☐
Corrective Therapy	If 'YES' record on Medication form	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Do you consider this a serious adverse experience by the definitions on the tab?		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
		AE Number <u> </u>	AE Number <u> </u>	AE Number <u> </u>
If "YES", report to SB by telephone within 24 hours				

If patient died, complete Form D

PROGRESS NOTES	PROTOCOL 29060/717	Medication Record

MEDICATION RECORD

Cycle	Start Date	Stop Date	Number of capsules dispensed (eg. 24)	Unused Medication Did the patient return capsules?	* Interruption of > 3 days ?
Treatment Cycle 1	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)		☐ No ☐ Yes, how many ? →	☐ No ☐ Yes
Treatment Cycle 2	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)		☐ No ☐ Yes, how many ? →	☐ No ☐ Yes
Treatment Cycle 3	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)		☐ No ☐ Yes, how many ? →	☐ No ☐ Yes
<i>* If there has been an interruption in medication for more than three consecutive days, SB should be contacted to confirm whether the patient must be withdrawn from the study.</i> <i>If patient has been withdrawn between visits, please ensure that the study medication record is completed</i>					

MEDICATION LABEL

Please affix study medication label for Treatment Cycles 1 to 3 to the Medication Label Record page (see separate pad) and record the 6-digit container number below

Container number :

PROGRESS NOTES	PROTOCOL 29060/717	Form D

FORM D

Certified Cause of Death _____ Date of Death <u> </u> / <u> </u> / <u> </u> (Day / Month / Year) → <i>Please complete Serious Adverse Experience section.</i> Was a post-mortem carried out? ☐ No ☐ Yes → <i>If 'Yes' please summarise findings (include diagnosis):</i> _____ _____ _____ _____

wg_formd_uk_01

PROGRESS NOTES	PROTOCOL 29060/717	Screening (Visit 1)	Date of Visit		
			Day	Month	Year

DEMOGRAPHY / PHYSICAL EXAMINATION

Date of birth : <u> </u> / <u> </u> / <u> </u> (Day / Month / Year)	Height: <u> </u> <u> </u> <u> </u> <u> </u> <u> </u> ☐ in ☐ cm	Pulse: <u> </u> bpm
Gender: Female	Weight: <u> </u> <u> </u> <u> </u> <u> </u> <u> </u> ☐ lbs ☐ kg	Sitting BP: <u> </u> / <u> </u> mmHg (systolic / diastolic) (after sitting for 3 mins)
Race: ☐ White ☐ Black ☐ Oriental ☐ Other → specify : <u> </u>		

SIGNIFICANT MEDICAL/SURGICAL HISTORY AND PHYSICAL EXAMINATION

All signs and symptoms referring to a single diagnosis must be recorded on the same line with the diagnosis. Signs and symptoms without an associated diagnosis must be recorded as a new sign and symptom on separate lines.

Record any significant medical or surgical condition that the patient is suffering from or has ever suffered from (excluding psychiatric disorders which are to be recorded at Visit 2(A)).

(tick both if applicable)

Diagnosis	Year of first diagnosis	Past	Current/Active
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐

PROGRESS NOTES	PROTOCOL 29060/717	Screening (Visit 1)

DSM-IV PREMENSTRUAL DYSPHORIC DISORDER**Research Criteria for Premenstrual Dysphoric Disorder**

	Yes	No
A. In most menstrual cycles during the past year, five (or more) of the following symptoms were present for most of the time during the last week of the luteal phase, began to remit within a few days after the onset of the follicular phase, and were absent in the week postmenses; with at least one of the symptoms being either (1*), (2*), (3*) or (4*) :	☐	☐
(1*) markedly depressed mood, feelings of hopelessness, or self-deprecating thoughts	☐	☐
(2*) marked anxiety, tension, feelings of being "keyed up" or "on edge"	☐	☐
(3*) marked affective lability (eg. feeling suddenly sad or tearful or increased sensitivity to rejection)	☐	☐
(4*) persistent and marked anger or irritability or increased interpersonal conflicts	☐	☐
(5) decreased interest in usual activities (eg. work, school, friends, hobbies)	☐	☐
(6) subjective sense of difficulty in concentrating	☐	☐
(7) lethargy, easy fatigability, or marked lack of energy	☐	☐
(8) marked change in appetite, overeating, or specific food cravings	☐	☐
(9) hypersomnia or insomnia	☐	☐
(10) a subjective sense of being overwhelmed or out of control	☐	☐
(11) other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of 'bloating', weight gain.	☐	☐

Note: In menstruating females, the luteal phase corresponds to the period between ovulation and the onset of menses, and the follicular phase begins with menses.

B. The disturbance markedly interferes with work or school or with social activities and relationships with others (eg. avoidance of social activities, decreased productivity and efficiency at work or school)	☐	☐
C. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as Major Depressive Disorder, Panic Disorder, Dysthymic Disorder or a Personality Disorder (although it may be superimposed on any of these disorders)	☐	☐
D. Criteria A, B and C must be confirmed by prospective daily ratings during at least two consecutive symptomatic cycles. The diagnosis may be made provisionally prior to this confirmation.		

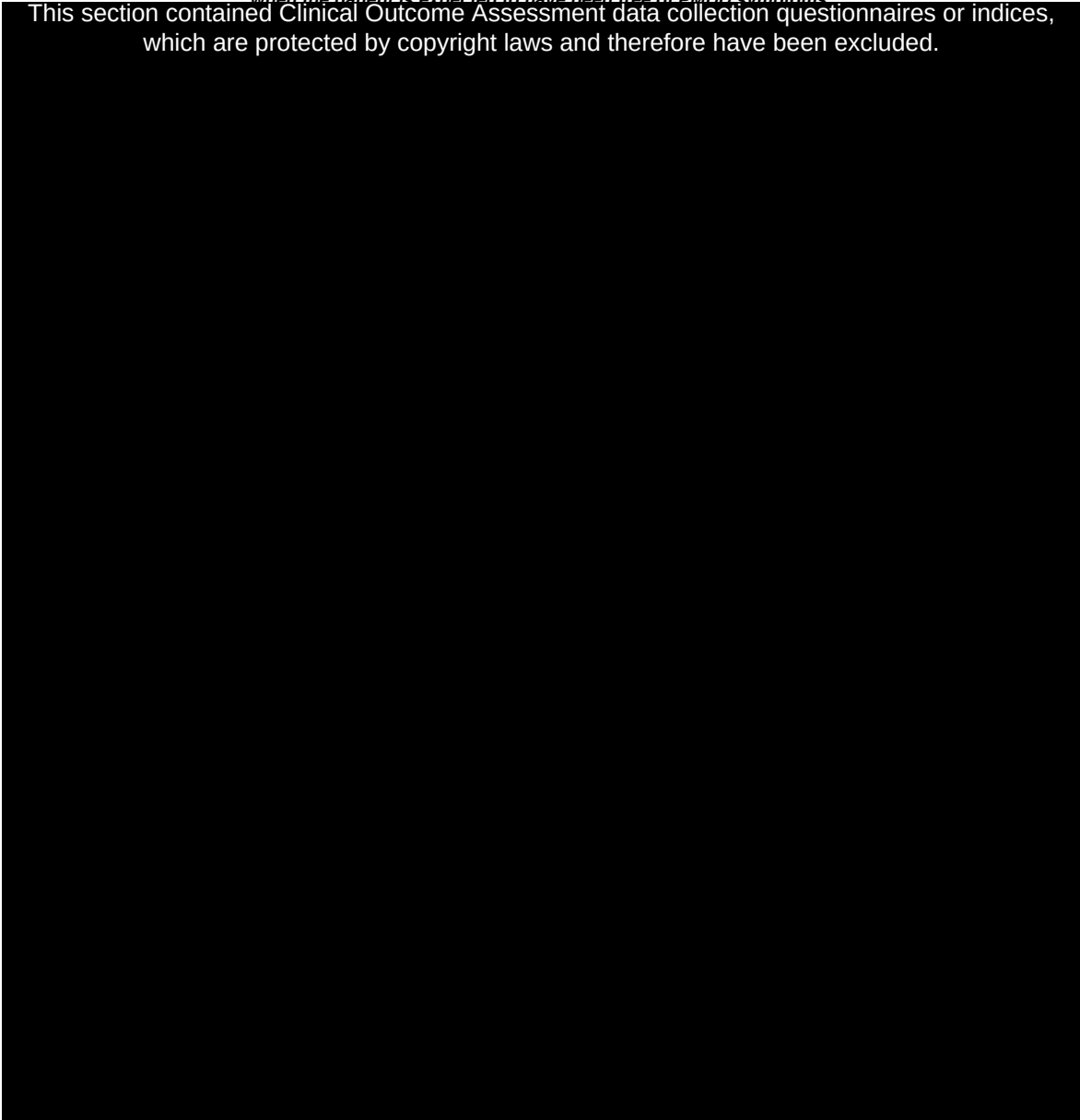
Do not enter the patient into the study if the answer to sections A, B or C is 'No'

PROGRESS NOTES	PROTOCOL 29060/717	Screening (Visit 1)

MONTGOMERY AND ASBERG DEPRESSION RATING SCALE (MADRS)

*Ratings should be based on symptoms and signs occurring during the WEEK prior to the interview,
when the patient is expected to have been free of PMDD symptoms.*

This section contained Clinical Outcome Assessment data collection questionnaires or indices,
which are protected by copyright laws and therefore have been excluded.



PROGRESS NOTES	PROTOCOL 29060/717	Screening (Visit 1)

