BELVIQ
A Pharmacotherapeutic Option for Chronic Weight Management

INDICATION
BELVIQ is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:
- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (eg, hypertension, dyslipidemia, type 2 diabetes).

Limitations of Use:
- The safety and efficacy of coadministration of BELVIQ with other products intended for weight loss, including prescription drugs (eg, phentermine), over-the-counter drugs, and herbal preparations, have not been established.
- The effect of BELVIQ on cardiovascular morbidity and mortality has not been established.

IMPORTANT SAFETY INFORMATION
Contraindication
- BELVIQ should not be taken during pregnancy or by women who are planning to become pregnant.

Please see additional Important Safety Information throughout the brochure.
Warnings and Precautions

BELVIQ is a serotoninergic drug. The development of potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported during use of serotoninergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors, tricyclic antidepressants, bupropion, triptans, dietary supplements such as St. John’s Wort and tryptophan, drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors), dextromethorphan, lithium, tramadol, antipsychotics or other dopamine antagonists, particularly when used in combination. Patients should be monitored for the emergence of serotonin syndrome symptoms or NMS-like reactions, including agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, nausea, vomiting, diarrhea, and muscle rigidity. Treatment with BELVIQ and any concomitant serotonergic or antidopaminergic agents should be discontinued immediately if the above events occur, and supportive symptomatic treatment should be initiated.

Please read US full Prescribing Information for BELVIQ located in the pocket.
OBESITY: A GROWING EPIDEMIC

Overweight and obesity is a condition that represents a multifactorial, interdisciplinary clinical challenge for healthcare providers. This burgeoning health problem, along with the elucidation of profuse comorbidities, has sparked a national health concern. Currently, being overweight or obese is a major problem and a growing epidemic in the United States. Historical attitudes, popular culture, and social pressure all complicate the healthcare practitioner’s interaction with overweight and obese patients.

Obesity Defined

The terms overweight and obesity are defined by the World Health Organization as “abnormal or excessive fat accumulation that may impair health.” For a clinical practitioner, precise definitions of overweight and obese are critical for appropriate treatment. Several organizations have developed clinical guidelines for assessing overweight and obese patients by body mass index (BMI). Typically, BMI is calculated using a patient’s height (h) and weight (w) (Figure 1). Definitions of underweight, normal, overweight, and obese, based on BMI, can be found in Table 1. BMI may not be accurate for all patients, therefore the National Heart, Lung, and Blood Institute recommends using waist circumference for all patients with a BMI between 25 kg/m² and 34.9 kg/m² as a secondary measurement. All patients should be regularly screened using these simple measurements. Any patient who meets the criteria for being overweight or obese should be counseled on the risks associated with overweight and obesity.

Figure 1 BMI* Conversion Chart

| Weight (lb) | 125 | 130 | 135 | 140 | 145 | 150 | 155 | 160 | 165 | 170 | 175 | 180 | 185 | 190 | 195 | 200 | 205 | 210 | 215 | 220 | 225 |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Height (in)|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 58         | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43  | 44  | 45  | 46  | 47 |
| 59         | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43  | 44  | 45  | 46 |
| 60         | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43  | 44 |
| 61         | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43  | 44 |
| 62         | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43 |
| 63         | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42 |
| 64         | 22  | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41 |
| 65         | 21  | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41 |
| 66         | 20  | 21  | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40 |
| 67         | 20  | 20  | 21  | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39 |
| 68         | 19  | 20  | 21  | 21  | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38 |
| 69         | 18  | 19  | 20  | 21  | 21  | 22  | 23  | 24  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 30  | 31  | 32  | 33  | 33  | 33 |
| 70         | 18  | 19  | 20  | 21  | 22  | 22  | 23  | 24  | 24  | 25  | 26  | 27  | 27  | 28  | 29  | 30  | 31  | 32  | 32  | 32  | 32 |
| 71         | 17  | 18  | 19  | 20  | 20  | 21  | 22  | 23  | 24  | 24  | 25  | 26  | 27  | 27  | 28  | 29  | 30  | 31  | 31  | 31  | 31 |
| 72         | 17  | 18  | 18  | 19  | 20  | 20  | 21  | 22  | 23  | 24  | 24  | 25  | 26  | 27  | 27  | 28  | 29  | 30  | 30  | 30  | 30 |
| 73         | 17  | 17  | 18  | 19  | 20  | 20  | 21  | 22  | 23  | 24  | 24  | 25  | 26  | 26  | 27  | 28  | 28  | 29  | 29  | 29  | 29 |
| 74         | 16  | 17  | 17  | 18  | 19  | 19  | 20  | 21  | 22  | 23  | 24  | 24  | 25  | 26  | 26  | 27  | 28  | 28  | 28  | 28  | 28 |
| 75         | 16  | 16  | 17  | 18  | 18  | 19  | 20  | 21  | 21  | 22  | 23  | 23  | 24  | 24  | 25  | 26  | 26  | 27  | 27  | 27  | 27 |
| 76         | 15  | 16  | 16  | 17  | 17  | 18  | 18  | 19  | 20  | 20  | 21  | 21  | 22  | 23  | 24  | 24  | 25  | 26  | 26  | 27  | 27 |

*BMI=w/h² x 703
w=weight [in pounds]; h=height [in inches].

