LTC NEWS+VIEWS
VOLUME 2 • SEPTEMBER 2025

Tardive Dyskinesia vs Drug-Induced Parkinsonism in the Long-Term Care Setting: Different Movements, Different Treatments

OVERVIEW OF TD AND DIP

Distinguishing Between Tardive Dyskinesia (TD) and Drug-Induced Parkinsonism (DIP): Why Accurate Diagnosis Matters

TD and DIP are 2 distinct movement disorders caused by dopamine receptor blocking agents (DRBAs) such as antipsychotics. Despite a common origin, they differ significantly in clinical features, pathophysiology, and treatment, and treatment for one may worsen the other. This article examines the distinguishing features of each disorder to help with accurate diagnosis and appropriate treatment.

TREATMENT

AUSTEDO XR®—A Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor for the Treatment of Tardive Dyskinesia (TD)

AUSTEDO XR is a VMAT2 inhibitor approved for the treatment of TD and chorea associated with Huntington's disease. This article highlights key findings from the pivotal clinical trials of AUSTEDO® (deutetrabenazine) tablets, including symptom control, long-term results, and safety profile. It also discusses the dosing flexibility of AUSTEDO XR and how to get residents started with AUSTEDO XR.

EXPERT COMMENTARY

Expert Commentary With Hany Mohamed and Tiffany Nelson

Hany Mohamed, PharmD, RPh, BCGP, BCMTM, CDTM
Director of Clinical Services
LI Script LLC
Yonkers, New York

Tiffany Nelson, DNP-C, CCM
Owner and Nurse Practitioner
It Is Well
Kennett, Missouri

This newsletter is produced by Teva Pharmaceuticals, and Dr Hany Mohamed and Tiffany Nelson were compensated by Teva for their insights.

INDICATIONS AND USAGE

AUSTEDO XR® (deutetrabenazine) extended-release tablets and AUSTEDO® (deutetrabenazine) tablets are indicated in adults for the treatment of chorea associated with Huntington's disease and for the treatment of tardive dyskinesia.

IMPORTANT SAFETY INFORMATION

Depression and Suicidality in Patients with Huntington's Disease: AUSTEDO XR and 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 XR and AUSTEDO are contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

OVERVIEW OF TD AND DIP

Distinguishing Between Tardive Dyskinesia (TD) and Drug-Induced Parkinsonism (DIP): Why Accurate Diagnosis Matters

TD and DIP Are Common but Distinct Movement Disorders

DRBAs such as antipsychotics are commonly used to treat patients with schizophrenia, major depressive disorder, and bipolar disorder.[1,2] In some patients, these medications can cause involuntary movements.[2] Historically, the term extrapyramidal symptoms (EPS) was used to describe any drug-induced movement disorder, such as dystonia, akathisia, DIP, and TD. This term is now considered overly broad, as these disorders, despite being caused by the same offending agents, differ in their underlying pathophysiology, clinical manifestations, and treatments.[1-5]

The most common drug-induced movement disorders, occurring in as many as 1 in 3 patients taking antipsychotics, are TD and DIP.[1,2,6] Although both are caused by disruptions in the brain's dopaminergic signaling, they each arise through different mechanisms. DIP is caused by reduced postsynaptic signaling resulting from the acute blockade of dopamine receptors.[1] In contrast, TD develops from the upregulation or increased sensitivity of dopamine receptor function due to chronic blockade of these receptors with antipsychotic drugs.[1,2]

TD and DIP exhibit distinct clinical characteristics that allow for differentiation based on the timing of their onset and associated symptoms.[1] DIP typically appears within weeks to months of initiating an antipsychotic medication, whereas TD generally develops after prolonged use of an antipsychotic drug, spanning several months to years.[1,7] Notably, in older adults aged 60 and above, TD may develop as early as 1 month.[1,7] Symptoms of TD also emerge following discontinuation or a change in medication dosage. Persistent symptoms lasting at least 3 months in adults or 1 month in older patients are indicative of TD. **(Figure 1.1)**.[1,7]