SCREENING ELIGIBILITY CRITERIA

INCLUSION CRITERIA		Yes	No
The patient is not eligible if any of the following inclusion criteria is answered "No"			
1.	Is the patient a female outpatient who is between 18 - 45 years of age?	☐	☐
2.	Does the patient have regular menstrual cycles (duration between 22 - 35 days)?	☐	☐
3.	Does the patient meet preliminary DSM-IV criteria for PMDD? <i>Note: Criteria A-C are to be fulfilled at Visit 1 Screening interview. Criterion D to be fulfilled following the two reference cycles.</i>	☐	☐
4.	Have PMDD symptoms been present for at least the past year during which symptoms were present in at least 9 out of 12 menstrual cycles?	☐	☐
5.	Is the patient using an adequate non-hormonal form of contraception? (Methods such as IUD, tubal ligation and double-barrier contraception (any two of diaphragm / spermicidal foam / condom) are acceptable while the use of oral contraceptives or systemic contraception are not).	☐	☐
6.	Has the patient given written informed consent to participate in the study?	☐	☐
Do not admit the patient into the study if any of the above boxes have been marked "NO".			
EXCLUSION CRITERIA		Yes	No
The patient is not eligible if any of the following exclusion criteria is answered "Yes"			
1.	Does the patient have a history of any Axis 1 disorder (other than PMDD or specific phobias) in the 6 months prior to this Screening Visit?	☐	☐
2.	Does the patient suffer from any severe, clinically significant, co-existing condition(s) which, in the investigator's opinion, would render the patient unsuitable for the study?	☐	☐
3.	Is the patient diagnosed as having a gynaecological disease (eg. uterine fibroids, ovarian/uterine/cervical carcinoma, or endometriosis).	☐	☐
4.	Does the patient have a MADRS score of ≥ 10 during the follicular phase of the menstrual cycle?	☐	☐
5.	Is the patient a significant suicidal risk?	☐	☐
6.	Is the patient using any ongoing medication (including herbal medication and any use of sedatives/hypnotics) which in the opinion of the investigator could affect the patient's PMDD symptomatology (within one month prior to the Screening Visit and for the duration of the study period) except the following permitted treatments. Permitted medications include the occasional use of fibrinolysis inhibitors for abundant menstrual bleeding. Also permitted are the occasional use of paracetamol (acetaminophen), acetylsalicylic acid or other NSAIDs to treat menstrual cramps or headaches (their use must be documented in the Concomitant Medication section).	☐	☐
7.	Has the patient previously received adequate treatment with an SSRI for premenstrual symptoms (defined as continuous or intermittent treatment for at least 3 consecutive menstrual cycles on an adequate dose equivalent to Prozac 20mg)?	☐	☐
8.	Does the patient have a history of hypersensitivity or adverse reaction to paroxetine or other SSRI's?	☐	☐
9.	Has the patient participated in a psychiatric drug trial (including PMDD trials) in the past 6 months?	☐	☐
10.	Is the patient breast-feeding, pregnant, or planning to become pregnant during the study period?	☐	☐
11.	Has the patient used an investigational drug within 30 days or 5 half-lives (whichever is longer) prior to this Screening Visit?	☐	☐
12.	Has the patient shown any characteristics which, in the opinion of the investigator, are likely to reduce compliance with the protocol (eg. poor medication compliance, poor diary card compliance)?	☐	☐
Do not admit the patient into the study if any of the questions in the Exclusion Criteria have been marked "YES".			

PROGRESS
NOTESPROTOCOL
29060/717

Screening (Visit 1)

PATIENT ELIGIBILITY

I have assessed the patient and checked the Screening Inclusion/Exclusion Criteria and the patient :

- ☐ is not eligible to participate in the study
- Please complete the Patient Continuation/Withdrawal record (Page 20)
 - Advise the patient where to seek help for premenstrual complaints
- ☐ is eligible to participate in the study
- **Please issue the patient with diaries for Reference Cycle 1 (Study Cycle 1 diary) and Reference Cycle 2 (Study Cycle 2 diary).**
Explain to her how and when these diaries should be completed.
 - Remind the patient to start recording her symptoms from the first day of her next menstrual cycle (Reference Cycle 1), **remembering that Day 1 is the first day of continuous bleeding, not spotting.**
 - Remind the patient to begin recording her symptoms in the second diary from Day 1 of Reference Cycle 2 (Study Cycle 2 diary).
 - Make an appointment with the patient to return for her next clinic visit between Days 1 - 3 of the next menstrual cycle. The patient must take the completed Study Cycle 1 diary card to the clinic at this visit for collection and review. They should also bring the Study Cycle 2 diary.

PROGRESS NOTES	PROTOCOL 29060/717	End Of Reference Cycle 1 (Visit 2)	Date of Visit	/	/
			Day	Month	Year

PATIENT ELIGIBILITY

Collect the patient diary for Reference Cycle 1 (Study Cycle 1 diary) and check the scores. The patient must rate at least 200 % higher (ie. worse) on one, or at least 100 % higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ((\text{mean luteal score} - \text{mean follicular score}) / \text{mean follicular score})$) - (For these items, the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$). Patients do not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores should also be low and SB must be consulted prior to inclusion of a patient if these scores are not $\leq 25\text{mm}$.

Is the patient still eligible for inclusion in the study based on the Reference Cycle 1 VAS Scores? ☐ Yes ☐ No

Is the patient still eligible for inclusion in the study based on all considerations (eg. changes in prohibited medication, poor diary card compliance) ? ☐ Yes ☐ No

Overall, is the patient still eligible for inclusion in the study?

- ☐ Yes → If "Yes", please do not complete any further assessments in this visit. Please go to the End of Reference Cycle 1(A) Visit and continue to complete assessments there, beginning with "Vital Signs" (i.e. "Patient Eligibility" should not be rated again).
- ☐ No → If "No", there are two options : (please indicate (✓) which one is being taken in the boxes provided)
- ☐ Exclude the patient from the study
- Collect unused diary card
 - Complete the Vital Signs, Concomitant Medication and Baseline Adverse Experience panels for this visit
 - Complete the Patient Continuation/Withdrawal Record
 - Advise the patient where to seek help for premenstrual complaints
- ☐ Ask the patient to complete an additional Reference Cycle
- Complete the Vital Signs, Concomitant Medication and Baseline Adverse Experience panels for this visit
 - Mark the current patient diary "Study Cycle 1(A)"
 - Instruct the patient to continue recording the symptoms for her current menstrual cycle in the Study Cycle 1(A) diary
 - Issue the patient with a diary card for "Study Cycle 2"
 - Remind the patient to begin completing the Study Cycle 2 diary from the first day of her next menstrual cycle, remembering that Day 1 is the first day of continuous bleeding, not spotting
 - Make an appointment with the patient to return for her next clinic visit between Days 1 - 3 of her next menstrual cycle. The patient must take the completed Study Cycle 1(A) diary card to the clinic at this visit for collection and review

VITAL SIGNS

Pulse: _____ beats/min

Sitting B.P: _____ / _____ mmHg
(systolic / diastolic)
(after sitting for 3 mins)

PROGRESS NOTES	PROTOCOL 29060/717	End Of Reference Cycle 1(A) (Visit 2A)	Date of Visit	/	/	
			Day	Month	Year	

PATIENT ELIGIBILITY

Collect the patient diary for Reference Cycle 1(A) (Study Cycle 1(A) diary) and check the scores*. The patient must rate at least 200 % higher (ie. worse) on one, or at least 100 % higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ((\text{mean luteal score} - \text{mean follicular score}) / \text{mean follicular score})$) - (For these items, the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$). Patients do not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores should also be low and SB must be consulted prior to inclusion of a patient if these scores are not $\leq 25\text{mm}$.

Is the patient still eligible for inclusion in the study based on the Reference Cycle 1(A) VAS Scores? ☐ Yes ☐ No

Is the patient still eligible for inclusion in the study based on all considerations (eg. changes in prohibited medication, poor diary card compliance)? ☐ Yes ☐ No

Overall, is the patient still eligible for inclusion in the study?

- ☐ Yes → If "Yes", please complete the procedures for this visit
- ☐ No → If "No", the patient must be excluded from the study
- Collect Study Cycle 2 diary card
 - Complete the Vital Signs, Concomitant Medication and Baseline Adverse Experience panels for this visit
 - Complete the Patient Continuation/Withdrawal record
 - Advise the patient where to seek help for premenstrual complaints

* The VAS data from the Study Cycle 1 diary will already have been checked at Visit 2

VITAL SIGNS

Pulse: _____ beats/min

Sitting B.P: _____ / _____ mmHg
(systolic / diastolic)
(after sitting for 3 mins)

PROGRESS
NOTESPROTOCOL
29060/717End Of Reference Cycle 1(A)
(Visit 2A)**HISTORY OF PREMENSTRUAL DYSPHORIC DISORDER (PMDD)**

Please provide a response to each item

Age at onset of first PMDD symptoms ?

Onset of PMDD coincided with :

Yes No

Menarche

Childbirth

Starting oral contraception

Stopping oral contraception

Sterilization

Other, specify :

Have PMDD symptoms persisted since initial onset ?

☐ Yes →

If "Yes", please specify:

Yrs

Mths

duration of episode

☐ No →

If "No", please specify:

Yrs

Mths

duration of current episode

duration of longest episode

OBSTETRICS/GYNAECOLOGICAL HISTORY

Please provide a response to each item

Number of pregnancies

Number of children

Number of spontaneous miscarriages

Number of terminations of pregnancy

Number of D&C's (dilatation and curettage)

Does the patient report a recent/current history of :

Yes No

Heavy periods (heavy bleeding during periods or excessive duration) ?

Painful periods ?

PROGRESS NOTES	PROTOCOL 29060/717	End Of Reference Cycle 1(A) (Visit 2A)

PREVIOUS TREATMENT FOR PREMENSTRUAL DYSPHORIC DISORDER

Has the patient used any of the following as a treatment for PMDD :		
(Rate response to treatment as follows : None = 0, Mild = 1, Moderate = 2 and Marked = 3. If the patient has used a given drug more than once then record the response rate for the most recent usage)		
	No	Yes Response
Antidepressants, anxiolytics, neuroleptics, lithium or other psychotropic drugs	☐	☐ → ☐
Oral contraception or hormone preparations	☐	☐ → ☐
Pyridoxine (vitamin B6)	☐	☐ → ☐
Gamma-linolenic acid (evening primrose oil)	☐	☐ → ☐
d-Fenfluramine	☐	☐ → ☐
Non-steroidal anti-inflammatory drugs	☐	☐ → ☐
Tryptophan	☐	☐ → ☐
L-Dopa	☐	☐ → ☐
Bromocriptine	☐	☐ → ☐
Mefenamic acid	☐	☐ → ☐
Diuretics	☐	☐ → ☐
Clonidine	☐	☐ → ☐
B-Blockers	☐	☐ → ☐
Verapamil	☐	☐ → ☐
Calcium	☐	☐ → ☐
Other, please specify : _____	☐	☐ → ☐
_____	☐	☐ → ☐
_____	☐	☐ → ☐

PROGRESS NOTES	PROTOCOL 29060/717	End Of Reference Cycle 1(A) (Visit 2A)

PSYCHIATRIC HISTORY

Please conduct a full psychiatric interview with the patient and, as part of this, complete the Mini International Neuropsychiatric Interview (MINI)

With reference to the Mini International Neuropsychiatric Interview (MINI) (version 4.4), please state if the patient has the following conditions (**please answer all questions below**) and, if applicable, either record the start and stop dates or record the start date and indicate that the condition is continuing.

Psychiatric condition	Yes	No	Start Date			End Date			Continuing
			Day	Mth	Yr	Day	Mth	Yr	
A. Major Depressive Episode	☐	☐	/	/		/	/		☐
B. Dysthymia	☐	☐	/	/		/	/		☐
C. (Hypo) Manic Episode	☐	☐	/	/		/	/		☐
D. Panic Disorder	☐	☐	/	/		/	/		☐
E. Agoraphobia	☐	☐	/	/		/	/		☐
F. Social Phobia	☐	☐	/	/		/	/		☐
G. Obsessive Compulsive Disorder	☐	☐	/	/		/	/		☐
H. Generalised Anxiety Disorder	☐	☐	/	/		/	/		☐
I. Alcohol (Dependence/Abuse)	☐	☐	/	/		/	/		☐
J. Drugs (Dependence/Abuse)(non-alcohol)	☐	☐	/	/		/	/		☐
K. Psychotic Disorders	☐	☐	/	/		/	/		☐
L. Anorexia Nervosa	☐	☐	/	/		/	/		☐
M. Bulimia Nervosa	☐	☐	/	/		/	/		☐
N. Suicidality	☐	☐	/	/		/	/		☐
O. Post Traumatic Stress disorder	☐	☐	/	/		/	/		☐

Any relevant additional psychiatric conditions not identified by the MINI but by the Full Psychiatric Interview should be recorded below.