Under/Normal weight | Overweight | Obese
Prevalence of Overweight and Obesity

The incidence of overweight and obesity has become an increasingly urgent issue for national health. The US Food and Drug Administration (FDA) has stated that “Obesity threatens the overall well-being of patients and is a major public health concern." The prevalence of overweight and obesity in the United States has risen dramatically in recent years, and currently 69% of American adults are either overweight or obese. The condition of overweight and obesity represents a major concern across the United States, as a study of self-reported obesity found that there is no state with less than 20% of its population qualifying as obese (Figure 2).

Figure 2  Prevalence of Self-Reported Obesity

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>Normal</td>
</tr>
<tr>
<td>25–29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>≥30</td>
<td>Obese</td>
</tr>
</tbody>
</table>
**Etiology of Obesity**

Being overweight or obese is a multifactorial disease with several contributing factors. The combination of social, biological, and psychological factors makes it difficult for clinicians to narrow down specific risk factors or causes of a patient’s difficulty with weight management. Understanding the effect each aspect of a patient’s lifestyle and physiology has on his/her weight can help to develop an effective management strategy (Figure 3).

**Figure 3  Factors Influencing Weight Management**

**Lifestyle**

Accumulation of fat can result from caloric intake that is in excess of caloric output, resulting in excess energy that the body stores as fat. Caloric balance is primarily determined by diet and exercise. The increasing prevalence of overweight and obesity has been attributed to a combination of poor diet and increasingly sedentary lifestyles. The per capita daily caloric intake in the United States has increased by 20% since 1970. Indeed, diet and physical activity are two of the most important factors that determine an individual’s weight, and should be the first line of defense for both patients and healthcare providers in combating and preventing overweight and obesity. Several national and statewide campaigns aimed at battling obesity on a public level promote healthy lifestyle choices, including regular physical activity and balanced eating habits. Individual physiology affects how a patient processes food and registers food intake, and this also has major implications for developing overweight or obesity.

**Genetics**

It has long been postulated that there is a significant genetic contribution to the development of overweight or obesity in individual patients. Several genomic studies have found genetic markers associated with the incidence of overweight or obesity. These genetic variations may cause certain individuals to be more susceptible than others to developing overweight or obesity. These factors are not deterministic, and their clinical impact on the development, progression, and treatment of the disease remains unclear.
Endocrinology and Neurology

Physiologically, susceptibility to overweight and obesity is influenced by the function of neural and endocrine systems that function in part to regulate food intake and energy expenditure. These bidirectional signals work between the central nervous system (CNS) and the organs involved in food processing and energy storage (Figure 4). The perception of hunger that leads to food consumption results from a combination of signals from the body to the brain, along with external factors such as social and learned behaviors. The integration of these signals remains poorly understood.

After food has been consumed, the brain receives that information and produces satiety signals which cause the feeling of satisfaction and “fullness.” Satiety signals trigger cessation of feeding. The balance and timing of hunger and satiety signals regulate an individual’s feeding desires and regimen. These pathways are also involved in regulating the amount of fat accumulation in response to biological cues. Physiologically, these signals can induce the body to store fat in excess of what is necessary, leading to weight gain and overweight or obesity.

Figure 4  Endocrine and Neurologic Processing of Food

[Diagram showing the interaction between lifestyle, genetic/developmental factors, food intake, nutrient absorption, energy expenditure, and energy storage.]
Challenges for Healthcare Providers and Patients

Combatting overweight or obesity and its associated medical, social, and economic consequences starts with healthcare providers. It is imperative that all medical professionals be educated on overweight or obesity and appropriate courses of treatment, as well as how to accurately convey this information to patients.1

The idea that overweight or obesity is a “disease” has only recently become prominent in the medical community.10 With the identification of risk factors and the definition of patient screening parameters comes the responsibility to discuss appropriate treatment options.1

Initiating the Conversation

Discussing weight management with patients can be extremely challenging. Overweight or obese patients may avoid seeking medical care due to shame or concern about the associated stigma.14 It also can be difficult for the physician to initiate a discussion of weight management for fear of triggering these reactions. Furthermore, physicians who are themselves overweight or obese tend to avoid the topic of weight management with their patients.15 It is the responsibility of healthcare providers and the medical community as a whole to create an environment that eases these fears and concerns on both sides and encourages communication.14 Patient motivation is a key component for success in a weight loss program,1 and a patient’s primary healthcare provider can play a large role in helping to maintain this motivation.16

Setting Realistic Goals

Once the issue of weight management has been brought to the attention of the patient, the next step is to set realistic goals and to outline a plan to achieve them. Some factors to consider when setting goals include:

- Weight loss at the rate of 1 to 2 pounds per week (with a calorie deficit of 500 to 1000 kcal/day) commonly occurs for up to 6 months1
- The rate of weight loss usually declines after 6 months due to lesser energy expenditure at the lower weight1
- A patient’s goals should be individually determined based on factors such as comorbidities and current lifestyle3

It is important to set individualized, realistic goals for each patient because achieving predetermined goals is an important factor in maintaining patient motivation.17
Choosing Patient-Appropriate Therapies

There are several weight management strategies available to doctors and patients. Each therapy is appropriate for a distinct patient set and has a different safety profile associated with it. Lifestyle modification is advised for overweight or obese patients with BMI ≥25 kg/m², though choosing a form of intervention can be difficult. Patient motivation is a key component for success in a weight loss program, so it is a critical factor in choosing an appropriate therapy. Practitioners need to assess the patient’s motivation to enter weight loss therapy, assess the readiness of the patient to implement the plan, and then take appropriate steps to motivate these patients.

