Teva cordially invites you to a presentation & discussion entitled:

Demystifying Extrapyramidal Symptoms (EPS): Tardive Dyskinesia Is Distinct and Informing Treatment Decisions in TD Patient Assessment and Monitoring

Moderated by:

Arvinder Walia, MD
Chief Medical Officer and Medical Director
DBT Intensive Outpatient Program Austin Center for Psychological Care, Austin, Texas

On

Wednesday, February 6, 2019 at 6:30 PM

At
Paesano's Lincoln Heights
555 East Basse Road
San Antonio, TX 78209
(210) 828-5191

Please RSVP to:
Kristin Caddell - (318) 426-2424

In accordance with the PhRMA Code on Interactions with Healthcare Professionals, attendance at this program is limited to healthcare professionals. Accordingly, attendance by non-clinical guests or spouses is not permitted.

2019-TEVA-US-SB-0008926

Indications and Usage
AUSTEDO® is indicated for the treatment of chorea associated with Huntington’s disease and for the treatment of tardive dyskinesia in adults.

Important Safety Information
Depression and Suicidality in Patients with Huntington’s Disease: AUSTEDO® can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington’s disease. Balance the risks of depression and suicidality with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior. Inform patients, their caregivers, and families of the risk of depression and suicidality and instruct them to report behaviors of concern promptly to the treating physician. Exercise caution when treating patients with a history of depression or prior suicide attempts or ideation. AUSTEDO® is contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression.

Please see Important Safety Information continued on next page and accompanying full Prescribing Information, including Boxed Warning.
Important Safety Information (continued)

Contraindications: AUSTEDO® (deutetrabenazine) tablets is contraindicated in patients with Huntington’s disease who are suicidal, or have untreated or inadequately treated depression. AUSTEDO® is also contraindicated in: patients with hepatic impairment; patients taking reserpine or within 20 days of discontinuing reserpine; patients taking monoamine oxidase inhibitors (MAOIs), or within 14 days of discontinuing MAOI therapy; and patients taking tetrabenazine (Xenazine®) or valbenazine (Ingrezza™).

Clinical Worsening and Adverse Events in Patients with Huntington’s Disease: AUSTEDO® may cause a worsening in mood, cognition, rigidity, and functional capacity. Prescribers should periodically re-evaluate the need for AUSTEDO® in their patients by assessing the effect on chorea and possible adverse effects.

QTc Prolongation: Tetrabenazine, a closely related VMAT2 inhibitor, causes an increase in the corrected QT (QTc) interval. A clinically relevant QT prolongation may occur in some patients treated with AUSTEDO® who are CYP2D6 poor metabolizers or are co-administered a strong CYP2D6 inhibitor. Dose reduction may be necessary. The use of AUSTEDO® in combination with other drugs known to prolong QTc may result in clinically significant QT prolongations. For patients requiring AUSTEDO® doses greater than 24 mg per day who are using AUSTEDO® with other drugs known to prolong QTc, assess the QTc interval before and after increasing the dose of AUSTEDO® or the other drugs. AUSTEDO® should be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias.

Neuroleptic Malignant Syndrome (NMS), a potentially fatal symptom complex reported in association with drugs that reduce dopaminergic transmission, has been observed in patients receiving tetrabenazine. The risk may be increased by concomitant use of dopamine antagonists or antipsychotics. The management of NMS should include immediate discontinuation of AUSTEDO®, intensive symptomatic treatment and medical monitoring; and treatment of any concomitant serious medical problems.

Akathisia, Agitation, and Restlessness: AUSTEDO® may increase the risk of akathisia, agitation, and restlessness. The risk of akathisia may be increased by concomitant use of dopamine antagonists or antipsychotics. If a patient develops akathisia, the AUSTEDO® dose should be reduced; some patients may require discontinuation of therapy.

Parkinsonism in Patients with Huntington’s Disease: AUSTEDO® may cause parkinsonism in patients with Huntington’s disease. The risk of parkinsonism may be increased by concomitant use of dopamine antagonists or antipsychotics. If a patient develops parkinsonism, the AUSTEDO® dose should be reduced; some patients may require discontinuation of therapy.

Sedation and Somnolence: Sedation is a common dose-limiting adverse reaction of AUSTEDO®. Patients should not perform activities requiring mental alertness, such as operating a motor vehicle or hazardous machinery, until they are on a maintenance dose of AUSTEDO® and know how the drug affects them. Concomitant use of alcohol or other sedating drugs may have additive effects and worsen sedation and somnolence.

Hyperprolactinemia: Tetrabenazine elevates serum prolactin concentrations in humans. If there is a clinical suspicion of symptomatic hyperprolactinemia, appropriate laboratory testing should be done and consideration should be given to discontinuation of AUSTEDO®.

Binding to Melanin-Containing Tissues: Deutetrabenazine or its metabolites bind to melanin-containing tissues and could accumulate in these tissues over time. Prescribers should be aware of the possibility of long-term ophthalmologic effects.

Please see Important Safety Information continued on next page and accompanying full Prescribing Information, including Boxed Warning.
Important Safety Information (continued)

**CYP2D6 Metabolism:** In patients who are poor CYP2D6 metabolizers or are taking strong CYP2D6 inhibitors, the total daily dosage of AUSTEDO® (deutetrabenazine) tablets should not exceed 36 mg (maximum single dose of 18 mg).

**Common Adverse Reactions:** The most common adverse reactions for AUSTEDO® (>8% and greater than placebo) in a controlled clinical study in patients with Huntington’s disease were somnolence, diarrhea, dry mouth, and fatigue. The most common adverse reactions for AUSTEDO® (4% and greater than placebo) in controlled clinical studies in patients with tardive dyskinesia were nasopharyngitis and insomnia.

Please see accompanying full Prescribing Information, including Boxed Warning.
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AUSTEDO safely and effectively. See full prescribing information for AUSTEDO.