Additional Psychiatric condition(s)	Yes	No	Start Date			End Date			Continuing
			Day	Mth	Yr	Day	Mth	Yr	
Hypochondriasis	☐	☐	/	/		/	/		☐
Somatization Disorder	☐	☐	/	/		/	/		☐
Adjustment Disorder with Anxiety/Depressed Mood	☐	☐	/	/		/	/		☐
Specify other DSM-IV conditions:									
☐ ☐ ☐ • ☐ ☐ ☐	☐	☐	/	/		/	/		☐
☐ ☐ ☐ • ☐ ☐ ☐	☐	☐	/	/		/	/		☐
☐ ☐ ☐ • ☐ ☐ ☐	☐	☐	/	/		/	/		☐
☐ ☐ ☐ • ☐ ☐ ☐	☐	☐	/	/		/	/		☐

Patients who fulfill DSM-IV criteria for any Axis I disorder other than PMDD or specific phobias within 6 months prior to the Screening Visit (Visit 1) are not eligible.

PROGRESS NOTES	PROTOCOL 29060/717	End Of Reference Cycle 1(A) (Visit 2A)

PREGNANCY TEST

Please take a blood sample for serum pregnancy test.

Sample Date: / /
(Day / Month / Year)

Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly (please ensure to include the sample for laboratory evaluation).

To be completed when the laboratory results are available

Was the serum pregnancy test positive ?

☐ No

☐ Yes → If "Yes", please withdraw the patient from the study.

LABORATORY EVALUATION

Please take a blood sample for routine analysis.

Sample Date: / /
(Day / Month / Year)

Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly (please ensure to include the sample for the pregnancy test).

To be completed when the laboratory results are available

Were any clinically significant abnormalities detected at the end of Reference Cycle 1(A) (Visit 2(A)) ?

☐ No

☐ Yes → If "Yes", please record details in the Significant Medical/Surgical History and Physical Examination page (Page 1). Repeat laboratory tests should be taken.

Attach the Quest Diagnostics laboratory report in the plastic wallet at the end of this workbook.

A repeat of these tests prior to the Baseline Visit (Visit 3) should be performed if there are any abnormalities in the screening laboratory results and details recorded at Visit 2(B) (which is an optional visit to perform repeat laboratory assessments only).

Please record the laboratory numbers below or affix the laboratory label in the box provided

ACCT

REQ

Attach label here

PROGRESS NOTES	PROTOCOL 29060/717	End Of Reference Cycle 1(A) (Visit 2A)

PATIENT ELIGIBILITY

I have carried out the assessments for this visit and on the patient Study Cycle 1 diary (and Study Cycle 1(A) diary if applicable) the patient:

- ☐ **is not eligible** to continue in the study
- Please complete the Patient Continuation/Withdrawal record (Page 20)
 - Retain the Study Cycle 2 diary
 - Advise the patient where to seek help for premenstrual complaints
- ☐ **is eligible** to continue in the study
- Instruct the patient to continue recording the symptoms for her current menstrual cycle in the Study Cycle 2 diary.
 - Issue the patient with a diary card for Treatment Cycle 1 (Study Cycle 3 diary)
 - Remind the patient to begin completing the Study Cycle 3 diary from the first day of her next menstrual cycle remembering that Day 1 is the first day of continuous bleeding, not spotting.
 - Dispense study medication for Reference Cycle 2. Give the patient both verbal and written instructions in taking the medication. Advise the patient to start taking the study medication approximately 14 days prior to the expected time of next menses and continue until the first day of menses.
 - Make an appointment with the patient to return for her next clinic visit between Days 1 - 3 of her next menstrual cycle. The patient must take the completed Study Cycle 2 diary card to the clinic at this visit for collection and review.

PROGRESS NOTES	PROTOCOL 29060/717	REPEAT LABORATORY TESTS (Visit 2B)	Date of		
			Visit	/	/
			Day	Month	Year

LABORATORY EVALUATION

Please take a blood sample for routine analysis if an abnormality was detected at the End of Reference Cycle 1(A) visit.

Sample Date: / / or ☐ Not required
(Day / Month / Year)

Now read the instructions on the Quest Diagnostics shipment document and dispatch the samples for analysis accordingly.

To be completed when the laboratory results are available

Were any clinically significant abnormalities detected at this visit ?

☐ No

☐ Yes → If "Yes", please record details in the Baseline Adverse Experiences section and withdraw the patient.

Attach the Quest Diagnostics laboratory report in the plastic wallet at the end of this workbook.

Please record the laboratory numbers below or affix the laboratory label in the box provided

ACCT

REQ

Attach label here

PROGRESS NOTES	PROTOCOL 29060/717	Baseline (Visit 3)	Date of Visit		
			Day	Month	Year

PATIENT ELIGIBILITY

Collect unused Reference Cycle 2 medication, check compliance **and complete the Study Medication record page (Page 26).**

Collect the patient diary for Reference Cycle 2 (Study Cycle 2 diary) and check the scores. The patient must rate at least 200 % higher (ie. worse) on one, or at least 100 % higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ((\text{mean luteal score} - \text{mean follicular score}) / \text{mean follicular score})$) - (For these items, the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$). Patients do not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores should also be low and SB must be consulted prior to inclusion of a patient if these scores are not $\leq 25\text{mm}$.

Is the patient still eligible for inclusion in the study based on the VAS Scores? ☐ Yes ☐ No

Is the patient still eligible for inclusion in the study based on all considerations (eg. changes in prohibited medication, poor diary card compliance)? ☐ Yes ☐ No

Overall, is the patient still eligible for inclusion in the study?

☐ Yes → If "Yes", please complete the procedures for this visit

☐ No → If "No", the patient must be excluded from the study

- Collect Study Cycle 3 diary card
- Complete the Vital Signs, Concomitant Medication and Baseline Adverse Experience panels for this visit
- Complete the Patient Continuation/Withdrawal record
- Advise the patient where to seek help for premenstrual complaints

CLINICAL GLOBAL IMPRESSION

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

WEIGHT

Weight:		☐ lbs ☐ kg

PROGRESS NOTES	PROTOCOL 29060/717	Baseline (Visit 3)

ISCO-88

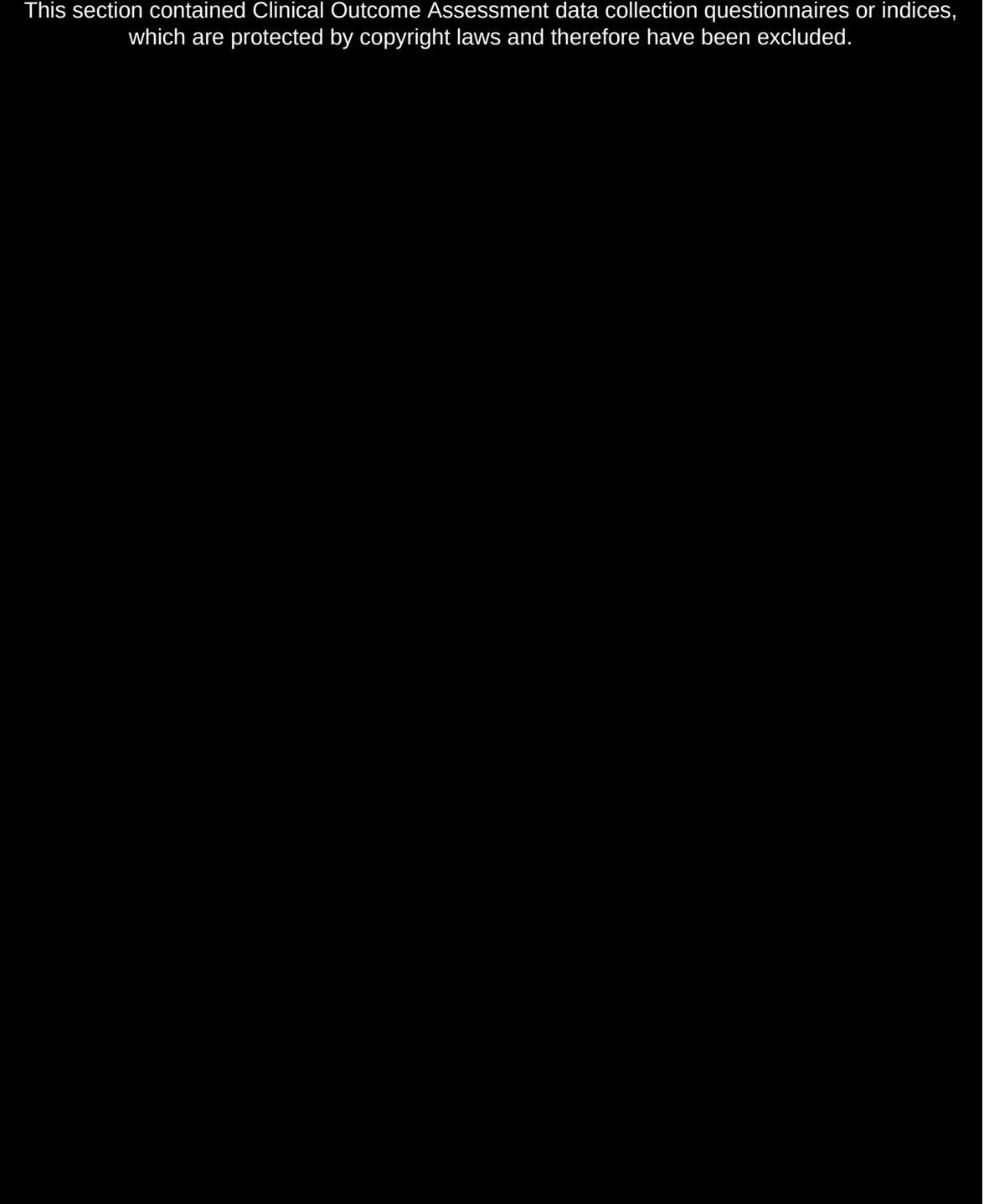
Please mark the one box below which best describes the patient's **current** occupation : (International Standard Classification of Occupations (ISCO-88 (COM)))

- ☐ Legislator, senior official or manager (e.g. specialist managers, directors and chief executives)
- ☐ Professional (e.g. teaching, legal, science and health professionals)
- ☐ Technician or associate professional (computer associates, nurses/midwives, ship and aircraft controllers, police inspectors, finance and sales)
- ☐ Clerk (e.g. secretaries, cashiers and other office clerks)
- ☐ Service worker or shop and market sales worker (e.g. housekeeping and restaurant services, shop salesperson and demonstrators and models)
- ☐ Skilled agricultural or fishery worker (e.g. animal/crop producers, market gardeners, fishery workers, hunters or trappers)
- ☐ Craft and related trades worker (e.g. miners, builders, blacksmiths, potters, glass-makers, textile workers)
- ☐ Plant and machine operator or assembler (e.g. metal processing plant operators, food and related products machine operators)
- ☐ Elementary occupation (e.g. street vendors, building caretakers, mining and construction labourers)
- ☐ Military
- ☐ Not Applicable