TD and DIP are associated with distinct movement patterns. The key symptoms distinguishing these 2 disorders can be categorized by the nature and degree of movement.[1,8] TD is marked by an excess of movements that are irregular, jerky, and unpredictable,

Figure 1.1. TD and DIP Have Differences in Onset of Symptoms[1,7]

Drug-Induced Parkinsonism (DIP)	Tardive Dyskinesia (TD)
Within a few weeks to months of **Starting an antipsychotic**	*After using an antipsychotic for* ***at least a few months to years***
Increasing the dosage of an antipsychotic	Elderly persons may develop TD symptoms in a shorter period of time
Reducing the dosage of an anticholinergic medication used to treat EPS	**Movements may appear after discontinuation** or after a change or reduction in dosage; if symptoms persist for >4 to 8 weeks, it is considered TD

The minimum antipsychotic exposure history required for the diagnosis of TD is at least 3 months (or 1 month in patients ≥60 years)

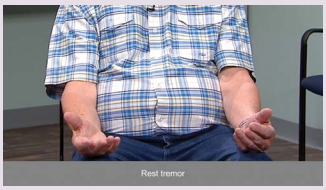
IMPORTANT SAFETY INFORMATION (CONTINUED)

Contraindications: AUSTEDO XR® (deutetrabenazine) extended-release tablets and AUSTEDO® (deutetrabenazine) tablets are contraindicated in patients with Huntington's disease who are suicidal, or have untreated or inadequately treated depression. AUSTEDO XR and AUSTEDO are 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 or valbenazine.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

Videos. TD and DIP are associated with different types of movements

Scan QR code to view considerations for differential diagnosis

	DIP	TD
Nature of movements	 Rest tremor Movements are rhythmic	 Trunk, finger, and foot movements Movements are irregular, unpredictable, jerky, and twitchy
Degree of movements	 Masked face Overall paucity of movements	 Blinking Movements are excessive and continuous

with normal muscle tone.[7,8] DIP is characterized by a paucity of movement; however, when movements do occur, they are rhythmic, and patients may also exhibit muscle rigidity **(Videos)**.[8,9]

TD and DIP Are Different and so Are Their Treatments

Given the differences between TD and DIP, it is essential to diagnose and treat TD appropriately, as treatment for one disorder can worsen the other.[1] The American Psychiatric Association (APA) guidelines recommend that symptoms of TD that have an impact on the patient, regardless of severity, should be managed with a vesicular monoamine transporter 2 (VMAT2) inhibitor.[10]

A study examining clinical outcomes in long-term care (LTC) residents with TD found statistically significant differences in both frequency of falls and emergency department (ED) visits between those treated with a VMAT2 inhibitor and those who were not. Fall rates were 2.67 (standard deviation [SD]: 5.67) in the treated group versus 4.23 (SD: 8.92) in the untreated group (P=0.013), while ED visit rates were 0.11 (SD: 0.55) for the treated group compared with 0.22 (SD: 0.79) for the untreated group (P=0.004).[11] Furthermore, the APA and the DSM-5-TR caution against using anticholinergics in the treatment of TD.[7,10] The DSM-5-TR notes that anticholinergic medications such as benztropine can worsen TD symptoms.[7] Despite these recommendations, anticholinergics are widely prescribed for the treatment of TD. An online survey of psychiatry providers revealed that 40% would initiate benztropine to treat TD.[12] In an additional analysis of patients with TD, ~75% were treated with benztropine for >3 months, and ~35% of patients were treated for >1 year.[11] Furthermore, The Beers Criteria®, from the American Geriatric Association, advises against anticholinergic use in individuals over 65 years of age due to an increased risk of side effects such as constipation, confusion, dry mouth, delirium, and cognitive decline **(Figure 1.2)**.[13]

Figure 1.2. Anticholinergics Such as Benztropine Should Not Be Used to Treat or Prevent TD[13,14]