AUSTEDO® (deutetrabenazine) tablets, for oral use
Initial U.S. Approval: 2017

WARNING: DEPRESSION AND SUICIDALITY IN PATIENTS WITH HUNTINGTON’S DISEASE
See full prescribing information for complete boxed warning.
• Increases the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington’s disease (5.1)
• Balance risks of depression and suicidality with the clinical need for treatment of chorea when considering the use of AUSTEDO (5.1)
• Monitor patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior (5.1)
• Informs patients, caregivers, and families of the risk of depression and suicidality and instructs to report behaviors of concern promptly to the treating physician (5.1)
• Exercise caution when treating patients with a history of depression or prior suicide attempts or ideation (5.1)
• AUSTEDO is contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression (4.5, 5.1)

RECENT MAJOR CHANGES
Boxed Warning
8/2017
Indications and Usage (1) 08/2017
Dosage and Administration (2.1) 08/2017
Contraindications (4) 08/2017
Warnings and Precautions (5.1, 5.2, 5.3, 5.5, 5.7) 08/2017

INDICATIONS AND USAGE
AUSTEDO is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of:
• Chorea associated with Huntington’s disease (1)
• Tardive dyskinesia in adults (1)

DOSEAGE AND ADMINISTRATION

<table>
<thead>
<tr>
<th>Chorea associated with Huntington’s disease</th>
<th>Initial Dose</th>
<th>Recommended Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mg/day</td>
<td>6 mg-48 mg/day</td>
<td>48 mg/day</td>
<td></td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td>12 mg/day</td>
<td>12 mg-48 mg/day</td>
<td>48 mg/day</td>
</tr>
</tbody>
</table>

• Titrate at weekly intervals by 6 mg per day based on reduction of chorea or tardive dyskinesia, and tolerability, to a maximum recommended daily dosage of 48 mg (24 mg twice daily) (2.1)
• Administer total daily doses of 12 mg or above in two divided doses (2.1)

FULL PRESCRIBING INFORMATION: CONTENTS*
WARNING: DEPRESSION AND SUICIDALITY IN PATIENTS WITH HUNTINGTON’S DISEASE
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Dosing Information
2.2 Switching Patients from Tetrabenazine (XENAZINE®) to AUSTEDO
2.3 Dosage Adjustment with Strong CYP2D6 Inhibitors
2.4 Dosage Adjustment in Poor CYP2D6 Metabolizers
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FULL PRESCRIBING INFORMATION

WARNING: DEPRESSION AND SUICIDALITY IN PATIENTS WITH HUNTINGTON’S DISEASE
AUSTEDO can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington’s disease. Anyone considering the use of AUSTEDO must balance the risks of depression and suicidality with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior. Patients, their caregivers, and families should be informed of the risk of depression and suicidality and should be instructed to report behaviors of concern promptly to the treating physician.

Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency with Huntington’s disease. AUSTEDO is contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression (see Contraindications (4) and Warnings and Precautions (6.1)).

1 INDICATIONS AND USAGE
AUSTEDO is indicated for the treatment of:

- chorea associated with Huntington’s disease (see Clinical Studies [14.1])
- tardive dyskinesia in adults (see Clinical Studies [14.2])

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The dose of AUSTEDO is determined individually for each patient based on reduction of chorea or tardive dyskinesia and tolerability. When first prescribed to patients who are not being switched from tetrabenazine (a related VMT2 inhibitor), the recommended starting dose of AUSTEDO is 6 mg administered orally once daily for patients with Huntington’s disease and 12 mg per day (6 mg twice daily) for patients with tardive dyskinesia.

- The dose of AUSTEDO may be increased at weekly intervals in increments of 6 mg per day to a maximum recommended daily dosage of 48 mg.
- Administer total daily doses of 12 mg or above in two divided doses.
- Administer AUSTEDO with food (see Clinical Pharmacology [12.5]).
- Slow AUSTEDO titration. Do not chew, crush, or break tablets.
- For patients at risk for QT prolongation, assess the QT interval before and after increasing total AUSTEDO dosage above 24 mg per day (see Warnings and Precautions [5.3] and Drug Interactions [7.2]).

2.2 Switching Patients from Tetrabenazine (XENAZINE) to AUSTEDO

Discontinue tetrabenazine (XENAZINE) and initiate AUSTEDO the following day. The recommended initial dosing regimen of AUSTEDO in patients switching from tetrabenazine (XENAZINE) to AUSTEDO is shown in Table 1.

Table 1: Recommended Initial Dosing Regimen when Switching from Tetrabenazine (XENAZINE) to AUSTEDO

<table>
<thead>
<tr>
<th>Current tetrabenazine daily dosage</th>
<th>Initial regimen of AUSTEDO</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5 mg</td>
<td>6 mg once daily</td>
</tr>
<tr>
<td>25 mg</td>
<td>6 mg twice daily</td>
</tr>
<tr>
<td>37.5 mg</td>
<td>5 mg twice daily</td>
</tr>
<tr>
<td>50 mg</td>
<td>12.5 mg twice daily</td>
</tr>
<tr>
<td>62.5 mg</td>
<td>15 mg twice daily</td>
</tr>
<tr>
<td>75 mg</td>
<td>18 mg twice daily</td>
</tr>
<tr>
<td>87.5 mg</td>
<td>21 mg twice daily</td>
</tr>
<tr>
<td>100 mg</td>
<td>24 mg twice daily</td>
</tr>
</tbody>
</table>

After patients are switched to AUSTEDO, the dose may be adjusted at weekly intervals (see Dosage and Administration [2.1]).

2.3 Dosage Adjustment with Strong CYP2D6 Inhibitors

In patients receiving strong CYP2D6 inhibitors (e.g., quinidine, antidepressants such as paroxetine, fluoxetine, and bupropion), the total daily dosage of AUSTEDO should not exceed 35 mg (maximum single dose of 15 mg) (see Drug Interactions [7.1] and Clinical Pharmacology [12.3]).

2.4 Dosage Adjustment in Poor CYP2D6 Metabolizers

In patients who are poor CYP2D6 metabolizers, the total daily dosage of AUSTEDO should not exceed 35 mg (maximum single dose of 15 mg) (see Use in Specific Populations [8.7]).

2.5 Discontinuation and Interruption of Treatment

Treatment withdrawal can be discontinued without tapering. Follow-up treatment interruption of greater than one week, AUSTEDO therapy should be re-initiated when resumed. For treatment interruption of less than one week, treatment can be resumed at the previous maintenance dose without interruption.

3 DOSAGE FORMS AND STRENGTHS

AUSTEDO tablets are available in the following strengths:

- The 6 mg tablets are round, purple-coated tablets, with “SD” over “6” printed in black ink on one side.
- The 9 mg tablets are round, blue-coated tablets, with “SD” over “9” printed in black ink on one side.
- The 12 mg tablets are round, beige-coated tablets, with “SD” over “12” printed in black ink on one side.