PROGRESS NOTES	PROTOCOL 29060/717	Baseline (Visit 3)

~~PREMENSTRUAL TENSION SCALE - observer rated~~ *(must refer to luteal phase)*

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



PROGRESS NOTES	PROTOCOL 29060/717	Baseline (Visit 3)

PREMENSTRUAL TENSION SCALE - observer rated cont. (must refer to luteal phase)

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

VITAL SIGNS

Pulse: _____ beats/min

Sitting B.P: _____ / _____ mmHg
(systolic / diastolic)
(after sitting for 3 mins)

PROGRESS NOTES	PROTOCOL 29060/717	Baseline (Visit 3)

BASELINE INCLUSION CRITERIA**INCLUSION CRITERIA**

The patient is not eligible if any of the following inclusion criteria is answered "No"

	Yes	No
1. Does the patient have a Baseline luteal phase Clinical Global Impression Severity of Illness score ≥ 3 ?	☐	☐
2. During 2 consecutive Reference Cycles, does the patient rate at least 200% higher (ie. worse) on one, or at least 100% higher on two or more of the four core symptoms (irritability, depressed mood, tension or affective lability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ((\text{mean luteal score} - \text{mean follicular score}) / \text{mean follicular score})$) - (For these items, the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$). Patients do not need to qualify on the same symptom(s) in both reference cycles. For the "non-qualifying symptoms" (i.e. the remainder of the four core symptoms other than the 1 or 2 qualifying symptoms) the mean follicular phase scores should also be low and SB must be consulted prior to inclusion of a patient if these scores are not $\leq 25\text{mm}$.	☐	☐
3. Does the patient meet DSM-IV criteria for PMDD after analysis of the Study Cycle 1 and Study Cycle 2 diaries (and Study Cycle 1(A) diary if applicable) and following the psychiatric interview (including the MINI)?	☐	☐

Do not admit the patient into the study if any of the above boxes have been marked "NO".

BASELINE EXCLUSION CRITERIA**EXCLUSION CRITERIA**

The patient is not eligible if any of the following exclusion criteria is answered "Yes"

	Yes	No
1. Does the patient have any clinically significant abnormalities in screening blood tests ?	☐	☐
2. Does the patient have a positive pregnancy test ?	☐	☐
3. Has the patient shown any characteristics which, in the opinion of the investigator, are likely to reduce compliance with the protocol (eg. poor medication compliance, poor diary card compliance) ?	☐	☐
4. Did the patient fulfil DSM-IV criteria for any Axis 1 disorder (other than PMDD or specific phobias) in the 6 months prior to the Screening Visit (Visit 1) ?	☐	☐

Do not admit the patient into the study if any of the above boxes have been marked "YES".

PATIENT ELIGIBILITY

I have carried out the assessments for this visit and on the patient diary for Reference Cycle 2 (Study Cycle 2 diary) the patient:

- ☐ **is not eligible** to continue in the study
- Please complete the Patient Continuation/Withdrawal record (Page 20)
 - Retain the Study Cycle 3 diary
 - Advise the patient where to seek help for premenstrual complaints
- ☐ **is eligible** to continue in the study
- Please randomise the patient and record the randomisation number below

RANDOMISATION NUMBER :

- Instruct the patient to continue recording the symptoms for her current menstrual cycle in the Study Cycle 3 diary.
- Issue the patient with a diary card for Study Cycle 4
- Remind the patient to begin completing the Study Cycle 4 diary from the first day of her next menstrual cycle remembering that Day 1 is the first day of continuous bleeding, not spotting.
- Dispense study medication for Treatment Cycles 1, 2 and 3. Give the patient both verbal and written instructions in taking the medication. Advise the patient to start taking the study medication approximately 14 days prior to the expected time of next menses and continue until the first day of menses.
- Make an appointment with the patient to return for her next clinic visit between Days 1 - 3 of her next menstrual cycle. The patient must take the completed Study Cycle 3 diary card to the clinic at this visit for collection and review.

PROGRESS NOTES	PROTOCOL 29060/717	

PATIENT CONTINUATION / WITHDRAWAL

Is the patient continuing in the study?

☐ Yes

☐ No → If 'No' please mark the **primary** reason for withdrawal below.

☐ Baseline adverse experience (complete BAE form)

☐ Does not meet inclusion/exclusion criteria

☐ Protocol deviation (including non-compliance)

☐ Lost to follow-up

☐ Other, please specify: _____

Which was the last visit the patient attended : ☐ Screening

☐ End of Reference Cycle 1

☐ End of Reference Cycle 1(A)

Please complete the Investigator Signature page if the patient is withdrawing from the study.

PRIOR AND CONCOMITANT MEDICATION***ROUTE KEY***

PO	=	by mouth
IV	=	intravenous
IM	=	intramuscular
IAR	=	intra-arterial
TO	=	topical
SL	=	sublingual
IT	=	intrathecal
VA	=	vaginal
NA	=	nasal
IA	=	intra-articular injection
TD	=	transdermal
IH	=	inhaled
SC	=	subcutaneous
PR	=	rectal
ID	=	intradermal

BASELINE ADVERSE EXPERIENCES**DEFINITIONS****INTENSITY (Maximum)**

MILD	Baseline event which is easily tolerated
MODERATE	Baseline event which is sufficiently discomforting to interfere with daily activity
SEVERE	Baseline event which is incapacitating and prevents normal everyday activities and/or requires therapeutic intervention such as the use of prescribed drugs, hospitalization or prolongation of hospital stay

SERIOUS ADVERSE EXPERIENCE**SERIOUS ADVERSE EXPERIENCE**

A serious baseline event is any event which is :-

- fatal
- life threatening
- permanently or temporarily disabling
- incapacitating
- results in hospitalisation (excluding elective surgery or routine clinical procedures)
- prolongs a hospital stay
- associated with congenital abnormality, carcinoma or overdose

In addition any event which the investigator regards as serious or which would suggest any significant hazard, contraindication, side effect or precaution that may be associated with the study procedures should be reported as a serious experience

PLEASE REMEMBER ALL QUESTIONS ON BASELINE ADVERSE EXPERIENCES FORM
MUST BE COMPLETED

Use each form for a maximum of three events. If additional events are noted please use a separate form

PROGRESS NOTES	PROTOCOL 29060/717	

BASELINE ADVERSE EXPERIENCES

PLEASE SEE INSTRUCTIONS ON TAB BEFORE COMPLETION

PLEASE RECORD ANY ADVERSE EXPERIENCE OBSERVED OR ELICITED BY THE FOLLOWING DIRECT QUESTION TO PATIENT: "Have you felt different in any way since your last visit ?"

Please record one experience per column or mark this box to indicate no baseline adverse events ☐

EXPERIENCE				
Date Started		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Date Stopped		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Duration if less than 24 hours		<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins
Experience continuing at end of Baseline Visit		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Course	Continuous	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	If NO, no of episodes			
Intensity	1. Mild	☐	☐	☐
	2. Moderate	☐	☐	☐
	3. Severe	☐	☐	☐
Corrective Therapy	If 'YES' record on Concomitant Medication form	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Do you consider this a serious baseline adverse experience by the Baseline Adverse Experience definitions ?		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
		AE Number <u> </u>	AE Number <u> </u>	AE Number <u> </u>

If "YES", report to SB by telephone within 24 hours

PROGRESS NOTES	PROTOCOL 29060/717	

BASELINE ADVERSE EXPERIENCES

PLEASE SEE INSTRUCTIONS ON TAB BEFORE COMPLETION

PLEASE RECORD ANY ADVERSE EXPERIENCE OBSERVED OR ELICITED BY THE FOLLOWING DIRECT QUESTION TO PATIENT: "Have you felt different in any way since your last visit ?"

Please record one experience per column or mark this box to indicate no baseline adverse events ☐

EXPERIENCE				
Date Started		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Date Stopped		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Duration if less than 24 hours		<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins
Experience continuing at end of Baseline Visit		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Course	Continuous	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	If NO, no of episodes			
Intensity	1. Mild	☐	☐	☐
	2. Moderate	☐	☐	☐
	3. Severe	☐	☐	☐
Corrective Therapy	If 'YES' record on Concomitant Medication form	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Do you consider this a serious baseline adverse experience by the Baseline Adverse Experience definitions ?		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
		AE Number <u> </u>	AE Number <u> </u>	AE Number <u> </u>

If "YES", report to SB by telephone within 24 hours

PROGRESS NOTES	PROTOCOL 29060/717	

BASELINE ADVERSE EXPERIENCES

PLEASE SEE INSTRUCTIONS ON TAB BEFORE COMPLETION

PLEASE RECORD ANY ADVERSE EXPERIENCE OBSERVED OR ELICITED BY THE FOLLOWING DIRECT QUESTION TO PATIENT: "Have you felt different in any way since your last visit ?"

Please record one experience per column or mark this box to indicate no baseline adverse events ☐

EXPERIENCE				
Date Started		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Date Stopped		<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)
Duration if less than 24 hours		<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins	<u> </u> hrs <u> </u> mins
Experience continuing at end of Baseline Visit		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Course	Continuous	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
	If NO, no of episodes			
Intensity	1. Mild	☐	☐	☐
	2. Moderate	☐	☐	☐
	3. Severe	☐	☐	☐
Corrective Therapy	If 'YES' record on Concomitant Medication form	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Do you consider this a serious baseline adverse experience by the Baseline Adverse Experience definitions ?		☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
		AE Number <u> </u>	AE Number <u> </u>	AE Number <u> </u>

If "YES", report to SB by telephone within 24 hours

PROGRESS NOTES	PROTOCOL 29060/717	Medication Record

MEDICATION RECORD

Cycle	Start Date	Stop Date	Number of capsules dispensed (eg. 24)	Unused Medication Did the patient return capsules?	* Interruption of > 3 days ?
Reference Cycle 2	<u> / / </u> (Day / Month / Year)	<u> / / </u> (Day / Month / Year)		☐ No ☐ Yes, how many ? →	☐ No ☐ Yes
<i>* If there has been an interruption in medication for more than three consecutive days, SB should be contacted to confirm whether the patient must be withdrawn from the study.</i> <i>If patient has been withdrawn between visits, please ensure that the study medication record is completed</i>					

MEDICATION LABEL

Please attach the relevant medication label in the space below.

Please attach label here for Reference Cycle 2

PROGRESS NOTES	PROTOCOL 29060/717	Form D

FORM D

Certified Cause of Death _____

Date of Death (Day / Month / Year) *→ Please complete Serious Adverse Experience section.*

Was a post-mortem carried out?

☐ No

☐ Yes *→ If 'Yes' please summarise findings (include diagnosis):*

wg_formd_uk_01

Protocol	Centre Number	Patient Number	Patient Initials
29060/717			

CONFIDENTIAL



STUDY CYCLE 3

PROTOCOL 29060/717

PATIENT DIARY

IMPORTANT PATIENT INSTRUCTIONS

Record the start and stop date for the corresponding medication bottle.

Start End
Day Month Yr Day Month Yr

When you have completed this diary you should bring it back to the next clinic visit as instructed by your investigator.