Lifestyle modification, pharmacotherapy, and surgery are options that should be considered for certain patient sets based on BMI (Table 3) and past and current medical conditions. Social and historical factors influence attitudes toward the weight management therapies among both healthcare providers and patients. Many overweight or obese patients, particularly women, are more likely to try fad diets and over-the-counter weight loss supplements rather than a balanced diet and an exercise program. In addition, recent history has seen several pharmacologic weight loss agents enter the market only to be recalled due to safety concerns. This can lead to a hesitation to use other medical weight management treatment options, particularly pharmacotherapies. It is important to be aware of all available and appropriate therapies for each patient, and the associated clinically proven benefits as well as risk profiles.

Table 3 Summary of Clinical Recommendations for Weight Loss Therapies

<table>
<thead>
<tr>
<th>Treatment</th>
<th>BMI Category (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24–26.9</td>
</tr>
<tr>
<td>Lifestyle modification</td>
<td>Overweight</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>Recommended with comorbidities</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
</tbody>
</table>
A Novel Pharmacotherapeutic Option for Chronic Weight Management
INDICATION

BELVIQ is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (eg, hypertension, dyslipidemia, type 2 diabetes).

Limitations of Use:

- The safety and efficacy of coadministration of BELVIQ with other products intended for weight loss, including prescription drugs (eg, phentermine), over-the-counter drugs, and herbal preparations, have not been established.
- The effect of BELVIQ on cardiovascular morbidity and mortality has not been established.

Mechanism of Action

Although the exact mechanism of action is not known, BELVIQ is believed to decrease food consumption and promote satiety. Satiety is the signal from the brain of “fullness” or “satisfaction” that indicates the body has ingested enough nutrients and feeding should cease. One mechanism believed to relay this signal is the release of serotonin in areas of the brain where it can specifically bind to and activate the 5-HT$_2C$ receptor. This receptor is one subtype within the 5-HT$_2$ family of receptors that have diverse functions throughout the body (Figure 6). BELVIQ, at the recommended dose, is believed to decrease food consumption and promote satiety by selectively activating the 5-HT$_2C$ receptors. At the recommended daily dose, BELVIQ selectively interacts with 5-HT$_2C$ receptors as compared to 5-HT$_2A$ and 5-HT$_2B$ receptors.

Figure 6  BELVIQ Mechanism of Action

CONTRAINDICATION

BELVIQ should not be taken during pregnancy or by women who are planning to become pregnant.

Please see additional Important Safety Information throughout this monograph.
**Table 4** **BELVIQ Potency**

<table>
<thead>
<tr>
<th>Receptor</th>
<th>BELVIQ EC50 (nM)*</th>
</tr>
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<tbody>
<tr>
<td>5-HT2A</td>
<td>553</td>
</tr>
<tr>
<td>5-HT2B</td>
<td>2380</td>
</tr>
<tr>
<td>5-HT2C</td>
<td>39</td>
</tr>
</tbody>
</table>

*Potency is a measure of drug activity expressed in terms of the amount required to produce an effect of given intensity. A highly potent drug elicits a larger response at lower concentrations. EC50 is the concentration of drug that produces 50% of the maximal effect. The smaller the EC50, the higher the potency.*

**Pivotal Phase 3 Clinical Trials**

The efficacy of BELVIQ in conjunction with reduced caloric intake and increased physical activity was established in three randomized, double-blind, multicenter, placebo-controlled clinical trials: Behavioral Modification and Lorcaserin for Overweight and Obesity Management (BLOOM), Behavioral Modification and Lorcaserin Second Study for Obesity Management (BLOSSOM), and Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus (BLOOM-DM). The third study focused on the efficacy of BELVIQ for weight loss in patients already diagnosed with type 2 diabetes mellitus.

**Efficacy and Safety in Patients Without Diabetes**

BLOOM (N=3182) and BLOSSOM (N=4008) were concurrent clinical trials to examine the efficacy and safety of BELVIQ. Treatment duration was 1 year in BLOSSOM, and 2 years in BLOOM. In BLOSSOM and Year 1 of BLOOM, patients were randomly assigned to receive BELVIQ 10 mg twice daily (BID) or placebo. In Year 2 of BLOOM, patients in the placebo group continued to receive placebo, but patients in the BELVIQ group were randomly reassigned to either remain on BELVIQ 10 mg BID or switch to placebo. Throughout the duration of both trials, all patients received diet-and-exercise counseling. Patients were instructed to exercise moderately for 30 minutes each day, and to reduce daily caloric intake to 600 kcal below estimated energy requirements. Patient demographics for BLOOM and BLOSSOM were similar. Study participants were adults ages 18–65 years, with an average age of approximately 44 years. Patients had either a BMI of 30–45 kg/m² or a BMI of 27–45 kg/m² with at least one coexisting condition (hypertension, dyslipidemia, cardiovascular disease, impaired glucose tolerance, or sleep apnea). The average BMI of enrolled patients was approximately 36 kg/m². More than 80% of participants were women, and more than 67% of participants were Caucasian. Key exclusion criteria included diabetes mellitus, medical conditions that would preclude participation in a nutritional and physical exercise program, and valvulopathy (BLOOM) or recent cardiovascular event.