4 CONTRAINDICATIONS

AUSTEDO is contraindicated in patients:

- With Huntington’s disease who are suicidal, or have untreated or inadequately treated depression [see Warnings and Precautions (5.1)]
- With hepatic impairment [see Use in Specific Populations (1.6), Clinical Pharmacology (12.3)]
- Taking reserpine. At least 20 days should elapse after stopping reserpine before starting AUSTEDO [see Drug Interactions (7.6)]
- Taking monoamine oxidase inhibitors (MAOIs). AUSTEDO should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with an MAOI [see Drug Interactions (7.7)]
- Taking tetrabenazine (XENAZINE) or valbenzine [see Drug Interactions (7.7)].

5.1 Depression and Suicidality in Patients with Huntington’s Disease

Patients with Huntington’s disease are at increased risk for depression, and suicidal ideation or behaviors (suicidality). AUSTEDO may increase the risk for suicidality in patients with Huntington’s disease.

In a 12-week, double-blind, placebo-controlled trial, suicidal ideation was reported by 2% of patients treated with AUSTEDO compared to 0% of placebo; no suicide attempts and no completed suicides were reported. Depression was reported by 4% of patients treated with AUSTEDO.

When considering the use of AUSTEDO, the risk of suicidality should be balanced against the need for treatment of chorea. All patients treated with AUSTEDO should be observed for new or worsening depression or suicidality. If depression or suicidality does not resolve, consideration of discontinuing treatment with AUSTEDO should be given. Patients, their caregivers, and families should be informed of the risks of depression, worsening depression, and suicidality associated with AUSTEDO, and should be instructed to report behaviors of concern promptly to the treating physician. Patients with Huntington’s disease who express suicidal ideation should be evaluated immediately.

5.2 Clinical Worsening and Adverse Events in Patients with Huntington’s Disease

Huntington’s disease is a progressive disorder characterized by changes in mood, cognition, chorea, rigidity, and functional capacity over time. VA123 inhibitors, including AUSTEDO, may cause a worsening in mood, cognition, rigidity, and functional capacity. Prescribers should periodically re-evaluate the need for AUSTEDO in their patients by assessing the effect on chorea and possible adverse effects, including sedation/somnia, depression, and suicidality, parkinsonism, akathisia, restlessness, and cognitive decline. It may be difficult to distinguish between adverse reactions and symptoms that are part of the underlying disease; decreasing the dose or stopping the drug may help the clinician to distinguish between the two possibilities. In some patients, the underlying disease itself may improve over time, decreasing the need for AUSTEDO.

5.3 QTc Prolongation

Tetrabenazine, a closely related VMAT2 inhibitor, causes an increase (about 8 msec) in the corrected QT (QTc) interval. A clinically relevant QTc prolongation may occur in some patients treated with AUSTEDO who are CYP2D6 poor metabolizers or are co-administered a strong CYP2D6 inhibitor [see Clinical Pharmacology (12.2, 12.3)].

For patients who are CYP2D6 poor metabolizers or are taking a strong CYP2D6 inhibitor, dose reduction may be necessary [see Dosage and Administration (2.3, 2.4)]. The use of AUSTEDO in combination with other drugs that are known to prolong QTc may result in clinically significant QT prolongations [see Drug Interactions (7.2)].

Patients requiring AUSTEDO dose reduction should be avoided with AUSTEDO with other drugs known to prolong QTc, assess the QTc interval before and after increasing the dose of AUSTEDO or other medications that are known to prolong QTc. AUSTEDO should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. Certain circumstances may increase the risk of occurrence of torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval, including (1) bradycardia, (2) hypokalemia or hypomagnesemia, (3) concomitant use of other drugs that prolong the QTc interval, and (4) presence of congenital prolongation of the QT interval.

5.4 Neuroleptic Malignant Syndrome (NMS)

A potentially fatal symptom complex sometimes referred to as Neuromuscular Malignant Syndrome (NMS) has been reported in association with drugs that reduce dopamine transmission. While NMS has been observed in patients receiving AUSTEDO, it has been observed in patients receiving tetrabenazine (a closely related VMAT2 inhibitor). Clinicians should be alerted to the signs and symptoms associated with NMS. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria, rhabdomyolysis, and acute renal failure. The diagnosis of NMS may be complicated by other serious medical illness (e.g., pneumonia, systemic infection) and untreated or inadequately treated extrapyramidal disorders can present with similar signs and symptoms. Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology. The management of NMS should include (1) immediate discontinuation of AUSTEDO; (2) supportive symptomatic treatment and medical monitoring; and (3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for NMS.

Recurrence of NMS has been reported with resumption of drug therapy. If treatment with AUSTEDO is needed after recovery from NMS, patients should be monitored for signs of recurrence.
5.5 Akathisia, Agitation, and Restlessness

*AUSTEDO* increase the risk of akathisia, agitation, and restlessness in patients with Huntington’s disease and tardive dyskinesia. In a 12-week, double-blind, placebo-controlled trial in Huntington’s disease patients, akathisia, agitation, or restlessness was reported by 4% of patients treated with *AUSTEDO*, compared to 2% of patients on placebo. In patients with tardive dyskinesia, 2% of patients treated with *AUSTEDO* and 1% of patients on placebo experienced these events.

Patients receiving *AUSTEDO* should be monitored for signs and symptoms of restlessness and agitation, as these may be indicators of developing akathisia. If a patient develops akathisia during treatment with *AUSTEDO*, the *AUSTEDO* dose should be reduced; some patients may require discontinuation of therapy.

5.6 Parkinsonism in Patients with Huntington’s Disease

*AUSTEDO* may cause parkinsonism in patients with Huntington’s disease. Because rigidity can develop as part of the underlying disease process in Huntington’s disease, it is difficult to distinguish between this potential drug-induced adverse reaction and progression of the underlying disease process. Drug-induced parkinsonism has the potential to cause more functional disability than untreated chorea for some patients with Huntington’s disease. If a patient develops parkinsonism during treatment with *AUSTEDO*, the *AUSTEDO* dose should be reduced; some patients may require discontinuation of therapy.