Anticholinergics Such as Benztropine
Should **not be used to treat or prevent TD**
Can make **TD symptoms worse**
Are **not appropriate for many older adults** (Beers Criteria®) due to side effects (constipation, confusion, dry mouth, delirium) and association with cognitive decline

Reducing Inappropriate or Unnecessary Drug Use Is a Key Focus for LTC Facilities

The risks associated with inappropriate treatment for TD underscore broader efforts to reduce unnecessary or inappropriate drug use in the LTC setting, a key focus of several Centers for Medicare & Medicaid Services initiatives.[15] To support these efforts,

several Federal tags (F-tags) have been established that provide a standardized framework to ensure compliance with mandated quality and safety standards.[15] F-tags F-605, F-757, and F-841 are important when addressing TD in LTC facilities, particularly when there is a failure to prevent or reduce the unnecessary use of antipsychotic drugs **(Figure 1.3)**.[16] These tags are also significant when TD is misdiagnosed or inappropriately treated with an anticholinergic drug such as benztropine.[17]

It is therefore crucial for providers to accurately differentiate between TD and DIP to ensure that residents in LTC facilities receive the most appropriate treatment. When addressing TD, it is important to note that simply discontinuing the antipsychotic medication does not typically lead to improvement of TD symptoms. Instead, a VMAT2 inhibitor should be considered as first-line treatment, while anticholinergic medications should be avoided **(Figure 1.4)**.[1,10,18]

Figure 1.3. Resident Health and Safety Inspections Evaluate Antipsychotic Use Through F-Tags[16]

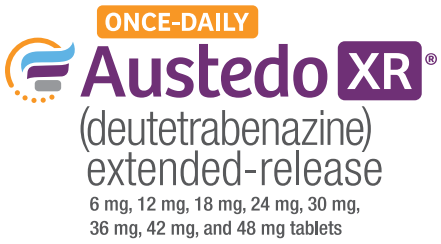
F-tag F-605	Provides residents with the right to be treated with respect and dignity Ensures freedom from physical or chemical restraints used for discipline or convenience
F-tag F-757	Requires that each resident's treatment plan must be free from unnecessary medications (excessive dosage, prolonged duration, inadequate indication, or adverse consequences warranting dose reduction or discontinuation)
F-tag F-841	Ensures that a physician serves as the medical director to implement resident care policies for safe and effective use of medications and for the coordination of medical care

Figure 1.4. TD and DIP Require Different Treatments[1,10,18]

	DIP	TD
Antipsychotic discontinuation	✓ May improve DIP	✗ May not improve TD
Anticholinergics	✓ Indicated for DIP	✗ May worsen TD
VMAT2 inhibitors	✗ May worsen DIP	✓ Only FDA-approved treatment for TD

Summary

TD and DIP are common movement disorders caused by exposure to antipsychotic medications.[1] However, they are distinct conditions that require different treatment approaches.[1] Selecting the appropriate therapy should be done based on an accurate diagnosis through careful observation and examination, as treatment for one disorder can worsen symptoms of the other.[1] Many patients with TD mistakenly receive treatment with anticholinergics intended for DIP, emphasizing the importance of following expert guidelines, such as those from the APA and the DSM-5-TR.[12] The Code of Federal Regulations includes F-tags that have been designed to identify unnecessary medication use and ensure the safe and effective administration of medications in LTC facilities.[16] Therefore, to improve patient outcomes, it is important to accurately diagnose and treat the movement disorder according to clinical guidelines and federal regulations. ■



TREATMENT

AUSTEDO XR—A Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor for the Treatment of Tardive Dyskinesia (TD)

Tardive dyskinesia (TD) is a persistent, often irreversible, hyperkinetic movement disorder of the face, jaw, trunk, or extremities. It is one of several drug-induced movement disorders caused by dopamine receptor blocking agents, including antipsychotics, antiemetics, and prokinetics.[2,3] The symptoms of TD are often mistaken for those of other movement disorders, such as drug-induced parkinsonism (DIP). This misidentification may lead to the use of anticholinergics, which are not recommended for TD and can actually worsen its symptoms.[4-6]