**Warnings and Precautions**

BELVIQ is a serotonergic drug. The development of potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported during use of serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors, tricyclic antidepressants, bupropion, triptans, dietary supplements such as St. John’s Wort and tryptophan, drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors), dextromethorphan, lithium, tramadol, antipsychotics or other dopamine antagonists, particularly when used in combination. Patients should be monitored for the emergence of serotonin syndrome symptoms or NMS-like reactions, including agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, nausea, vomiting, diarrhea, and muscle rigidity. Treatment with BELVIQ and any concomitant serotonergic or antidopaminergic agents should be discontinued immediately if the above events occur, and supportive symptomatic treatment should be initiated.
Coprimary endpoints for both trials included percent of patients who achieved ≥5% and ≥10% weight loss and mean weight change from baseline after 1 year of treatment. In BLOOM, primary endpoints also included the proportion of patients who sustained ≥5% weight loss from baseline after 2 years of treatment. Select secondary efficacy endpoints for both trials included change from baseline of lipids, glycemic variables, blood pressure, waist circumference, BMI, and body composition (BLOSSOM only).25,26

Collectively, between the BLOOM and BLOSSOM trials, 3098 patients were assigned to BELVIQ 10 mg BID, and 3038 patients were assigned to placebo. Efficacy at Year 1 was analyzed by patients achieving ≥5% or ≥10% weight loss and change in weight from baseline. After 1 year of treatment, more patients met their weight loss goals when BELVIQ was taken in conjunction with lifestyle modification than with lifestyle modification and placebo (Figure 7).* Of patients taking BELVIQ, 47.1% lost ≥5% body weight, compared with 22.6% of patients taking placebo (P<0.001) (Table 5). Furthermore, 22.4% of patients taking BELVIQ 10 mg BID lost ≥10% body weight, compared with 8.7% of patients taking placebo (P<0.001). At Week 52, the mean weight loss was 5.8% with BELVIQ versus 2.5% with placebo (P<0.001).20

**Figure 7  Weight Loss in Patients Without Diabetes**

*Intent-to-treat (ITT) population using last-observation-carried-forward (LOCF) method; all patients who received study medication and had a post-baseline measurement. 44% of BELVIQ patients and 51% of placebo patients withdrew prior to Week 52.

**Warnings and Precautions (cont’d)**

- Patients should not take BELVIQ in combination with drugs that have been associated with valvular heart disease (eg, cabergoline). In clinical trials, 2.4% of patients taking BELVIQ and 2.0% of patients taking placebo developed valvular regurgitation: none of these patients were symptomatic. BELVIQ should be used with caution in patients with congestive heart failure (CHF). Patients who develop signs and symptoms of valvular heart disease, including dyspnea, dependent edema, CHF, or a new cardiac murmur, should be evaluated and discontinuation of BELVIQ should be considered.
Patients taking BELVIQ exhibited a significantly greater decrease in blood pressure (Figure 8) and an improved lipid profile (Figure 9) compared to those taking placebo. Patients taking BELVIQ had a 1.8 mmHg and 1.6 mmHg least-squares mean reduction in systolic and diastolic blood pressure, respectively, compared to 1.0 mmHg and 1.0 mmHg in patients taking placebo.‡20

**Figure 8 Changes in Blood Pressure‡20**

<table>
<thead>
<tr>
<th>Change From Baseline (mmHg)</th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>†</td>
<td>-1.8</td>
<td>-1.6</td>
</tr>
<tr>
<td>*</td>
<td>-1.0</td>
<td>-1.0</td>
</tr>
</tbody>
</table>

**Figure 9 Changes in Lipid Profiles‡20**

<table>
<thead>
<tr>
<th>Change From Baseline (%)</th>
<th>Total Cholesterol</th>
<th>LDL Cholesterol</th>
<th>HDL Cholesterol</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>†</td>
<td>-0.9%</td>
<td>1.6%†</td>
<td>1.8%†</td>
<td>-5.3%†</td>
</tr>
</tbody>
</table>

Limitation of Use:

- The effect of BELVIQ on cardiovascular morbidity and mortality has not been established

Warnings and Precautions (cont’d):

- Impairment in attention, memory, somnolence, confusion, and fatigue, have been reported in patients taking BELVIQ. Patients should not drive a car or operate heavy machinery until they know how BELVIQ affects them.

*ITT population using LOCF method, all patients who received study medication and had a post-baseline measurement. 44% of BELVIQ patients and 51% of placebo patients withdrew prior to Week 52.

† Statistically significant versus placebo.
In the BLOOM study, of the 3182 patients who were randomized in Year 1, 1553 (48.8%) were randomized in Year 2, 1128 of whom completed 2 years of treatment. Patients in all three groups regained weight in Year 2, but remained below their mean baseline weight (Figure 10). Among patients in the BELVIQ 10 mg BID group in Year 1 who had ≥5% weight loss and continued onto Year 2, the 5% loss was maintained in 67.9% of patients who continued to receive BELVIQ 10 mg BID versus 50.3% of patients who were reassigned to placebo (P<0.001).20,25

![Figure 10 Weight Loss in Completer Population Over Two Years of Treatment (BLOOM)](image)

Response to therapy should be evaluated by Week 12. If a patient has not lost at least 5% of baseline body weight, discontinue BELVIQ, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.20 Adverse reactions from the pooled BLOOM/BLOSSOM trials that occurred in more than 5% of patients and more frequently in patients treated with BELVIQ than placebo are listed in Table 5.