5.7 Sedation and Somnolence

Sedation is a common dose-limiting adverse reaction of *AUSTEDO*. In a 12-week, double-blind, placebo-controlled trial examining patients with Huntington’s disease, 11% of *AUSTEDO*-treated patients reported somnolence compared with 4% of patients on placebo and 9% of *AUSTEDO*-treated patients reported fatigue compared with 4% of placebo-treated patients.

Patients should not perform activities requiring mental alertness to maintain the safety of themselves or others, such as operating a motor vehicle or operating hazardous machinery, until they are on a maintenance dose of *AUSTEDO* and know how the drug affects them.

5.8 Hyperprolactinemia

Serum prolactin levels were not evaluated in the *AUSTEDO* development program. Tetrabenazine, a closely related VMAT2 inhibitor, elevates serum prolactin concentrations in humans following administration of 25 mg of tetrabenazine to healthy volunteers, peak plasma prolactin levels increased 4- to 5-fold. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent in vitro, a factor of potential importance if *AUSTEDO* is being considered for a patient with previously detected breast cancer. Although amenorrhea, galactorrhea, gynecomastia, and impotence can be caused by elevated serum prolactin concentrations, the clinical significance of elevated serum prolactin concentrations for most patients is unknown. Chronic increase in serum prolactin levels (although not evaluated in the *AUSTEDO* or tetrabenazine development programs) has been associated with low levels of estrogen and increased risk of osteoporosis. If there is a clinical suspicion of symptomatic hyperprolactinemia, appropriate laboratory testing should be done and contraception should be given to discontinuation of *AUSTEDO*.

5.9 Binding to Melanin-Containing Tissues

Since deuterobenazine or its metabolites bind to melanin-containing tissues, it could accumulate in these tissues over time. This raises the possibility that *AUSTEDO* may cause toxicity in these tissues after extended use. Neither ophthalmologic nor microscopic examination of the eye has been conducted in the chronic toxicity studies in a pigmented species such as dogs. Ophthalmologic monitoring in humans was insufficient to exclude the possibility of injury occurring after long-term exposure. The clinical relevance of deuterobenazine’s binding to melanin-containing tissues is unknown. Although there are no specific recommendations for periodic ophthalmologic monitoring, prescribers should be aware of the possibility of long-term ophthalmic effects [see Clinical Pharmacology (12.5)].

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Depression and Suicidality in Patients with Huntington’s disease [see Warnings and Precautions (5.1)]
- QT Prolongation [see Warnings and Precautions (5.5)]
- Neuroleptic Malignant Syndrome (NMS) [see Warnings and Precautions (5.4)]
- Akathisia, Agitation, and Restlessness [see Warnings and Precautions (5.5)]
- Parkinsonism in Patients with Huntington’s disease [see Warnings and Precautions (5.6)]
- Sedation and Somnolence [see Warnings and Precautions (5.7)]
- Hyperprolactinemia [see Warnings and Precautions (5.8)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Patients with Huntington’s Disease

Study 1 was a randomized, 12-week, placebo-controlled study in patients with chorea associated with Huntington’s disease. A total of 45 patients received *AUSTEDO*, and 45 patients received placebo. Patients ranged in age between 25 and 74 years (mean 54.4, median 61); 69% were male, and 31% were female. The most common adverse reactions occurring in greater than 5% of *AUSTEDO*-treated patients were somnolence, diarrhea, dry mouth, and fatigue. Adverse reactions occurring in 4% or more of patients treated with *AUSTEDO*, and with a greater incidence than in patients on placebo, are summarized in Table 2.

Table 2: Adverse Reactions in Patients with Huntington’s Disease (Study 1) Experienced by at Least 4% of Patients on *AUSTEDO* and with a Greater Incidence than on Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>AUSTEDO</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=45)</td>
<td>(N=45)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Insomnia</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Anxiety</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Constipation</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Contusion</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

One or more adverse reactions resulted in a reduction of the dose of study medication in 7% of patients in Study 1. The most common adverse reaction resulting in dose reduction in patients receiving *AUSTEDO* was dizziness (4%).

Although agitation led to discontinuation in 2% of patients treated with *AUSTEDO* in study 1.

Patients with Tardive Dyskinesia

The data described below reflect 410 patients with tardive dyskinesia patients participating in clinical trials. *AUSTEDO* was studied primarily in two 12-week, placebo-controlled trials (fixed dose, dose escalation). The population was 18 to 80 years of age, and had tardive dyskinesia and had concurrent diagnoses of mood disorder (33%) or schizophrenia/schizoaffective disorder (65%). In these studies *AUSTEDO* was administered in doses ranging from 12-48 mg per day. All patients continued on previous stable regimens of antipsychotics, 71% and 14% respective atypical and typical antipsychotic medications at study entry.

The most common adverse reaction occurring in greater than 5% of *AUSTEDO*-treated patients and greater than placebo were nasopharyngitis and insomnia. The adverse reactions occurring in 2% or more patients treated with *AUSTEDO* (12.48 mg per day) and greater than in placebo patients in two double-blind, placebo-controlled studies in patients with tardive dyskinesia (Study 1 and Study 2) are summarized in Table 3:

Table 3: Adverse Reactions in Placebo-Controlled Tardive Dyskinesia Studies (Study 1 and Study 2) of 12-week Treatment with *AUSTEDO* Reported in at Least 2% of Patients and Greater than Placebo

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>AUSTEDO (N=275)</th>
<th>Placebo (N=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>4 (1.5)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4 (1.5)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Depression/Dysphoric disorder</td>
<td>4 (1.5)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Akathisia/Agiton/Restlessness</td>
<td>2 (0.7)</td>
<td>2 (1.5)</td>
</tr>
</tbody>
</table>

One or more adverse reactions resulted in a reduction of the dose of study medication in 4% of *AUSTEDO*-treated patients and in 2% of placebo-treated patients.

7 DRUG INTERACTIONS

7.1 Strong CYP2D6 Inhibitors

A reduction in *AUSTEDO* dose may be necessary when increasing a strong CYP2D6 inhibitor in patients maintained on a stable dose of *AUSTEDO*. Concurrent use of strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) has been shown to increase the systemic exposure to the active dehydrometabolites of deuterobenazine by approximately 5-fold. The daily dose of *AUSTEDO* should not exceed 50 mg per day, and the maximum single dose of *AUSTEDO* should not exceed 10 mg in patients taking strong CYP2D6 inhibitors [see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)].