In the United States, TD affects approximately 785,000 individuals, yet only 15% have received a formal diagnosis, and less than 6% have received appropriate treatment with a VMAT2 inhibitor.[4] A recent study showed that residents with TD who were treated with a VMAT2 inhibitor had fewer falls and visits to the emergency department.[4] TD is of particular concern in long-term care (LTC) facilities, as older age is itself a risk factor, and an estimated 700,000 LTC residents are treated with antipsychotics for conditions such as schizophrenia, depression, and bipolar disorder.[4,7]

Symptoms of TD can be observed by staff members during routine interactions and must be monitored during gradual dose reduction (GDR) of antipsychotics, as reducing the antipsychotic can unmask symptoms of TD.[8] The physical impact of TD is also more prominent and merits greater consideration in residents in the LTC setting.[9] Therefore, residents who are older and on antipsychotic drugs should be routinely monitored by LTC staff at every interaction. If TD is suspected, a formal diagnosis should be made and the resident should be treated appropriately. Once-daily AUSTEDO XR is a VMAT2 inhibitor approved in adults for the treatment of TD.[1]

TD Symptom Control Was Studied in a Fixed-Dose, a Flexible-Dose, and a Long-Term Open-Label Extension Study

The efficacy and safety profile of AUSTEDO was established in two 12-week, randomized, double-blind, placebo-controlled pivotal clinical trials, ARM-TD (Aim to Reduce Movements in Tardive Dyskinesia) and AIM-TD (Addressing Involuntary Movements in Tardive Dyskinesia). The studies included adult patients up to 81 years of age.[1,10,11]

- ARM-TD was a randomized, double-blind, parallel-group study in adult patients with TD. In this flexible-dose clinical trial, patients' doses were titrated to an individualized dosage that reduced abnormal movements and was tolerated by the patient. Patients were randomized 1:1 to receive AUSTEDO twice daily (BID) or placebo[11]
- AIM-TD was a randomized, double-blind, placebo-controlled, phase 3 clinical trial in adult patients with TD. Patients were randomly assigned 1:1:1:1 to receive 1 of 3 fixed doses of AUSTEDO (12 mg/day, 24 mg/day, or 36 mg/day) or placebo[10]

IMPORTANT SAFETY INFORMATION (CONTINUED)

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 XR and AUSTEDO; intensive symptomatic treatment and medical monitoring; and treatment of any concomitant serious medical problems.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

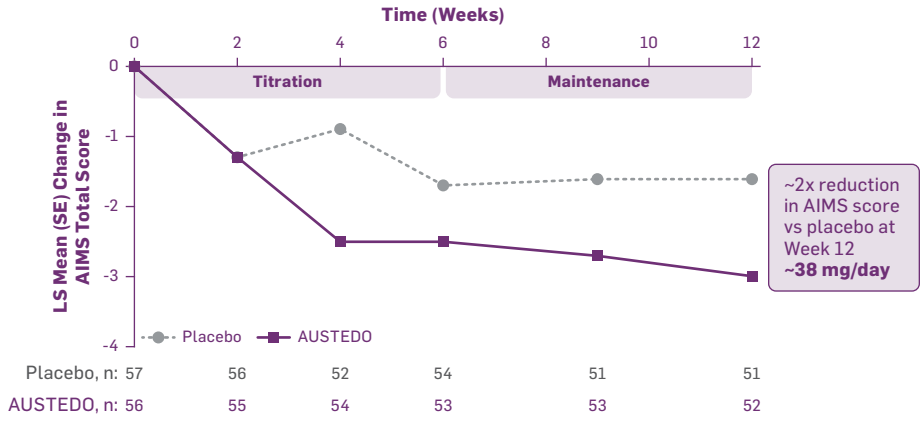
The primary efficacy endpoint in both studies was the change in Abnormal Involuntary Movement Scale (AIMS) total score (sum of items 1 through 7) from baseline (defined for each patient as the value from the day 0 visit) to Week 12.[10,11]