| Table 5 Most Common Adverse Reactions in Patients Without Diabetes20 |
|----------------------------------|-------------------|------------------|
| Reaction                        | BELVIQ 10 mg BID (%) | Placebo (%)      |
| Headache                        | 16.8              | 10.1             |
| Dizziness                       | 8.5               | 3.8              |
| Fatigue                         | 7.2               | 3.6              |
| Nausea                          | 8.3               | 5.3              |
| Dry mouth                       | 5.3               | 2.3              |
| Constipation                    | 5.8               | 3.9              |

**Warnings and Precautions (cont’d)**

- The recommended dose of 10 mg twice daily should not be exceeded, as higher doses may cause euphoria, hallucination, and dissociation. Monitor patients for the development or worsening of depression, suicidal thoughts or behaviors, and/or any changes in mood. Discontinue BELVIQ in patients who develop suicidal thoughts or behaviors.
- Men who experience priapism should immediately discontinue BELVIQ and seek emergency medical attention. BELVIQ should be used with caution with erectile dysfunction medications. BELVIQ should be used with caution in men who have conditions that might predispose them to priapism (eg, sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (eg, angulation, cavernosal fibrosis, or Peyronie’s disease).
Efficacy and Safety in Overweight Patients With Diabetes

BLOOM-DM was a randomized, double-blind, placebo-controlled, multicenter Phase 3 clinical trial. A total of 604 patients were randomly assigned to receive BELVIQ 10 mg BID or placebo, and all patients received lifestyle modification counseling. Patients were instructed to exercise moderately for 30 minutes each day and to reduce daily caloric intake to 600 kcal below estimated energy requirements. Treatment duration was 1 year.\textsuperscript{20,27}

Eligible patients had a BMI between 27 kg/m\textsuperscript{2} and 45 kg/m\textsuperscript{2} (average patient BMI was approximately 36 kg/m\textsuperscript{2}) and type 2 diabetes mellitus treated with metformin, a sulfonylurea, or both. Participants were 18–65 years of age, and they had baseline A1C of 7%–10% (mean baseline A1C was 8.1%). More than 54% of trial participants were women, and over 60% of trial participants were Caucasian. Key exclusion criteria included use of insulin in any form, or use of exenatide or pramlintide; history of cardiac valve disease or pulmonary artery hypertension, myocardial infarction, or stroke within 6 months, or unstable angina; bariatric surgery, change in weight ≥5 kg within 3 months; and medical conditions that would preclude participation in a nutritional and physical exercise program.\textsuperscript{20,27}

Coprimary endpoints included percent of patients who achieved ≥5% weight loss and ≥10% weight loss and mean weight change from baseline after 1 year of treatment. Select secondary efficacy endpoints included change from baseline in glycemic control measures, lipids, blood pressure, BMI, and waist circumference.\textsuperscript{27}

251 patients were treated with BELVIQ 10 mg BID, and 248 patients were treated with placebo. Among these patients, 37.5% of patients taking BELVIQ 10 mg BID achieved ≥5% weight loss, and 16.3% achieved ≥10% weight loss, versus 16.1% and 4.4%, respectively, of patients taking placebo (\(P<0.001\) for both)* (see Figure 11). At Week 52, the mean weight loss was 4.5% with BELVIQ versus 1.5% with placebo (\(P<0.001\)).\textsuperscript{20}

![Figure 11 Weight Loss in Overweight Patients With Diabetes*\textsuperscript{20}](image)

> *ITT population using LOCF method, all patients who received study medication and had a post-baseline measurement. 34% of BELVIQ patients and 38% of placebo patients withdrew prior to Week 52.

**Warnings and Precautions (cont’d)**

- Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus who are being treated with antidiabetic medications, so measurement of blood sugar levels before and during treatment with BELVIQ is recommended. Decreases in doses of antidiabetic medications or changes in medication regimen should be considered.
Overweight patients with type 2 diabetes treated with BELVIQ exhibited significant improvements in glycemic control compared to those treated with placebo (Figure 12). Patients taking BELVIQ demonstrated a least-squares means decrease from baseline of 0.9% in HbA1c, compared to 0.4% with placebo. Patients taking BELVIQ also had a decrease of 27.4 mg/dL in fasting plasma glucose levels, compared to 11.9 mg/dL in patients taking placebo.*²⁰

**Figure 12**  Improvement in Glycemic Control*²⁰

<table>
<thead>
<tr>
<th></th>
<th>BELVIQ 10 mg BID (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypoglycemia</strong></td>
<td>29.3</td>
<td>21.0</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td>14.5</td>
<td>7.1</td>
</tr>
<tr>
<td><strong>Back pain</strong></td>
<td>11.7</td>
<td>7.9</td>
</tr>
<tr>
<td><strong>Cough</strong></td>
<td>8.2</td>
<td>4.4</td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td>7.4</td>
<td>4.0</td>
</tr>
</tbody>
</table>

*ITT population using LOCF method, all patients who received study medication and had a post-baseline measurement. 34% of BELVIQ patients and 38% of placebo patients withdrew prior to Week 52.

†Statistically significant versus placebo.