Protocol	Centre Number	Patient Number	Patient Initials
29060/717			

INSTRUCTIONS FOR COMPLETION**General Instructions**

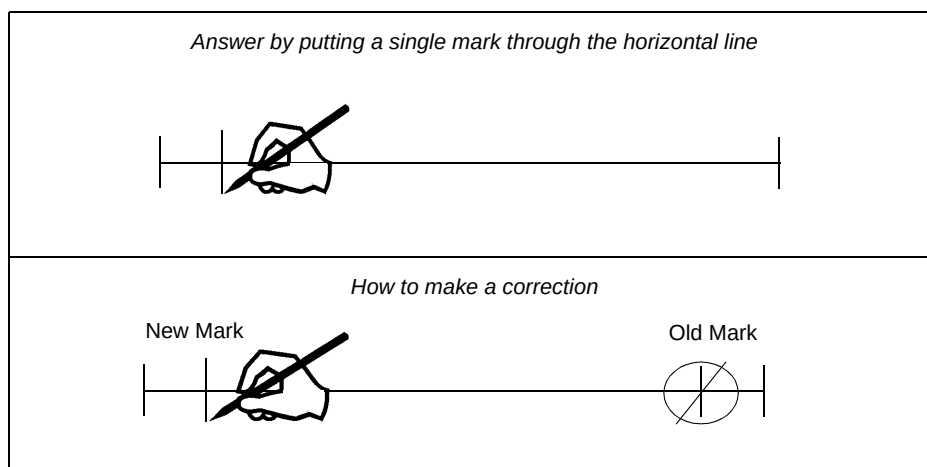
- *Please complete all pages using a black ink ballpoint pen.*
- *Ensure that all entries are complete and legible.*
- *Ensure that the diary pages are kept together. **Do not rip out or substitute pages.***
- *The diary should be completed each day before going to bed.*
- *If you do forget to fill in the diary, you must not try to remember afterwards, but to fill in the date and write "NOT FILLED IN" on the questionnaire.*
- *NOTE: on the day menstruation starts, you should begin completing a new diary regardless of how many pages that remain in this diary.*
- *If you have any questions regarding the completion of this diary please contact your study nurse/doctor.*

INSTRUCTIONS FOR COMPLETION**VAS**

- Record the date in the following format :

1	2	N	O	V	0	1

 = 12th November 2001
- Answer all questions in relation to how you have felt **on that day**.
- Answer by putting a single mark through the horizontal lines (see below).
- Position the mark to give the best indication of how you have felt that day.**
- If you do change your mind after you have marked the line, please make the change by putting a single line through the wrong answer and circling it. Then answer again by making a new mark (see example below).
- If you suffer from only one of the example symptoms for a particular VAS item, then you should rate that item.
- Otherwise, if you suffer from a number of the example symptoms for a particular VAS item, then you should rate the most severe symptom for that item.

**MARKING BOXES**

- Please mark boxes like this 
- Do **not** mark boxes like this   


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 131

DAY 01

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 132

DAY 02

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 133

DAY 03

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 134

DAY 04

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 135

DAY 05

Today's Date:

Day		Month		Year	

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day		Month		Year	

Signature 2.

Day		Month		Year	

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 136

DAY 06

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 137

DAY 07

Today's Date:

Day		Month		Year	

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day		Month		Year	

Signature 2.

Day		Month		Year	

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 138

DAY 08

Today's Date:

Day		Month		Year	

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day		Month		Year	

Signature 2.

Day		Month		Year	

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 139

DAY 09

Today's Date:

Day		Month		Year	

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day		Month		Year	

Signature 2.

Day		Month		Year	

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 140

DAY 10

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 141

DAY 11

Today's Date:

Day		Month		Year	

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day		Month		Year	

Signature 2.

Day		Month		Year	

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 142

DAY 12

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 143

DAY 13

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 144

DAY 14

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 145

DAY 15

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 146

DAY 16

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 147

DAY 17

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 148

DAY 18

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 149

DAY 19

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 150

DAY 20

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 151

DAY 21

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 152

DAY 22

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 153

DAY 23

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 154

DAY 24

Today's Date:

Day		Month		Year	

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day		Month		Year	

Signature 2.

Day		Month		Year	

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 155

DAY 25

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 156

DAY 26

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 157

DAY 27

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 158

DAY 28

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 159

DAY 29

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 160

DAY 30

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 161

DAY 31

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 162

DAY 32

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 163

DAY 33

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 164

DAY 34

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 165

DAY 35

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 166

DAY 36

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)Not
at allExtreme
Symptoms

Office Use

TENSION (tense, anxious, "keyed up", or "on edge")Not
at allExtreme
Symptoms

Office Use

AFFECTIVE LABILITY (sad, tearful, more sensitive to rejection)Not
at allExtreme
Symptoms

Office Use

IRRITABILITY (angry, irritable, had conflicts with people)Not
at allExtreme
Symptoms

Office Use

DECREASED INTEREST (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)Not
at allExtreme
Symptoms

Office Use

DIFFICULTY CONCENTRATINGNot
at allExtreme
Symptoms

Office Use

LACK OF ENERGY (fatigued, lethargic, lacking in energy)Not
at allExtreme
Symptoms

Office Use

CHANGE IN APPETITE (marked appetite changes, binge eating, food cravings)Not
at allExtreme
Symptoms

Office Use

CHANGE IN SLEEP PATTERN (hypersomnia (slept more), insomnia (trouble sleeping))Not
at allExtreme
Symptoms

Office Use

FEELING OUT OF CONTROL (felt overwhelmed, felt could not cope, felt out of control)Not
at allExtreme
Symptoms

Office Use

PHYSICAL SYMPTOMS (breast tenderness/swelling, headaches, sensations of 'bloating')Not
at allExtreme
Symptoms

Office Use

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 167

DAY 37

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 168

DAY 38

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 169

DAY 39

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

***IF YOU HAVE HAD MENSTRUAL BLEEDING TODAY (NOT SPOTTING),
DO NOT COMPLETE THE REST OF THIS DIARY.
INSTEAD, START A NEW DIARY.***


SmithKline Beecham
 Pharmaceuticals

Protocol: 29060/717

Page: 170

DAY 40

Today's Date:

Day	Month	Year		

1. Have you had menstrual bleeding today (not spotting)?

☐ No ☐ Yes → **If "Yes", please begin new diary.**

 2. Have your premenstrual symptoms affected your family, work/studies, everyday activities or relations with others today? ☐ No ☐ Yes

3. Answer each item below by putting a mark through the horizontal line to give the best indication of how you are feeling today (see instructions at front of diary).

Not at all = How you normally feel when you don't have premenstrual symptoms
Extreme Symptoms = How you feel when your premenstrual symptoms are at their worst

DEPRESSED MOOD (depressed, sad, "down", "blue", hopeless, worthless or guilty)

Office Use

Not
at allExtreme
Symptoms**TENSION** (tense, anxious, "keyed up", or "on edge")

Office Use

Not
at allExtreme
Symptoms**AFFECTIVE LABILITY** (sad, tearful, more sensitive to rejection)

Office Use

Not
at allExtreme
Symptoms**IRRITABILITY** (angry, irritable, had conflicts with people)

Office Use

Not
at allExtreme
Symptoms**DECREASED INTEREST** (less interest in usual activities (work, school, friends, hobbies), withdrawal from social relationships)

Office Use

Not
at allExtreme
Symptoms**DIFFICULTY CONCENTRATING**

Office Use

Not
at allExtreme
Symptoms**LACK OF ENERGY** (fatigued, lethargic, lacking in energy)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN APPETITE** (marked appetite changes, binge eating, food cravings)

Office Use

Not
at allExtreme
Symptoms**CHANGE IN SLEEP PATTERN** (hypersomnia (slept more), insomnia (trouble sleeping))

Office Use

Not
at allExtreme
Symptoms**FEELING OUT OF CONTROL** (felt overwhelmed, felt could not cope, felt out of control)

Office Use

Not
at allExtreme
Symptoms**PHYSICAL SYMPTOMS** (breast tenderness/swelling, headaches, sensations of 'bloating')

Office Use

Not
at allExtreme
Symptoms

OFFICE USE

Signature 1.

Day	Month	Year		

Signature 2.

Day	Month	Year		

Office Use: 717002

Office Use: 000000

NOTE

***PLEASE DO NOT COMPLETE THE
FOLLOWING ASSESSMENTS
UNTIL THE CLINIC VISIT***

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Pharmaceuticals

Protocol: 29060/717

Page: 171

PLEASE DO NOT COMPLETE THIS PAGE UNTIL THE CLINIC VISIT
(Please note that these questions refer to the
premenstrual phase which has just ended)

Date Completed

Day	Month	Year		

EUROOOL

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.