Patients in the ARM-TD study showed a significant improvement in AIMS total score from baseline (P=0.019) at Week 12 vs placebo (3.0-point reduction vs 1.6-point reduction) **(Figure 2.1)**. Results were consistent with those observed in AIM-TD at Week 12.[4,10,11]

Long-term efficacy and safety of AUSTEDO® (deutetrabenazine) tablets were studied in Reducing Involuntary Movements in Participants With Tardive Dyskinesia, an open-label, long-term maintenance study in patients who successfully completed ARM-TD or AIM-TD. AUSTEDO was discontinued for 1 week and then started at a dose of 12 mg/day, which was titrated for up to 6 weeks. The dose was increased in a response-driven manner on a weekly basis by 6 mg/day until the maximum allowable dose was reached, a clinically significant adverse event (AE) occurred, or adequate dyskinesia control was achieved. Patients were followed for approximately 3 years.[12]

Among the 335 patients evaluated, 257 were 21-64 years and 78 were 65-81 years. All patients received treatment at baseline and 160 received treatment through the end of Week 145. Mean dose at Week 145 was similar for both age groups. For both age groups, there was a rapid response beginning at Week 2 as assessed by improvement in the AIMS total score. Thereafter, increasing improvement was observed for about 3 years **(Figure 2.2)**.[4]

Figure 2.1. Patients Achieved Significant and Meaningful Reduction in TD Severity at Week 12[4,10]



Patients in the ARM-TD study received the AUSTEDO BID formulation.

Baseline AIMS total scores were similar between AUSTEDO and placebo: AUSTEDO 9.7 (SD, 4.1); Placebo 9.6 (SD, 3.8). LS, least squares; SD, standard deviation; SE, standard error.

AUSTEDO Has a Demonstrated Safety and Tolerability Profile

The most common AEs reported by patients treated with AUSTEDO (≥2% and greater than placebo) in the placebo-controlled pivotal studies are shown in **Table 2.1**.[1] Discontinuation due to AEs occurred in 4% of patients taking AUSTEDO vs 3% of patients taking placebo.[10] Dose reduction due to AEs was required in 4% of patients taking AUSTEDO vs 2% of patients taking placebo.[1] Once patients were titrated to their maintenance dose, dry mouth, nausea, and hypertension were no longer reported in AIM-TD and somnolence and dry mouth were no longer reported in ARM-TD.[4] Adverse reactions with AUSTEDO XR® (deutetrabenazine) extended-release tablets are expected to be similar to those with AUSTEDO BID.[1]

No Dose Restrictions up to 36 mg/day for Patients Starting AUSTEDO XR

Given the prevalence of polypharmacy in residents, the risk of drug-drug interactions (DDIs) is significantly increased.[13]

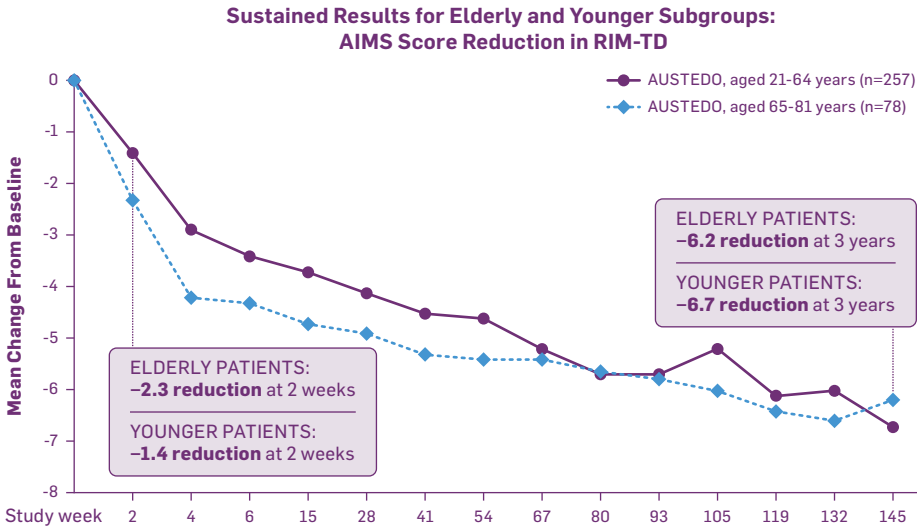
Adverse reactions with AUSTEDO XR are expected to be similar to the AUSTEDO BID formulation.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Akathisia, Agitation, and Restlessness: AUSTEDO XR and 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 XR or AUSTEDO dose should be reduced; some patients may require discontinuation of therapy.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