7.2 Drugs that Cause QT Prolongation

Tetrahydrobenazine, a closely related VMAT2 inhibitor, may cause increase in the corrected QT (QTc) interval. Clinically relevant QT prolongation may also occur with *AUSTEDO* [see Warnings and Precautions (5.3), Clinical Pharmacology (12.3)]. For patients receiving *AUSTEDO* doses above 24 mg per day who are using *AUSTEDO* in combination with other drugs known to prolong QTc, assess the QTc interval before and after increasing the dose of *AUSTEDO* or other medications that are known to prolong QTc. Drugs known to prolong QTc include anticholinergic medications (e.g., chlorpromazine, haloperidol, thioridazine, ziprasidone), antidepressants (e.g., mirtazapine), Class 1A (e.g., quinidine, procainamide), and Class III (e.g., amiodarone, sotalol) antiarrhythmic medications.

7.3 Reserpine

Reserpine binds irreversibly to VMAT2 and the duration of its effect is several days. Prescribers should wait for chorea or dyskinesia to remerge before administering *AUSTEDO* to help reduce the risk of overdose and major depletions of serotonin and norepinephrine. At least 30 days should elapse after stopping reserpine before starting *AUSTEDO*. *AUSTEDO* and reserpine should not be used concomitantly [see Contraindications (4)].
4

7.4 Monoamine Oxidase Inhibitors (MAOIs)

AUSTEDO® (deuterobenzamine) tablets are contraindicated in patients taking MAOIs. AUSTEDO should not be used in combination with a MAOI, or within 14 days of discontinuing therapy with a MAOI (see Contraindications (4)).

7.5 Neuroleptic Drugs

The risk of parkinsonism, EPS, and akathisia may be increased by concomitant use of AUSTEDO and dopamine antagonists or antipsychotics.

7.6 Sedative Drugs or Other Ongoing Drugs

Concomitant use of alcohol or other sedating drugs may have additive effects and worsen sedation and somnolence (see Warnings and Precautions (5.7)).

7.7 Concomitant Tetrabenazine or Valbenzamine

AUSTEDO is contraindicated in patients currently taking tetrabenazine or valbenzamine. AUSTEDO may be initiated the day following discontinuation of tetrabenazine (see Dosage and Administration (2.2)).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of AUSTEDO in pregnant women. Administration of deuterobenzamine to rats during organogenesis produced no clear adverse effect on embryofetal development. However, administration of tetrabenazine to rats through pregnancy and lactation resulted in an increase in stillbirths and postnatal offspring mortality (see Data). In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2.4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data

Oral administration of deuterobenzamine (5 mg/kg/day) or tetrabenazine (30 mg/kg/day) to pregnant rats during organogenesis had no clear effect on embryofetal development. The highest dose tested was 5 times the maximum recommended human dose of 48 mg/day, on a body surface area (mg/m²) basis.

The effects of deuterobenzamine when administered during organogenesis to rabbits or during pregnancy and lactation to rats have not been assessed.

Tetrabenazine had no effects on embryofetal development when administered to pregnant rabbits during the period of organogenesis at oral doses up to 64 mg/kg/day. When tetrabenazine was administered to female rats (doses of 5, 15, and 30 mg/kg/day) from the beginning of organogenesis through the lactation period, an increase in stillbirths and offspring postnatal mortality was observed at 15 and 30 mg/kg/day and delayed pup maturation was observed at all doses.

8.2 Lactation

Risk Summary

There are no data on the presence of deuterobenzamine or its metabolites in human milk. The effects on breastfed infants, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for AUSTEDO and any potential adverse effects on the breastfed infant from AUSTEDO or from the underlying maternal condition.

8.3 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.4 Geriatric Use

Clinical studies of AUSTEDO did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be based on the same principles that apply to all age groups (see Clinical Pharmacology (12.3)).

8.5 Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics of deuterobenzamine and its primary metabolite has not been studied; however, in a clinical study conducted with tetrabenazine, a closely related VMAT2 inhibitor, there was a large increase in exposure to tetrabenazine and its active metabolites in patients with hepatic impairment. The clinical significance of this increased exposure has not been assessed, but because of the potential for serious adverse reactions, the use of AUSTEDO in patients with hepatic impairment is contraindicated (see Contraindications (4), Clinical Pharmacology (12.3)).

8.7 Poor CYPID2 Metabolizers

Although the pharmacokinetics of deuterobenzamine and its metabolites have not been systematically evaluated in patients who do not express the drug metabolizing enzyme, it is likely that the exposure to both deuterobenzamine and its metabolites would be increased similarly to that seen with strong CYP2D6 inhibitors (approximately 3-fold). In patients who are CYP2D6 poor metabolizers, the daily dose of AUSTEDO should not exceed 36 mg (maximum single dose of 18 mg) (see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)).

10 OVERDOSAGE

Overdoses ranging from 100 mg to 1 g have been reported in the literature with tetrabenazine, a closely related VMAT2 inhibitor. The following adverse reactions occurred with overdosing: acute dystonia, orthostatic crisis, nausea and vomiting, sweating, sedation, hyponatremia, confusion, diarrhea, hallucinations, rubor, and tremor. Treatment should consist of those general measures employed in the management of overdosage with any central nervous system active drug. General supportive and symptomatic measures are recommended. Cardiac rhythm and vital signs should be closely monitored. In managing overdosage, the possibility of multiple drug involvement should always be considered. The physician should consider contacting a poison control center on the treatment of any overdose. Telephone numbers for certified poison control centers are listed on the American Association of Poison Control Centers website www.aapcc.org.

11 DESCRIPTION

AUSTEDO (deuterobenzamine) is a vesicular monoamine transporter 2 (VMAT2) inhibitor for central nervous system function. The molecular formula for deuterobenzamine is C10H12D5NO4. Deuterobenzamine is a racemic mixture containing the following structures:

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+ CO2H
+ CO2H

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Deuterobenzamine is a white to slightly yellow crystalline powder that is sparingly soluble in water and soluble in ethanol.