Adverse reactions from the BLOOM-DM trial that occurred in more than 5% of patients and more frequently in patients treated with BELVIQ than placebo are listed in Table 6.²⁰

**Table 6 Most Common Adverse Reactions in Overweight Patients With Diabetes²⁰**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>BELVIQ 10 mg BID (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia</td>
<td>29.3</td>
<td>21.0</td>
</tr>
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<td>Fatigue</td>
<td>7.4</td>
<td>4.0</td>
</tr>
</tbody>
</table>

**Limitation of Use:**

- The effect of BELVIQ on cardiovascular morbidity and mortality has not been established

**Warnings and Precautions (cont’d)**

- Because BELVIQ may cause a slow heartbeat, it should be used with caution in patients with a history of bradycardia or heart block greater than first degree.
- Consider monitoring for CBC changes, prolactin excess, and pulmonary hypertension.
Between the three pivotal Phase 3 clinical trials, 3451 patients were exposed to BELVIQ 10 mg BID, and 3437 patients were exposed to placebo. Of patients taking BELVIQ, 8.6% prematurely discontinued treatment due to adverse reactions, compared with 6.7% for placebo-treated patients. The most common adverse reactions leading to discontinuation more often among patients treated with BELVIQ than placebo were headache (1.3% versus 0.8%), depression (0.9% versus 0.5%) and dizziness (0.7% versus 0.2%).

**Valvular Heart Disease**
Regurgitant cardiac valvular disease has been reported in patients who took serotonergic drugs with 5-HT\textsubscript{2B} receptor agonist activity. The etiology of the regurgitant valvular disease is thought to be activation of 5-HT\textsubscript{2B} receptors on cardiac interstitial cells. At therapeutic concentrations, BELVIQ is selective for 5-HT\textsubscript{2C} receptors as compared to 5-HT\textsubscript{2B} receptors.

Patients enrolled in the clinical trials were also evaluated for incidence of valvulopathy. The incidence of FDA-defined valve abnormalities (mild or greater aortic insufficiency and/or moderate or greater mitral insufficiency) was 2.4% in patients taking BELVIQ 10 mg BID, and 2.0% in patients taking placebo. None of the patients were symptomatic. The pooled relative risk of FDA-defined valvulopathy after 1 year of treatment was 1.16 (95% CI: 0.81, 1.67) for BELVIQ versus placebo.

**Dosing and Administration**
The recommended dose of BELVIQ is 10 mg twice daily, administered orally. Patients should be advised to not exceed the recommended dose. BELVIQ can be taken with or without food. No titration is required.

Response to therapy should be evaluated by Week 12. If a patient has not lost at least 5% of baseline body weight, discontinue BELVIQ, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

**How Supplied/Storage and Handling**
BELVIQ 10-mg tablets are supplied as blue-colored, round, biconvex, film-coated tablets debossed with an “A” on one side and “10” on the other side. BELVIQ is available in bottles of 60 tablets. BELVIQ should be stored at 25°C (77°F), excursions of 15°C–30°C (59°F–86°F) are permitted.

**Most Common Adverse Reactions**
- In patients without diabetes: headache (17%), dizziness (9%), fatigue (7%), nausea (8%), dry mouth (5%), and constipation (6%)
- In patients with diabetes: hypoglycemia (29%), headache (15%), back pain (12%), cough (8%), and fatigue (7%)

**Nursing Mothers**
- BELVIQ should not be taken by women who are nursing.
Summary
Overweight or obesity is a chronic disease with which many patients struggle. For appropriate patients who have attempted to manage their weight with lifestyle modifications but have not achieved their weight loss goals, pharmacotherapy is an option that should be considered. BELVIQ is a novel pharmacotherapeutic agent for the treatment of overweight individuals with at least one weight-related comorbid condition or obesity (a summary of BELVIQ information presented in this monograph can be found in Table 7). Providing patients with tools to combat overweight or obesity, such as BELVIQ in appropriate patients, may help them progress in their weight management.

Table 7  BELVIQ Essential Information

| Indication | Patients with a BMI of ≥30 kg/m², or with a BMI of ≥27 kg/m² and at least one comorbid condition  
BELVIQ is indicated in conjunction with a reduced-calorie diet and increased physical activity  
Limitations of Use | The safety and efficacy of coadministration of BELVIQ with other products intended for weight loss, including prescription drugs (eg, phentermine), over-the-counter drugs, and herbal preparations, have not been established  
The effect of BELVIQ on cardiovascular morbidity and mortality has not been established  
Mechanism of Action | Believed to increase satiety and suppress appetite by selectively activating serotonin 2C receptors  
The exact mechanism of action is not known  
Efficacy | More patients taking BELVIQ lost ≥5% and ≥10% of baseline body weight compared to placebo  
Patients on BELVIQ exhibited improvements in cardiometabolic parameters, including blood pressure, HDL, triglycerides, and glycemic control, compared to patients on placebo  
Safety | Most common adverse reactions in overweight patients without diabetes were headache, dizziness, fatigue, nausea, dry mouth, and constipation  
Most common adverse reactions in overweight patients with diabetes were hypoglycemia, headache, back pain, cough, and fatigue  
Dosing | The recommended dose of BELVIQ is 10 mg administered orally twice daily  
BELVIQ can be taken with or without food  
Response to therapy should be evaluated by Week 12. If a patient has not lost at least 5% of baseline body weight, discontinue BELVIQ, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment |

For complete information on BELVIQ, please refer to the full Prescribing Information located in the pocket.