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Protocol: 29060/717

Page: 173

PLEASE DO NOT COMPLETE THIS PAGE UNTIL THE CLINIC VISIT

Date Completed

Day		Month		Year	

PATIENT GLOBAL EVALUATION

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Pharmaceuticals

Protocol: 29060/717

Page: 174

PLEASE DO NOT COMPLETE THIS PAGE UNTIL THE CLINIC VISIT

Date Completed

Day	Month	Year		

INSTRUCTIONS

Please circle the numbers in the Sheehan Disability Scale below like this →

0	1	2

SHEEHAN DISABILITY SCALE

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Office Use: 717007

Office Use: 00000

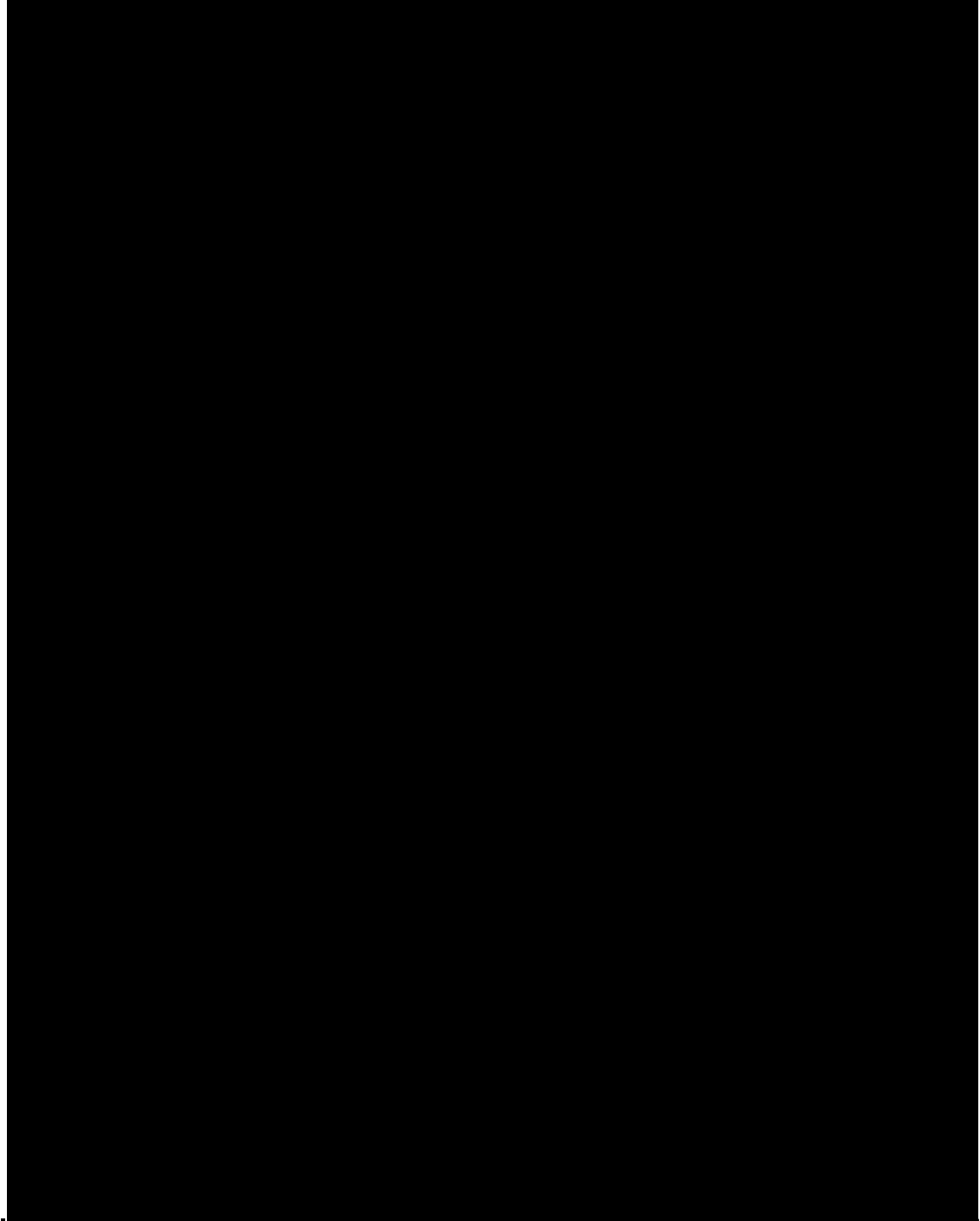
**SmithKline Beecham**
Pharmaceuticals

Protocol: 29060/717

Page: 175

WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT QUESTIONNAIRE (WPAI)

This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by copyright laws and therefore have been excluded.



Office Use: 717008

Office Use: 00000

PATIENT DECLARATION

INSTRUCTION - Please complete the following section in the clinic with your doctor.

I certify that I have reviewed all of the information that I have entered in this diary and that it is, to my knowledge, complete and accurate.

Patient's Signature _____

Date

Day	Month	Yr

29060 / 717

PATIENT ELIGIBILITY CALCULATION WORKSHEETS

VAS Eligibility Look Up Table Study BRL-29060/717		
(Column 1)	200% Change (Column 2)	100% Change (Column 3)
Mean Follicular Score	Mean Luteal Score	Mean Luteal Score
20	≥ 60	≥ 40
19	≥ 57	≥ 40
18	≥ 54	≥ 40
17	≥ 51	≥ 40
16	≥ 48	≥ 40
15	≥ 45	≥ 40
14	≥ 42	≥ 40
13	≥ 40	≥ 40
12	≥ 40	≥ 40
11	≥ 40	≥ 40
10	≥ 40	≥ 40
9	≥ 40	≥ 40
8	≥ 40	≥ 40
7	≥ 40	≥ 40
6	≥ 40	≥ 40
5	≥ 40	≥ 40
4	≥ 40	≥ 40
3	≥ 40	≥ 40
2	≥ 40	≥ 40
1	≥ 40	≥ 40
0	≥ 40	≥ 40

To assess patient eligibility for symptom 'on-offness' for each of the 4 core symptoms (*Irritability, Depressed Mood, Tension and Affective Lability*):

NOTE: If the **mean** follicular phase score is > 20mm then the patient is not eligible for study entry on this symptom.

NOTE: If the **mean** luteal phase score is < 40mm then the patient is not eligible for study entry on this symptom.

- 1 Look up the mean follicular phase score in Column 1.
- 2 If the mean luteal phase score for this symptom is **greater than or equal to** the corresponding value shown in Column 2, the patient has at least a 200% worsening for this symptom and is eligible.
- 3 If the mean luteal phase score for this symptom is **less than** that in column 2, please compare with the corresponding score shown in Column 3.
 - If the mean luteal phase score for this symptom is **greater than or equal to** that shown in Column 3, the patient has at least a 100% worsening for this symptom. The patient must show at least 100% worsening for another core symptom to be eligible.
 - If the mean luteal phase score for this symptom is less than that shown in Column 3 then the patient is not eligible for this symptom.

29060 / 717

PATIENT ELIGIBILITY CALCULATION WORKSHEET

1 Record the centre number, patient number, patient initials and the reference cycle number in the boxes below.

29060 / 717 / /
Centre Patient Initials

Reference Cycle (01 / 1A / 02)

2 Measure the scores on the patient's VAS diary for the 4 core PMDD symptoms (depressed mood, tension, affective lability and irritability) and complete the table below for days 6 - 10 and the last 5 days of the cycle (no more than one day's data should be missing for each of these calculations).

**FOLLICULAR PHASE
(DAYS 6 - 10 OF CYCLE)**

Day	6	7	8	9	10	Mean Score (Days 6-10)
Depressed Mood						
Tension						
Affective Lability						
Irritability						

**LUTEAL PHASE
(LAST 5 DAYS OF CYCLE)**

Day	-5	-4	-3	-2	-1	Mean Score (Last 5 days)
Depressed Mood						
Tension						
Affective Lability						
Irritability						

3 Now calculate the mean score for each of the 4 core symptoms over days 6 - 10 and the last 5 days of the cycle and complete the boxes indicated (shaded area). No more than one day's data should be missing for each of these calculations.

4 Remember that in order to be eligible, a patient must rate at least 200 % higher (ie. worse) on one, or at least 100% higher on two or more of the four core symptoms (depressed mood, tension, affective lability or irritability) for the mean luteal phase score compared with the mean follicular phase score (% worsening = $100 \times ([\text{mean luteal score} - \text{mean follicular score}] / \text{mean follicular score})$) - (For these items, the mean follicular phase score must be $\leq 20\text{mm}$ and the mean luteal phase score must be $\geq 40\text{mm}$). Patients do not need to qualify on the same symptom(s) in both reference cycles. Please use the table provided to help you check the patients' eligibility.

* The follicular phase score of $\leq 20\text{mm}$ applies only to the "qualifying items" (those core symptoms showing the 100% or 200% change). For the "non-qualifying symptoms" (ie. the remainder of the four core symptoms other than the qualifying symptoms) the mean follicular phase score should also be low and SB must be consulted prior to randomising a patient if these scores are not $\leq 25\text{mm}$

5 Please note if the patient was eligible based on these scores.

☐ No

☐ Yes → If "Yes", please tick the box to indicate on which item(s) the patient qualified.

	200%	100%
Depressed Mood	☐	☐
Tension	☐	☐
Affective Lability	☐	☐
Irritability	☐	☐

29060 / 717

PATIENT ELIGIBILITY CALCULATION WORKSHEET

1	Record the centre number, patient number, patient initials and the reference cycle number in the boxes below. 29060 / 717 Centre Patient Initials Reference Cycle (01 / 1A / 02)																																																																						
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29060 / 717

PATIENT ELIGIBILITY CALCULATION WORKSHEET

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29060 / 717

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Protocol	Centre Number	Patient Number	Patient Initials		
29060/717					

**LABEL**

LABEL :	Medication Label Record
CRF Pages :	501
Unprocessed Forms :	None

FOR OFFICE USE ONLY

Module Comments:



Sent to Data Mngt



Review Complete

Date:

User:



First Entry Complete

Date:

User:



Second Entry Complete

Date:

User:



Validation Complete

Date:

User:

Clintrial PID:

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Page	501

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MEDICATION LABEL RECORD

Please affix study medication label for Treatment Cycles 1 to 3 in the box below

Please attach label here for
Treatment Cycles 1 to 3

**INSTRUCTIONS FOR REPORTING SERIOUS ADVERSE EXPERIENCES (SAE)
(PAROXETINE)**

SAEs MUST BE REPORTED TO SMITHKLINE BEECHAM WITHIN 24 HOURS

COMPLETE THE SAE PAGES OVERLEAF

Please complete these pages as fully and accurately as possible in order to minimise the time you spend dealing with data queries

If the SAE is still ongoing at the time of reporting, please leave 'Experience Course' blank and update it later

SIGN AND DATE THE SAE PAGE

PLEASE ENSURE THAT ALL OF THE INFORMATION ON THE FOLLOWING eCRF SCREENS IS COMPLETE

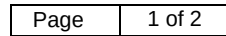
- Demography
- Significant Medical/Surgical History and Physical Examination
- Study Medication Record
- Concomitant Medication
- Adverse Experiences/Baseline Adverse Experiences
- Form D (if applicable)

REPLICATE YOUR LAPTOP DATA WITHIN 24 HOURS

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Protocol	Center Number	Patient Number	Patient Initials	SB Receipt Date		
				Day	Month	Year
29060/717						

Person Reporting SAE <i>(Please print clearly)</i>		AEGIS Number _____ . _____
Serious Adverse Experience <i>(Please print clearly)</i>		→ Specify reason(s) for considering this a serious AE. Mark all that apply. [1] ☐ fatal [2] ☐ life threatening [3] ☐ disabling/incapacitating [4] ☐ results in hospitalisation (excluding elective surgery or routine clinical procedures) [5] ☐ hospitalisation prolonged [6] ☐ congenital abnormality [7] ☐ cancer [8] ☐ overdose [9] ☐ Investigator considers serious or a significant hazard, contraindication, side effect or precaution Did the SAE abate? ☐ Yes ☐ No If study medication was stopped or dose decreased: Was study medication reintroduced (or dose increased)? ☐ Yes ☐ No If yes, did SAE recur? ☐ Yes ☐ No
For SmithKline Beecham		
Date Started	Day Month Yr	
Date Stopped	Day Month Yr	
Duration if less than 24hrs	hrs mins	
Experience continuing at end of study	YES ☐ NO ☐	
Course	Continuous YES ☐ NO ☐ If NO, no of episodes	
Intensity	☐ Mild ☐ Moderate ☐ Severe	
Action Taken on Study Medication	☐ None ☐ Dose decreased ☐ Dose increased ☐ Drug stopped	Assessment The SAE is probably associated with: ☐ Protocol design or procedures (but not to study drug) Please specify _____ ☐ Another condition (eg, condition under study, intercurrent illness) Please specify _____ ☐ Another drug Please specify _____
Relationship to Investigational Drug	☐ Unrelated ☐ Probably Unrelated ☐ Possibly Related ☐ Related	
Corrective Therapy <i>If 'Yes', record details in the Concomitant Medication section</i>	☐ Yes ☐ No	



Page	2 of 2

Protocol 29060/717	Center Number [][][]	Patient Number [REDACTED]	Patient Initials [][][][]	SB Receipt Date Day Month Year [][][][][][]	

SERIOUS ADVERSE EXPERIENCE (SAE) (cont) (PAROXETINE)
Relevant Laboratory Data

Please provide relevant abnormal laboratory data below

Test	Date	Value	Units	Normal Range
	[][][][][] Day Month Yr			
	[][][][][] Day Month Yr			
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	[][][][][] Day Month Yr			

Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)

If applicable, was randomisation code broken at investigational site?