AUSTEDO tablets contain 6 mg, 9 mg, or 12 mg deuterobenzamine, and the following inactive ingredients: ammonium hydroxide, black iron oxide, S-1-butyl alcohol, butylated hydroxyanisole, butylated hydroxytoluene, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol, polyethylene oxide, polysorbate 80, polyethylene alcohol, povidone, propylene glycol, shellac, talc, titanium dioxide, and FD&C blue #3 La. The 6 mg tablets also contain FD&C red #40 La. The 12 mg tablets also contain FD&C yellow #6 La.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The precise mechanism by which deuterobenzamine exerts its effects in the treatment of tardive dyskinesia and chorea in patients with Huntington’s disease is unknown but is believed to be related to its effect as a reversible depolarizing block of monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals.

The major circulating metabolites (S- and R-deuterobenzamine [HTZB] and β- and HTZB of deuterobenzamine) are reversible inhibitors of VMAT2, resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores.

12.2 Pharmacodynamics

Cardiac Electrophysiology

The effect of a single 12- to 24-mg dose of AUSTEDO on the QT interval was studied in a randomized, double-blind, placebo-controlled crossover study in healthy male and female subjects with moxifloxacin as a positive control. At 24 mg, AUSTEDO caused an approximately 4.5-msec mean increase in QTc at 6 (90% CL 2.4 to 6.5 msec). Effects at higher exposures to AUSTEDO or its metabolites have not been evaluated.

Malignant Binding

Deuterobenzamine or its metabolites bind to melanin-containing tissues (i.e., eye, skin, fur) in pigmented rats. After a single oral dose of radiolabeled deuterobenzamine, radioactivity was still detected in eye and fur at 35 days following dosing (see Warnings and Precautions (5.9)).

12.3 Pharmacokinetics

After oral dosing up to 25 mg, plasma concentrations of deuterobenzamine are generally below the limit of detection after oral dosing. Peak plasma concentrations (Cmax) of deuterated α- and HTZB are reached within 3 to 4 hours after dosing.

Effect of Food

The effects of food on the bioavailability of AUSTEDO were studied in subjects administered a single dose with and without food. Food had no effect on the area under the plasma concentration-time curve (AUC) of α- or HTZB, although Cmax was increased by approximately 50% in the presence of food (see Dosage and Administration (2.1)).

Distribution

The median volume of distribution (V/V) of the α- HTZB and the β- HTZB metabolites of AUSTEDO are approximately 500 L and 750 L, respectively.

Results of PET-scan studies in healthy human subjects show that following intravenous injection of [11C]-labeled tetrabenazine or α-HTZB, radioactivity is rapidly distributed to the brain, with the highest binding in the striatum and lowest binding in the cortex.

In vivo protein binding of tetrabenazine, α-HTZB, and β-HTZB was examined in human plasma for concentrations ranging from 50 to 200 ng/mL. Tetrabenazine binding ranged from 82% to 85%, α-HTZB binding ranged from 50% to 60%, and β-HTZB binding ranged from 59% to 63%.
AUSTEDO® (deutetrabenzamine) tablets

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
No carcinogenicity studies were performed with deutetrabenzamine.

Mutagenesis
No increase in tumors was observed in 2-year transgenic mice treated orally with tertabenzamine at doses of 0, 5, 15, and 30 mg/kg/day for 25 weeks.

Metabolism and Excretion
Deutetrabenzamine and its deuterated α-HT2β and β-HT2β metabolites were negative in vitro (bacterial reverse mutation and chromosome aberration in human peripheral blood lymphocytes) assays in the absence or presence of metabolic activation and in the in vitro micromass assay in mice.

Impairment of Fertility
The effects of deutetrabenzamine on fertility have not been evaluated. Oral administration of tertabenzamine (doses of 5, 10, or 50 mg/kg/day) to female rats for 3 months resulted in estrous cycle disruption at all doses; the lowest dose tested was similar to the maximum recommended human dose (48 mg/day) on a body surface area (mg/m²) basis.

14 CLINICAL STUDIES

14.1 Chorea Associated with Huntington’s Disease

Double-Blind, Placebo-Controlled Study

The efficacy of AUSTEDO as a treatment for chorea associated with Huntington’s disease was established primarily in Study 1, a randomized, double-blind, placebo-controlled, multicenter trial conducted in 90 ambulatory patients with manifest chorea associated with Huntington’s disease. The diagnosis of Huntington’s disease was based on family history, neurological exam, and genetic testing. Treatment duration was 12 weeks, including a 3-week dose titration period and a 9-week maintenance period, followed by a 1-week washout. Patients were not blinded to discontinuation.

AUSTEDO was started at 6 mg per day and titrated upward, at weekly intervals in 6 mg increments until satisfactory treatment of chorea was achieved. Intolerable side effects occurred, or up to a maximal dose of 48 mg per day was reached. The primary efficacy endpoint was the Total Maximal Chorea Score, an item of the Unified Huntington’s Disease Rating Scale (UHDRS). On this scale, chorea is rated from 0 to 4 (with 0 representing no chorea) for 7 different parts of the body. The total score range is from 0 to 28.

Of the 90 patients enrolled, 77 patients completed the study. The mean age was 54 (range 23 to 74). Patients were 56% male and 44% Caucasian. The mean dose after titration was 40 mg per day. Table 4 and Figure 1 summarize the effects of AUSTEDO on chorea based on the Total Maximal Chorea Score. Total Maximal Chorea Scores for patients receiving AUSTEDO improved by approximately 4.4 units from baseline to the maintenance period (average of Week 9 and Week 12), compared to approximately 1.9 units in the placebo group. The treatment effect of -2.5 units was statistically significant (p < 0.0001). The Maintenance Endpoint is the mean of the Total Maximal Chorea Scores for the Week 9 and Week 12 visits. At the Week 13 follow-up visit (1 week after discontinuation of the study medication), the Total Maximal Chorea Scores of patients who had received AUSTEDO returned to baseline (Figure 1).

Table 4: Change from Baseline to Maintenance Therapy in Total Maximal Chorea (TMC) Score in Patients with Huntington’s Disease Treated with AUSTEDO in Study 1

| Motor Endpoint | AUSTEDO | Placebo | p value
<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in Total Chorea Score* from Baseline to Maintenance Therapy*</td>
<td>-4.4</td>
<td>-1.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*TMC is a subscale of the Unified Huntington’s Disease Rating Scale (UHDRS)

Primary efficacy endpoint.
**Figure 2: Distribution of the Change in Total Maximal Chorea Scores in Study 1**

**Total Chorea Score: Change from Baseline to Maintenance**

Figure 2 shows the distribution of values for the change in Total Maximal Chorea Score in Study 1. Negative values indicate a reduction in chorea and positive numbers indicate an increase in chorea.