Warnings and Precautions
BELVIQ is a serotonergic drug. The development of potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported during use of serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors, tricyclic antidepressants, bupropion, triptans, dietary supplements such as St. John’s Wort and tryptophan, drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors), dextromethorphan, lithium, tramadol, antipsychotics or other dopamine antagonists, particularly when used in combination. Patients should be monitored for the emergence of serotonin syndrome symptoms or NMS-like reactions, including agitation, hallucinations, coma, tachycardia, labile blood pressure, hyperthermia, hyperreflexia, incoordination, nausea, vomiting, diarrhea, and muscle rigidity. Treatment with BELVIQ and any concomitant serotonergic or antidopaminergic agents should be discontinued immediately if the above events occur, and supportive symptomatic treatment should be initiated.
Warnings and Precautions (cont’d)

- Patients should not take BELVIQ in combination with drugs that have been associated with valvular heart disease (e.g., cabergoline). In clinical trials, 2.4% of patients taking BELVIQ and 2.0% of patients taking placebo developed valvular regurgitation: none of these patients were symptomatic. BELVIQ should be used with caution in patients with congestive heart failure (CHF). Patients who develop signs and symptoms of valvular heart disease, including dyspnea, dependent edema, CHF, or a new cardiac murmur, should be evaluated and discontinuation of BELVIQ should be considered.

### ADDITIONAL PHARMACOLOGICAL INFORMATION

The role of the pharmacist in supporting patients who are taking BELVIQ is extremely important. In this section you will find critical pharmacologic information about BELVIQ, as well as counseling tips for helping your patients adhere to a diet and physical activity regimen, which is essential while taking BELVIQ.

#### Pharmacodynamics

**Cardiac Electrophysiology**

The effect of multiple oral doses of lorcaserin 15 mg and 40 mg once daily on QTc interval was evaluated in a randomized, placebo- and active-controlled (moxifloxacin 400 mg) 4-treatment arm parallel QT study in 244 healthy subjects. In a study with demonstrated ability to detect small effects, the upper bound of the one-sided 95% confidence interval for the largest placebo-adjusted, baseline-corrected QTc based on individual correction method (QTci) was below 10 ms, the threshold for regulatory concern.20

#### Pharmacokinetics

For a summary of key pharmacokinetic parameters, see Table 8.

<table>
<thead>
<tr>
<th>Table 8 Pharmacokinetic Parameters of BELVIQ20</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absorption</strong></td>
</tr>
<tr>
<td>- Plasma half-life is ~11 hours</td>
</tr>
<tr>
<td>- C_{max} occurs within 2 hours</td>
</tr>
<tr>
<td>- Steady state occurs within 3 days</td>
</tr>
<tr>
<td>- Food does not significantly affect absorption</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
</tr>
<tr>
<td>- ~70% bound to plasma proteins</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
</tr>
<tr>
<td>- Lorcaserin is extensively metabolized in the liver</td>
</tr>
<tr>
<td>- The principal metabolites exert no pharmacological activity at serotonin receptors</td>
</tr>
<tr>
<td><strong>Elimination</strong></td>
</tr>
<tr>
<td>- Lorcaserin and related metabolites are excreted in the urine</td>
</tr>
<tr>
<td>- 94.5% of the initial dose is recovered</td>
</tr>
</tbody>
</table>

20
Pharmacokinetics in Special Populations

Renal Impairment

Exposure of M1 was increased in patients with impaired renal function by approximately 1.7-fold in mild, 2.3-fold in moderate, and 10.5-fold in severe renal impairment compared with normal subjects. Exposure of M5 was increased in patients with impaired renal function by approximately 1.5-fold in mild, 2.5-fold in moderate, and 5.1-fold in severe renal impairment compared with normal subjects. The terminal half-life of M1 is prolonged by 26%, 96%, and 508% in mild, moderate, and severe renal impairment, respectively. The terminal half-life of M5 is prolonged by 0%, 26%, and 22% in mild, moderate, and severe renal impairment, respectively. The metabolites M1 and M5 accumulate in patients with severely impaired renal function. Approximately 18% of M5 in the body was cleared during a standard 4-hour hemodialysis procedure. Lorcaserin and M1 were not cleared by hemodialysis. No dose adjustment of BELVIQ is required in patients with mild renal impairment. Use BELVIQ with caution in patients with moderate renal impairment. BELVIQ is not recommended for patients with severe renal impairment or patients with end-stage renal disease.20

Hepatic Impairment

Dose adjustment is not required for patients with mild to moderate hepatic impairment. Lorcaserin C_{max} was 7.8% and 14.3% lower in subjects with mild and moderate hepatic impairment, respectively, than in subjects with normal hepatic function. The half-life of lorcaserin is prolonged by 59% to 19 hours in patients with moderate hepatic impairment. Lorcaserin exposure (AUC) is approximately 22% and 30% higher in patients with mild and moderate hepatic impairment, respectively. The effect of severe hepatic impairment on BELVIQ was not evaluated, therefore use with caution.20

Gender

No dosage adjustment based on gender is necessary. Gender did not meaningfully affect the pharmacokinetics of lorcaserin.20

Geriatric

No dosage adjustment is required based on age alone. In a clinical trial of 12 healthy elderly subjects (ages greater than 65 years) and 12 matched adult patients, C_{max} was approximately 18% lower in the elderly group, and T_{max} was increased from 2 hours to 2.5 hours in the elderly group as compared to the non-elderly adult group.20

Race

No dosage adjustment based on race is necessary. Race did not meaningfully affect the pharmacokinetics of lorcaserin.20

Warnings and Precautions (cont’d)

- Impairment in attention, memory, somnolence, confusion, and fatigue, have been reported in patients taking BELVIQ. Patients should not drive a car or operate heavy machinery until they know how BELVIQ affects them.
- The recommended dose of 10 mg twice daily should not be exceeded, as higher doses may cause euphoria, hallucination, and dissociation. Monitor patients for the development or worsening of depression, suicidal thoughts or behaviors, and/or any changes in mood. Discontinue BELVIQ in patients who develop suicidal thoughts or behaviors.