Figure 2.2. Increasing Improvement Observed Over 3 Years in an OLE Study[12,*]



21-64 years of age=younger; 65-81 years of age=elderly.[12]

Patients in the RIM-TD study received the AUSTEDO BID formulation.
*In a post hoc subgroup analysis of the RIM-TD open-label extension.[12]

Table 2.1. Adverse Reactions Reported in ≥2% of Patients Treated With AUSTEDO

Adverse Reaction	AUSTEDO (n=279)	Placebo (n=131)
Headache	5%	8%
Somnolence	4%	7%
Diarrhea	4%	4%
Nasopharyngitis	4%	2%
Fatigue	4%	5%
Insomnia	4%	1%
Anxiety	4%	5%
Upper respiratory tract infection	3%	4%
Dry mouth	3%	5%
Nausea	2%	7%
Weight increased	2%	3%
Urinary tract infection	2%	2%
Depression/dysthymic disorder	2%	1%
Akathisia/agitation/restlessness	2%	1%
Arthralgia	2%	1%

A recent study of residents in LTC facilities reported that the average number of medications per resident was ~15, making safety a top priority when selecting a treatment for TD.[4] The unique metabolic profile of AUSTEDO XR allows for no DDI-related restrictions with strong CYP3A4/5 inducers and inhibitors. It can also be safely administered up to 36 mg/day with strong CYP2D6 inhibitors and poor metabolizers, making it a suitable option for treating TD in residents who are taking concomitant medications. Additionally, there is no need to reduce the dose of P-glycoprotein (P-gp) substrates when taking AUSTEDO XR **(Table 2.2)**.[1]

One Pill, Once Daily Dosing With AUSTEDO XR

AUSTEDO XR is available in 12 mg, 18 mg, 24 mg, 30 mg, 36 mg, 42 mg, and 48 mg extended-release tablets. The recommended starting dose of AUSTEDO XR for TD is 12 mg/day and the dose should be increased by 6 mg/day at weekly intervals for individual residents until desired symptom

The average dose in pivotal clinical trials was >36 mg/day for both younger (19-64 years) and elderly (≥65 years) subgroups.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Parkinsonism: AUSTEDO XR and AUSTEDO may cause parkinsonism in patients with Huntington's disease or tardive dyskinesia. Parkinsonism has also been observed with other VMAT2 inhibitors. The risk of parkinsonism may be increased by concomitant use of dopamine antagonists or antipsychotics. If a patient develops parkinsonism, the AUSTEDO XR or AUSTEDO dose should be reduced; some patients may require discontinuation of therapy.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

control is tolerably achieved **(Figure 2.3)**.[1] The average dose in the pivotal clinical trials was >36 mg/day for both younger (19-64 years) and elderly (≥65 years) subgroups.[4,11]

Once-daily AUSTEDO XR may be taken at any time of day with or without food. AUSTEDO XR tablets should be swallowed whole and not chewed, crushed, or broken.[1]

Getting Residents Started on AUSTEDO XR

Residents can get started on AUSTEDO XR at no cost with a prescription for the 4-week Titration Kit by using the 30-Day Free Trial Voucher **(Figure 2.3)**. At the same time, a prescription for the maintenance dose of 36 mg/day can be written. Higher doses of AUSTEDO XR, up to a maximum dose of 48 mg/day, may be prescribed based on the resident's needs and response.[4]