A patient-rated global impression of change assessed how patients rated their overall Huntington’s disease symptoms. Fifty-one percent of patients treated with AUSTEDO rated their symptoms as “Much Improved” or “Very Much Improved” at the end of treatment, compared to 20% of placebo-treated patients.

In a physician-rated clinical global impression of change, 42% of patients treated with AUSTEDO rated their symptoms as “Much Improved” or “Very Much Improved” at the end of treatment compared to 13% of placebo-treated patients.

**14.2 Tardive Dyskinesia**

The efficacy of AUSTEDO in the treatment of tardive dyskinesia was established in two 12-week, randomized, double-blind, placebo-controlled, multi-center trials conducted in 335 adult ambulatory patients with tardive dyskinesia caused by use of dopamine receptor antagonists. Patients had a history of using a dopamine receptor antagonist (antipsychotics, metoclopramide) for at least 3 months (or 1 month in patients 60 years of age and older). Concurrent diagnoses included schizophrenia/schizoaffective disorder (62%) and mood disorder (33%). With respect to concurrent antipsychotic use, 44% of patients were receiving typical antipsychotics, 12% were receiving atypical antipsychotics, and 24% were not receiving antipsychotics.

The Abnormal Involuntary Movement Scale (AIMS) was the primary efficacy measure for the assessment of tardive dyskinesia severity. The AIMS is a 12-item scale: items 1 to 7 assess the severity of involuntary movements across body regions, and items 8 to 11 assess the frequency and intensity of the movements. The AIMS total score (sum of items 1 to 11) should reach from 0 to 28, with a decrease in score indicating improvement.

In Study 1, a 12-week, placebo-controlled, fixed-dose trial, adults with tardive dyskinesia were randomized to receive 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, or 10 mg of AUSTEDO at baseline. Treatment duration included a 4-week dose escalation period and an 8-week maintenance period followed by a 1-week washout. The dose of AUSTEDO was started at 1 mg/day and increased at weekly intervals in 1 mg/day increments to a dose target of 10 mg/day. The population was 192 patients (mean age 55 years, 45% male, and 70% Caucasian). In Study 2, the AIMS total score for patients receiving AUSTEDO demonstrated statistically significant improvement from baseline to Week 12, of 3.3 and 3.2 units for the 6 mg and 4 mg arms, respectively, compared with 1.4 units in placebo (Study 1 in Table 5). The improvements on the AIMS total score over the course of the study are displayed in Figure 3. Data did not suggest substantial differences in efficacy across various demographic groups. The treatment response rate distribution, based on magnitude of AIMS total score from baseline to week 12 is displayed in Figure 4. The mean changes in the AIMS total score by visit are shown in Figure 5.

In Study 2, a 12-week, placebo-controlled, flexible-dose trial, adults with tardive dyskinesia (n=113) received daily doses of placebo or AUSTEDO, starting at 12 mg per day and increasing allowed in 6 mg increments at 1-week intervals until satisfactory control of dyskinesia was achieved, until intolerable side effects occurred, or until a maximum dose of 48 mg per day was reached. Treatment duration included a 6-week dose titration period and a 6-week maintenance period followed by a 1-week washout. The population was 25 to 75 years old (mean 55 years), 48% male, and 70% Caucasian. Patients were titrated to an optimal dose over 6 weeks. The average dose of AUSTEDO after treatment was 38.3 mg per day. There were no evidence suggesting substantial differences in efficacy across various demographic groups. In Study 2, AIMS total score for patients receiving AUSTEDO demonstrated statistically significant improvement by 3.0 units from baseline to endpoint (Week 12), compared with 1.6 units in the placebo group with a treatment effect of -1.4 units. Table 5 summarizes the effects of AUSTEDO on tardive dyskinesia based on the AIMS.

**Table 5: Improvement in AIMS Total Score in Patients Treated with AUSTEDO in Study 1 and Study 2**

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment Group</th>
<th>Primary Efficacy Measure: AIMS Total Score</th>
<th>Mean Baseline Score (SD)</th>
<th>LS Mean Change from Baseline (SE)</th>
<th>Treatment Effect (90% CI)</th>
</tr>
</thead>
</table>
| Study 1 | AUSTEDO 36 mg*  
(n=55) | | 10.1 (3.21) | -3.3 (0.42) | -1.9 (-3.09, -0.79) |
| | AUSTEDO 24 mg  
(n=49) | | 9.4 (2.95) | -3.2 (0.45) | -1.8 (-3.06, -0.63) |
| | AUSTEDO 12 mg  
(n=60) | | 9.6 (2.46) | -2.1 (0.42) | -0.7 (-1.84, 0.42) |
| | Placebo  
(n=56) | | 9.5 (2.71) | -1.4 (0.41) | -1.4 (-2.62, -0.2) |
| Study 2 | AUSTEDO (12-48 mg/day)*  
(n=56) | | 9.7 (4.14) | -3.0 (0.45) | -1.4 (-2.62, -0.2) |
| | Placebo  
(n=57) | | 9.6 (3.78) | -1.6 (0.46) | -1.4 (-2.62, -0.2) |

*Dose that was statistically significantly different from placebo after adjusting for multiplicity. LS Mean = Least-squares mean; SD = Standard deviation; SE = Standard error; CI = 2-sided 95% confidence interval

**Figure 3: Least Square Means of Change in AIMS Total Score from Baseline for AUSTEDO Compared to Placebo (Study 1)**

**Figure 4: Percent of Patients with Specified Magnitude of AIMS Total Score Improvement at the End of Week 12 (Study 1)**

**16 HOW SUPPLIED/STORAGE AND HANDLING**

**16.1 How Supplied**

AUSTEDO tablets are available in the following strengths and packages:

- 6 mg: round, purple-coated tablets, with "6D" over "6" printed in black ink on one side.

Bottles of 60 tablets: NDC 68546-170-60.

- 9 mg: round, blue-coated tablets, with "SD" over "9" printed in black ink on one side.

Bottles of 60 tablets: NDC 68546-171-60.

Bottles of 60 tablets: NDC 68546-170-60.