Nursing Mothers

- BELVIQ should not be taken by women who are nursing.
Potential Drug Interactions
Based on the mechanism of action of BELVIQ and the theoretical potential for serotonin syndrome, use with extreme caution in combination with other drugs that may affect the serotonergic neurotransmitter systems, including, but not limited to20:

- Triptans
- Monoamine oxidase inhibitors (MAOIs)
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin-norepinephrine reuptake inhibitors (SNRIs)
- Dextromethorphan

- Tricyclic antidepressants (TCAs)
- Bupropion
- Lithium
- Tramadol
- Tryptophan
- St. John’s Wort

Lorcaserin inhibits CYP2D6-mediated metabolism. In a clinical trial in 21 CYP2D6 extensive metabolizers, concomitant administration of lorcaserin (10 mg BID for 4 days) increased dextromethorphan peak concentrations ($C_{max}$) by approximately 76%, and exposure (AUC) by approximately 2-fold20.

PATIENT COUNSELING TIPS

The Role of the Pharmacist
Weight management is a chronic condition, and patients who are attempting any kind of weight loss therapy face several daily challenges. Regular support from a healthcare provider, such as a pharmacist, is critical for the success of the patient in achieving their weight management goals.5 It is important to take measures that encourage patients to feel comfortable seeking advice when facing difficulty with their treatment program. Successful weight management is associated with certain patient attitudes and behaviors which should be encouraged, such as57:

- Reaching a self-determined goal
- Having a physically active lifestyle
- A regular meal rhythm including breakfast and healthier eating
- Control of overeating
- Self-monitoring of behaviors
- Internal motivation to lose weight
- Social support
- Better coping strategies and ability to handle life stress
- Autonomy
- Assuming responsibility in life
- Overall, more psychological strength and stability

Warnings and Precautions (cont’d)
Weight loss may increase the risk of hypoglycemia in patients with type 2 diabetes mellitus who are being treated with antidiabetic medications, so measurement of blood sugar levels before and during treatment with BELVIQ is recommended. Decreases in doses of antidiabetic medications or changes in medication regimen should be considered.
Lifestyle Counseling
BELVIQ is indicated for chronic weight management only in conjunction with a reduced-calorie diet and increased physical activity. Patients should consult their doctor about appropriate goals for caloric intake and physical activity levels. A reasonable goal for weight loss while taking BELVIQ is to lose 5% of baseline body weight in 12 weeks. Individual results may vary, and response to therapy should be evaluated by Week 12. If a patient has not lost at least 5% of baseline body weight, discontinue BELVIQ, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.20

Nutrition
A balanced, healthful diet is an essential aspect of losing weight with BELVIQ. Important nutritional information about which patients should be educated include:

- Energy value of different foods
- Food composition—fats, carbohydrates (including dietary fiber), and proteins
- Reading nutritional labels to determine caloric content
- New habits of purchasing—preference for low-calorie foods
- Food preparation—avoiding adding high-calorie ingredients (eg, fats and oils)
- Avoiding overconsumption of high-calorie foods (both high-fat and high-carbohydrate foods)
- Maintaining adequate water intake
- Reducing portion sizes
- Limiting alcohol consumption

For education about nutritional requirements and meal planning, patients can be referred to www.choosemyplate.gov. If a more structured plan is necessary, or if a patient has specific dietary restrictions, he or she should be referred to a registered dietitian.

Physical Activity
Engaging in physical activity can be a challenge for overweight or obese patients. Fear of stigma may lead to overweight or obese patients avoiding exercise.28 Exercising with friends or a support group can ease some of these fears and make the experience more of a social outing than an arduous obligation. Encourage patients to take advantage of available technology such as pedometers or smartphone apps like MyFitnessPal to track their progress. For patients who have not been physically active in the past, advise them to start slowly to avoid injury. Counsel patients that they can incorporate physical activity into their everyday life, without having to go to the gym. Examples of ways to add more physical activity into daily routines can be found in Table 9. Overall, patients should be encouraged to try a variety of activities to find what is most enjoyable for them.29

Table 9  Physical Activities in Everyday Life29,30

<table>
<thead>
<tr>
<th>Activity</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take a walk with your coworker during lunchtime</td>
<td>Take a lap around the mall before starting to shop</td>
</tr>
<tr>
<td>Take the stairs instead of the elevator</td>
<td>Park your car at the farthest space</td>
</tr>
<tr>
<td>Get off the subway or bus a stop early and walk</td>
<td>Use hand weights or stretch while watching TV</td>
</tr>
</tbody>
</table>

Warnings and Precautions (cont’d)
- Men who experience priapism should immediately discontinue BELVIQ and seek emergency medical attention. BELVIQ should be used with caution with erectile dysfunction medications. BELVIQ should be used with caution in men who have conditions that might predispose them to priapism (eg, sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (eg, angulation, cavernosal fibrosis, or Peyronie’s disease).
REFERENCES

Please read US full Prescribing Information for BELVIQ® (lorcaserin HCl) located in the pocket.