☐ No ☐ Yes

Randomisation / Study Medication Number:

 [][][][][]

Investigator's Signature:

(confirming that the above data are accurate and complete)

Date

[][][]	[][][]	[][]
Day	Month	Year

Please PRINT Name

SB Medical Monitor's Signature:

Date

Please PRINT Name

[][][]	[][][]	[][]
Day	Month	Year

**INSTRUCTIONS FOR REPORTING SERIOUS ADVERSE EXPERIENCES (SAE)
(PAROXETINE)**

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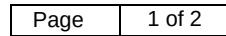
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Corrective Therapy <i>If 'Yes', record details in the Concomitant Medication section</i>	☐ Yes ☐ No	



Page	2 of 2

Protocol 29060/717	Center Number [][][]	Patient Number [][][][][][]	Patient Initials [][][][]	SB Receipt Date Day Month Year [][] [][] [][]

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Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)

If applicable, was randomisation code broken at investigational site?

☐ No ☐ Yes

Randomisation / Study Medication Number: [][][][][]

Investigator's Signature:

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Date

[][]	[][]	[][]
Day	Month	Year

Please PRINT Name

SB Medical Monitor's Signature:

Date

Please PRINT Name

[][]	[][]	[][]
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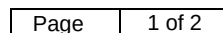
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Course Continuous If NO, no of episodes	YES ☐ NO ☐ 		
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Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)

[illegible]

If applicable, was randomisation code broken at investigational site?

☐ No ☐ Yes

Randomisation / Study Medication Number:

Investigator's Signature:

(confirming that the above data are accurate and complete)

Date

Day	Month		Year

Please PRINT Name

SB Medical Monitor's Signature:

Date

A horizontal timeline with three rectangular boxes. The first box is labeled 'Day', the second 'Month', and the third 'Year'. Each box has a vertical tick mark at its center.

Please PRINT Name

**INSTRUCTIONS FOR REPORTING SERIOUS ADVERSE EXPERIENCES (SAE)
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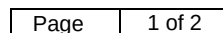
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Date Stopped	Day Month Yr	
Duration if less than 24hrs	hrs mins	
Experience continuing at end of study	YES ☐ NO ☐	
Course	Continuous YES ☐ NO ☐ If NO, no of episodes	
Intensity	☐ Mild ☐ Moderate ☐ Severe	
Action Taken on Study Medication	☐ None ☐ Dose decreased ☐ Dose increased ☐ Drug stopped	Did the SAE abate? ☐ Yes ☐ No If study medication was stopped or dose decreased: Was study medication reintroduced (or dose increased)? ☐ Yes ☐ No If yes, did SAE recur? ☐ Yes ☐ No
Relationship to Investigational Drug	☐ Unrelated ☐ Probably Unrelated ☐ Possibly Related ☐ Related	Assessment The SAE is probably associated with: ☐ Protocol design or procedures (but not to study drug) <i>Please specify</i> _____ ☐ Another condition (eg, condition under study, intercurrent illness) <i>Please specify</i> _____ ☐ Another drug <i>Please specify</i> _____
Corrective Therapy <i>If 'Yes', record details in the Concomitant Medication section</i>	☐ Yes ☐ No	



Page	2 of 2

Protocol 29060/717	Center Number [][][]	Patient Number [][][][][][]	Patient Initials [][][][]	SB Receipt Date Day Month Year [][][][][][][]	

SERIOUS ADVERSE EXPERIENCE (SAE) (cont) (PAROXETINE)**Relevant Laboratory Data**

Please provide relevant abnormal laboratory data below

Test	Date	Value	Units	Normal Range
	[][][][][][] Day Month Yr			
	[][][][][][] Day Month Yr			
	[][][][][][] Day Month Yr			
	[][][][][][] Day Month Yr			

Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)

If applicable, was randomisation code broken at investigational site?

☐ No ☐ Yes

Randomisation / Study Medication Number: [][][][][]

Investigator's Signature:

(confirming that the above data are accurate and complete)

Date

[][][]	[][][]	[][][]
Day	Month	Year

Please PRINT Name**SB Medical Monitor's Signature:**

Date

Please PRINT Name

[][][]	[][][]	[][][]
Day	Month	Year

**INSTRUCTIONS FOR REPORTING SERIOUS ADVERSE EXPERIENCES (SAE)
(PAROXETINE)**

SAEs MUST BE REPORTED TO SMITHKLINE BEECHAM WITHIN 24 HOURS

COMPLETE THE SAE PAGES OVERLEAF

Please complete these pages as fully and accurately as possible in order to minimise the time you spend dealing with data queries

If the SAE is still ongoing at the time of reporting, please leave 'Experience Course' blank and update it later

SIGN AND DATE THE SAE PAGE

PLEASE ENSURE THAT ALL OF THE INFORMATION ON THE FOLLOWING eCRF SCREENS IS COMPLETE

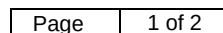
- Demography
- Significant Medical/Surgical History and Physical Examination
- Study Medication Record
- Concomitant Medication
- Adverse Experiences/Baseline Adverse Experiences
- Form D (if applicable)

REPLICATE YOUR LAPTOP DATA WITHIN 24 HOURS

FAX A COPY OF THE SAE PAGES TO:

Your local SB CRA/Medical Monitor (see Investigator Site File for appropriate fax number)

If no photocopier OR fax is available please telephone your local SB CRA/Medical monitor within 24 hours



Protocol	Center Number	Patient Number	Patient Initials	SB Receipt Date		
				Day	Month	Year
29060/717						

Person Reporting SAE (Please print clearly)		AEGIS Number	
Serious Adverse Experience (Please print clearly)		→ Specify reason(s) for considering this a serious AE. Mark all that apply.	
For SmithKline Beecham			
Date Started	Day Month Yr	[1] ☐ fatal [2] ☐ life threatening [3] ☐ disabling/incapacitating [4] ☐ results in hospitalisation (excluding elective surgery or routine clinical procedures)	
Date Stopped	Day Month Yr	[5] ☐ hospitalisation prolonged [6] ☐ congenital abnormality [7] ☐ cancer [8] ☐ overdose [9] ☐ Investigator considers serious or a significant hazard, contraindication, side effect or precaution	
Duration if less than 24hrs	hrs mins		
Experience continuing at end of study	YES ☐ NO ☐		
Course Continuous If NO, no of episodes	YES ☐ NO ☐ 		
Intensity	☐ Mild ☐ Moderate ☐ Severe		
Action Taken on Study Medication	☐ None ☐ Dose decreased ☐ Dose increased ☐ Drug stopped	Did the SAE abate? ☐ Yes ☐ No If study medication was stopped or dose decreased: Was study medication reintroduced (or dose increased)? ☐ Yes ☐ No If yes, did SAE recur? ☐ Yes ☐ No	
Relationship to Investigational Drug	☐ Unrelated ☐ Probably Unrelated ☐ Possibly Related ☐ Related	Assessment The SAE is probably associated with: ☐ Protocol design or procedures (but not to study drug) Please specify _____	
Corrective Therapy If 'Yes', record details in the Concomitant Medication section	☐ Yes ☐ No	☐ Another condition (eg, condition under study, intercurrent illness) Please specify _____ ☐ Another drug Please specify _____	



Page	2 of 2

Protocol 29060/717	Center Number [][][]	Patient Number [][][][][][]	Patient Initials [][][][]	SB Receipt Date Day Month Year [][] [][] [][]	

SERIOUS ADVERSE EXPERIENCE (SAE) (cont) (PAROXETINE)
Relevant Laboratory Data

Please provide relevant abnormal laboratory data below

Test	Date	Value	Units	Normal Range
	[][][][][][] Day Month Yr			
	[][][][][][] Day Month Yr			
	[][][][][][] Day Month Yr			
	[][][][][][] Day Month Yr			

Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)

If applicable, was randomisation code broken at investigational site?

☐ No ☐ Yes

Randomisation / Study Medication Number: [][][][][][]

Investigator's Signature:

(confirming that the above data are accurate and complete)

Date

[][][]	[][][]	[][][]
Day	Month	Year

Please PRINT Name

SB Medical Monitor's Signature:

Date

Please PRINT Name

[][][]	[][][]	[][][]
Day	Month	Year

**INSTRUCTIONS FOR REPORTING SERIOUS ADVERSE EXPERIENCES (SAE)
(PAROXETINE)**

SAEs MUST BE REPORTED TO SMITHKLINE BEECHAM WITHIN 24 HOURS

COMPLETE THE SAE PAGES OVERLEAF

Please complete these pages as fully and accurately as possible in order to minimise the time you spend dealing with data queries

If the SAE is still ongoing at the time of reporting, please leave 'Experience Course' blank and update it later

SIGN AND DATE THE SAE PAGE

PLEASE ENSURE THAT ALL OF THE INFORMATION ON THE FOLLOWING eCRF SCREENS IS COMPLETE

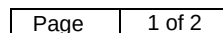
- Demography
- Significant Medical/Surgical History and Physical Examination
- Study Medication Record
- Concomitant Medication
- Adverse Experiences/Baseline Adverse Experiences
- Form D (if applicable)

REPLICATE YOUR LAPTOP DATA WITHIN 24 HOURS

FAX A COPY OF THE SAE PAGES TO:

Your local SB CRA/Medical Monitor (see Investigator Site File for appropriate fax number)

If no photocopier OR fax is available please telephone your local SB CRA/Medical monitor within 24 hours



Protocol	Center Number	Patient Number	Patient Initials	SB Receipt Date		
				Day	Month	Year
29060/717						

Person Reporting SAE <i>(Please print clearly)</i>		AEGIS Number _____ . _____
Serious Adverse Experience <i>(Please print clearly)</i>		→ Specify reason(s) for considering this a serious AE. Mark all that apply.
For SmithKline Beecham		
Date Started	____ Day ____ Month ____ Yr	[1] ☐ fatal
Date Stopped	____ Day ____ Month ____ Yr	[2] ☐ life threatening
Duration if less than 24hrs	____ hrs ____ mins	[3] ☐ disabling/incapacitating
Experience continuing at end of study	YES ☐ NO ☐	[4] ☐ results in hospitalisation (excluding elective surgery or routine clinical procedures)
Course Continuous If NO, no of episodes	YES ☐ NO ☐ _____	[5] ☐ hospitalisation prolonged
Intensity	☐ Mild ☐ Moderate ☐ Severe	[6] ☐ congenital abnormality
Action Taken on Study Medication	☐ None ☐ Dose decreased ☐ Dose increased ☐ Drug stopped	[7] ☐ cancer
Relationship to Investigational Drug	☐ Unrelated ☐ Probably Unrelated ☐ Possibly Related ☐ Related	[8] ☐ overdose
Corrective Therapy If 'Yes', record details in the Concomitant Medication section ←	☐ Yes ☐ No	[9] ☐ Investigator considers serious or a significant hazard, contraindication, side effect or precaution
		Did the SAE abate? ☐ Yes ☐ No If study medication was stopped or dose decreased: Was study medication reintroduced (or dose increased)? ☐ Yes ☐ No If yes, did SAE recur? ☐ Yes ☐ No
		Assessment The SAE is probably associated with: ☐ Protocol design or procedures (but not to study drug) Please specify _____ ☐ Another condition (eg, condition under study, intercurrent illness) Please specify _____ ☐ Another drug Please specify _____



Protocol	Center Number	Patient Number	Patient Initials	SB Receipt Date		
				Day	Month	Year
29060/717						

Relevant Laboratory Data

Please provide relevant abnormal laboratory data below

Test	Date	Value	Units	Normal Range
	Day Month Yr			
	Day Month Yr			
	Day Month Yr			
	Day Month Yr			

Remarks (Please provide a brief narrative description of the SAE, attaching extra pages eg. hospital discharge summary if necessary)

[illegible]

If applicable, was randomisation code broken at investigational site?