**16.2 Storage**

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Protect from light and moisture.
What is AUSTEDO®?
AUSTEDO® is a prescription medicine that is used to treat:
- the involuntary movements (chorea) of Huntington's disease.

AUSTEDO® does not cure the cause of the involuntary movements, and it does not treat other symptoms of Huntington's disease, such as problems with thinking or emotions.

- movements in the face, tongue, or other body parts that cannot be controlled (tardive dyskinesia).

It is not known if AUSTEDO is safe and effective in children.

Who should not take AUSTEDO®?
Do not take AUSTEDO® if you:
- have Huntington's disease and are depressed or have thoughts of suicide. See "What is the most important information I should know about AUSTEDO®?"
- have liver problems.
- are taking a monoamine oxidase inhibitor (MAOI) medicine. Do not take an MAOI within 14 days after you stop taking AUSTEDO®. Do not start AUSTEDO® if you stopped taking an MAOI in the last 14 days. Ask your healthcare provider or pharmacist if you are not sure.
- are taking reserpine. Do not take medicines that contain reserpine (such as Serpasil and Rensene-R) with AUSTEDO®. If your healthcare provider plans to switch you from taking reserpine to AUSTEDO®, you must wait at least 20 days after your last dose of reserpine before you start taking AUSTEDO®.
- are taking tetrabenazine (Xenazine). If your healthcare provider plans to switch you from tetrabenazine (Xenazine) to AUSTEDO®, take your first dose of AUSTEDO® on the day after your last dose of tetrabenazine (Xenazine).
- are taking valbenazine (Ingrezza).

Before taking AUSTEDO®, tell your healthcare provider about all of your medical conditions, including if you:
- have emotional or mental problems (for example, depression, nervousness, anxiety, anger, agitation, psychosis, previous suicidal thoughts or suicide attempts).
- have liver disease.
- have an irregular heart rhythm or heartbeat (QT prolongation, cardiac arrhythmia) or a heart problem called congenital long QT syndrome.
- have low levels of potassium or magnesium in your blood (hypokalemia or hypomagnesemia).
- have breast cancer or a history of breast cancer.
- are pregnant or plan to become pregnant. It is not known if AUSTEDO® can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if AUSTEDO® passes into breast milk.

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Taking AUSTEDO® with certain other medicines may cause side effects. Do not start any new medicines while taking AUSTEDO® without talking to your healthcare provider first.
**AUSTEDO**® (deutetrabenazine) tablets

How should I take AUSTEDO?
- Take AUSTEDO exactly as your healthcare provider tells you to take it.
- Take AUSTEDO by mouth and with food.
- Swallow AUSTEDO tablets whole with water. Do not chew, crush, or break AUSTEDO tablets before swallowing if you cannot swallow AUSTEDO tablets whole. Tell your healthcare provider. You may need a different medicine.
- If your dose of AUSTEDO is 12 mg or more each day, take AUSTEDO tablets 2 times a day in equal doses with food.
- Your healthcare provider will increase your dose of AUSTEDO each week for several weeks, until you and your healthcare provider find the right dose for you.
- Tell your healthcare provider if you stop taking AUSTEDO for more than 1 week. Do not take another dose until you talk to your healthcare provider.

What should I avoid while taking AUSTEDO?
Sleepiness (sedation) is a common side effect of AUSTEDO. While taking AUSTEDO, do not drive a car or operate dangerous machinery or heavy equipment without knowing how AUSTEDO affects you. Drinking alcohol and taking other drugs that may also cause sleepiness while you are taking AUSTEDO may increase any sleepiness caused by AUSTEDO.

What are the possible side effects of AUSTEDO?
AUSTEDO can cause serious side effects, including:
- Depression and suicidal thoughts or actions in people with Huntington’s disease. See “What is the most important information I should know about AUSTEDO?”
- Irregular heartbeat (QT prolongation). AUSTEDO increases your chance of having certain changes in the electrical activity in your heart. These changes can lead to a dangerous abnormal heartbeat. Taking AUSTEDO with certain medicines may increase this chance.
  - If you are at risk of QT prolongation, your healthcare provider should check your heart before and after increasing your AUSTEDO dose above 24 mg a day.
- Neuroleptic Malignant Syndrome (NMS). Call your healthcare provider right away and go to the nearest emergency room if you develop these signs and symptoms that do not have another obvious cause:
  - high fever
  - problems thinking
  - increased sweating
  - stiff muscles
  - very fast or uneven heartbeat
- Restlessness. You may get a condition where you feel a strong urge to move. This is called akathisia.
- Parkinsonism in people with Huntington’s disease. Symptoms of parkinsonism include: slight shaking, body stiffness, trouble moving, or keeping your balance.

The most common side effects of AUSTEDO in people with Huntington’s disease include:
- sleepiness (sedation)
- diarrhea
- tiredness
- dry mouth

The most common side effects of AUSTEDO in people with tardive dyskinesia include:
- inflammation of the nose and throat (nasopharyngitis)
- problems sleeping (insomnia)

These are not all the possible side effects of AUSTEDO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**AUSTEDO**® (deutetrabenazine) tablets

How should I store AUSTEDO?
- Store AUSTEDO tablets at room temperature, between 68°F to 77°F (20°C to 25°C).
- Keep the bottle tightly closed to protect AUSTEDO from light and moisture.
- Keep AUSTEDO tablets and all medications out of reach of children.

General Information about the safe and effective use of AUSTEDO. Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use AUSTEDO for a condition for which it was not prescribed. Do not give AUSTEDO to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about AUSTEDO that is written for health professionals.

What are the ingredients in AUSTEDO?
Active ingredient: deutetrabenazine
Inactive ingredients: ammonium hydroxide, black iron oxide, n-butyl alcohol, butylated hydroxyanisole, butylated hydroxytoluene, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol, polyethylene oxide, polysorbate 80, polyvinyl alcohol, propylene glycol, shellac, talc, titanium dioxide, and FD&C blue #2 lake. The 6 mg tablets also contain FD&C red #40 lake. The 12 mg tablets also contain FD&C yellow #6 lake.

Distributed by:
Teva Pharmaceuticals USA, Inc.
North Wales, PA 19454
AUSMG-002
For more information, go to www.AUSTEDO.com or call 1-888-483-9279.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: August 2017
AUS-40479