☐ No ☐ Yes

Randomisation / Study Medication Number:

Investigator's Signature:

(confirming that the above data are accurate and complete)

Date

Day Month Year

Please PRINT Name

SB Medical Monitor's Signature:

Date

Day	Month	Year

Please PRINT Name



Protocol	Centre Number	Patient Number	Patient Initials		
29060/717					

**SIG1**

SIG1 :	Investigator Signature
CRF Pages :	502
Unprocessed Forms :	None

FOR OFFICE USE ONLY

Module Comments:



Sent to Data Mngt



Review Complete



First Entry Complete



Second Entry Complete



Validation Complete

Clintrial PID:



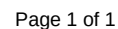
Protocol	Center Number	Patient Number	Patient Initials		
29060/717					

INVESTIGATOR SIGNATURE

I certify that I have reviewed the data in this electronic Case Report Form, including laboratory data and that in the Adverse Experience and Serious Adverse Experience sections (if appropriate) and that all information is complete and accurate.

Investigator's Signature _____ Date / /
(Day / Month / Year)

wg_inv_sig_01



Protocol	Centre Number	Patient Number	Patient Initials	Investigator
29060/717				-----

Please submit COMPLETE modules only. Do not submit whole blank modules.

☐ **Screening Failure (archive only)**

Module	Module Description	Page Range	Modules		Crash Number	Missing Pages (if Applicable)
			Sent to DM	Unused		
DIA1	Study Cycle 1 diary	1 - 40	☐	☐		-----
DIA2	Study Cycle 1(A) diary	41 - 85	☐	☐		-----
DIA3	Study Cycle 2 diary	86 - 130	☐	☐		-----
DIA4	Study Cycle 3 diary	131 - 175	☐	☐		-----
DIA5	Study Cycle 4 diary	176 - 220	☐	☐		-----
DIA6	Study Cycle 5 diary	221 - 265	☐	☐		-----
LABEL	Medication Label Record	501	☐	☐		-----
SIG1	Investigator Signature	502	☐	☐		-----

If multiple modules are submitted together, please ensure they are sorted according to the order above

Site Monitor's Comments (e.g. protocol violations or deviations)

[illegible]

Site Monitor's Signature _____ Date Submitted _____

/ /

(Day / Month / Year)

This section contained Principal Investigator's Curriculum Vitae and has been excluded to protect Principal Investigator privacy.

Certificates of Analysis

**Certificate of Analysis**

Product Name Overencapsulated Paroxetine CR tablets
Batch Number U00150 **Strength** 12.5 mg
Analytical Reference HA00/3912 **Formula** GL
Date of Manufacture 27 September 2000

New Frontiers Science Park
Third Avenue
Marlow
Essex
CM19 5AW
Tel: [REDACTED]
Fax: [REDACTED]
www.gsk.com

Test	Result
Description	A white powder, and a round, normal biconvex pale yellow coloured film coated tablet. This is all contained in a size NoSupro B capsule comprised of an opaque Swedish Orange body and cap. PASS
Identification	The tablet contained in the capsule is pale yellow in colour PASS
Disintegration	6.0 mins PASS

This product conforms with Release Specification CPSC/PDSH-2478/01 and has been manufactured and tested in accordance with Good Manufacturing Practice.

Approved by [REDACTED] on 01 June 2001
[REDACTED] BSc, MRPharmS 01 June 2001
[REDACTED] Head European Pharmaceutical Development QA

1 of 1

U00150.doc

01/06/2001

SmithKline Beecham Pharmaceuticals
is a business name of SmithKline Beecham plc
Registered in England & Wales
No. 2337959
Registered Office
New Horizons Court, Brentford, Middlesex TW8



GlaxoSmithKline

Certificate of Analysis

Product Name Overencapsulated Paroxetine CR tablets
Batch Number U00151 Strength 25 mg
Analytical Reference HA00/3913 Formula GM
Date of Manufacture 28 September 2001

New Frontiers Science Park
Third Avenue
Harlow
Essex
CM19 5AW
Tel: [REDACTED]
Fax: [REDACTED]
www.gsk.com

Test	Result
Description	An off white powder, and a round, normal biconvex dark almon coloured film coated tablet. This is all contained in a size No.Supro B capsule comprised of an opaque Swedish Orange body and cap. PASS
Identification	The tablet contained in the capsule is dark salmon in colour. PASS
Disintegration	6.0 mins PASS

This product conforms with Release Specification CPSC/PDSH 2479/01 and has been manufactured and tested in accordance with Good Manufacturing Practice.

Approved by [REDACTED] on 01 June 2001
[REDACTED] BSc, MRPharmS 01 June 2001
European Pharmaceutical Development QA

1 of 1

U00151.doc

01/06/2001

SmithKline Beecham Pharmaceuticals
is a business name of SmithKline Beecham /
Registered in England & Wales
No. 2337959
Registered Office
New Horizons Court, Brentford, Middlesex TW

**Certificate of Analysis**

Product Name Placebo to Match Overencapsulated Paroxetine
'Geomatrix' CR Tablets (12.5 and 25 mg)
Strength Placebo
Product Code HE
Batch Number N00349
Analytical Reference HA00/4084
Date of Manufacture 13 November 2000
Site of Manufacture GSK Harlow, UK.

New Frontiers Science Park
Third Avenue
Harlow
Essex
CM19 5AW
Tel: [REDACTED]
Fax: [REDACTED]
www.gsk.com

Test	Result
Description	A white to off white powder contained in a Supro B hard gelatin capsule comprised of an opaque Swedish Orange body and cap.
Disintegration	8.0 minutes

This product conforms with Release Specification CPSC/PDSH 2493/01 and has been manufactured and tested in accordance with Good Manufacturing Practice.

Approved by [REDACTED] on 22 Jan 2001
[REDACTED] 22 Jan 2001
[REDACTED] Quality Assurance, Harlow.



GlaxoSmithKline

GlaxoSmithKline1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA
19426-0989

Tel [REDACTED]

Fax [REDACTED]

www.gsk.com

Certificate of Analysis

Product Name	Overencapsulated Paroxetine CR Tablets		
Batch Number	U00175	Strength	12.5 mg
Analytical Reference	HA01/0533	Formula	GL
Date of Manufacture	27 Sep 2000		

Test	Result
Description	An off white powder and a round, normal biconvex, pale yellow coloured film coated tablet. This is all contained in a Size No. Supro B, capsule comprised of an opaque Swedish Orange body and cap.
Identification	The tablet contained in the capsule is pale yellow in colour.
Disintegration	6.0 minutes

This product conforms with Release Specification CPSC/PDSH 2478/01 and has been manufactured and tested in accordance with Good Manufacturing Practice.

Approved by [REDACTED]

on

02 April 2001

Quality Assurance



GlaxoSmithKline
1250 South Collegeville Road
P.O. Box 5089
Collegeville, PA
19426-0989

Tel [REDACTED]
Fax [REDACTED]
www.gsk.com

Certificate of Analysis

Product Name	Overencapsulated Paroxetine CR Tablets		
Batch Number	U00176	Strength	25 mg
Analytical Reference	HA01/1836	Formula	GM
Date of Manufacture	28 Sep 2000		
Site of Manufacture	Upper Providence, PA USA		

Test	Result
Description	A white powder and a round, normal biconvex, dark salmon coloured film coated tablet. This is all contained in a Size No. Supro B, capsule comprised of an opaque Swedish Orange body and cap.
Identification	The tablet contained in the capsule is dark salmon in colour.
Disintegration	3.0 minutes

This product conforms with Release Specification CPSC/PDSH 2479/01 and has been manufactured and tested in accordance with Good Manufacturing Practice.

Approved by [REDACTED] on 17 April 2001
Quality Assurance

29060/717 List of Investigators

Name	Address	Center	Country
■■■■■ ■■■■■	■■■■■■■■■	■■■	Sweden
	■■■■■■■ ■■■■■■■■■■		
	■■■■■		
■■■■■ ■■■■■ M.D., Ph.D.	■■■■■■■■■	■■■	Sweden
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■■■■■ ■■■■■	■■■■■■■■■	■■■	Sweden
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■■■■■ ■■■■■ M.D., Ph.D.	■■■■■■■■■	■■■	Sweden
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■■■■■ ■■■■■■ M.D.	■■■■■■■■■ ■■■■	■■■	Sweden
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■■■■■ ■■■■■ M.D.	■■■■■■■■■	■■■	Sweden
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■■■■■ ■■■■ ■■■	■■■■■ ■■■■■■ ■■■ ■■■■■■	■■■	Finland
	■■■ ■■■■■ ■■■■ ■■■■		
	■■■■■■■		
■■■■■ ■■■■■■■■ M.D., Ph.D.	■■■■■ ■■■■■■ ■■■ ■■■■■■	■■■	Finland
	■■■■■ ■■■■■		
	■■■■■		

Name	Address	Center	Country
██████████ M.D., Ph.D.	██████████ ██████████ ██████████	██████████	Finland
██████████	██████████ ██████████	██████████	Finland
██████████	██████████ ██████████	██████████	Finland
██████████ M.D.	██████████	██████████	Norway
██████████	██████████ ██████████	██████████	Norway
██████████ M.D.	██████████ ██████████	██████████	Norway
██████████	██████████ ██████████ ██████████	██████████	Norway
██████████	██████████ ██████████	██████████	Norway
██████████	██████████ ██████████	██████████	Norway
██████████ M.D.	██████████ ██████████	██████████	Netherlands
██████████ M.D.	██████████ ██████████	██████████	Netherlands
██████████	██████████ ██████████	██████████	Netherlands
██████████	██████████ ██████████	██████████	Netherlands
██████████ M.D.	██████████ ██████████	██████████	Netherlands
██████████ M.D., Ph.D.	██████████ ██████████	██████████	Netherlands
██████████ M.D.	██████████ ██████████	██████████	Netherlands
██████████ M.D.	██████████ ██████████	██████████	Germany

3

Name	Address	Center	Country
██████████ M.D.	██████████ ██████████	████	US
██████████ M.D.	██████████ ██████████	████	US
██████████ M.D.	██████████ ██████████	████	US
██████████ M.D.	██████████ ██████████	████	US
██████████ M.D.	██████████ ██████████ ██████████	████	US
██████████ M.D. ██████████ Ph.D.	██████████ ██████████	████	US

This section contained Principal Investigator's Curriculum Vitae and has been excluded to protect Principal Investigator privacy.