Summary

Factors such as older age and female sex increase the risk of TD, necessitating routine screening, assessment, and appropriate treatment for residents in LTC facilities.[1] The symptoms of TD are often mistaken for DIP. This misidentification may lead to the use of anticholinergics, which are not recommended for TD and can actually worsen its symptoms.[4-6] AUSTEDO XR, a once-daily VMAT2 inhibitor, is approved for the treatment of TD in adults.[1] The efficacy and safety profile of AUSTEDO has been demonstrated in clinical trials.[4,10,11] The open-label extension study showed increasing improvement for up to 3 years.[12] AUSTEDO XR is available in 7 dosages, allowing flexible titration to achieve effective symptom control.[1] Additionally, a 4-week Titration Kit is available through prescription at no cost, using the 30-Day Free Trial Voucher, to get residents started on AUSTEDO XR.[4] ■

Table 2.2. Metabolic Profile of AUSTEDO XR® (deutetrabenazine) extended-release tablets Allows for Few Restrictions Related to Drug-Drug Interactions[4,14]

	AUSTEDO XR	Valbenazine/ Valbenazine Sprinkle
Strong CYP3A4/5 inducer	No dose restriction	Concomitant use is not recommended
Strong CYP3A4/5 inhibitor	No dose restriction	40 mg/day lowest dose available
Strong CYP2D6 inhibitor (or if patient is a poor CYP2D6 metabolizer)	Up to 36 mg/day	40 mg/day lowest dose available
P-gp substrate (eg, calcium channel blockers, statins, antimicrobials, and digoxin)	No dose adjustment to P-gp substrate required	Dose adjustment to P-gp substrate may be required

These differences should not be construed to imply differences in safety, efficacy, or clinical outcome.

No clinically significant QT prolongation up to the maximum recommended dose of AUSTEDO® (deutetrabenazine) tablets (48 mg/day).

Figure 2.3. Flexibility for Effective and Tolerable Control

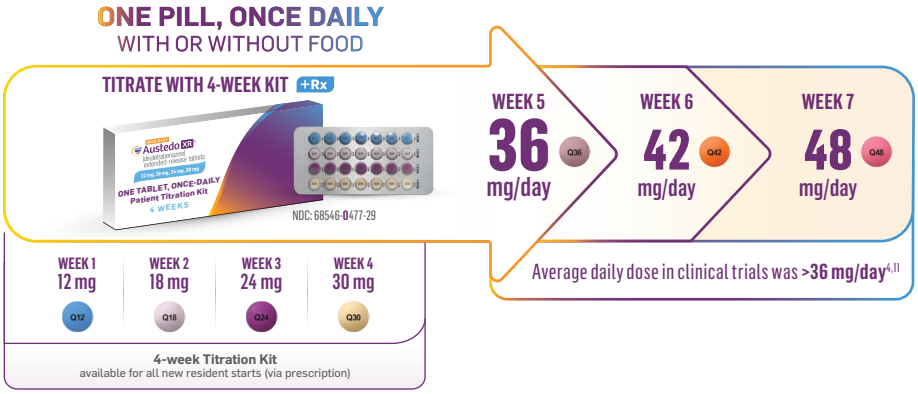


Image shown is not the actual 4-week Titration Kit. Tablets not shown to actual size.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Sedation and Somnolence: Sedation is a common dose-limiting adverse reaction of AUSTEDO XR and 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 XR or 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.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

Expert Commentary With Hany Mohamed and Tiffany Nelson

Hany Mohamed, PharmD, RPh, BCGP, BCMTM, CDTM
Director of Clinical Services
LI Script LLC
Yonkers, New York

Tiffany Nelson, DNP-C, CCM
Owner and Nurse Practitioner
It Is Well
Kennett, Missouri

This newsletter is produced by Teva Pharmaceuticals, and Dr Hany Mohamed and Tiffany Nelson were compensated by Teva for their insights.

Q: Can you speak about the overall use of antipsychotics in the long-term care (LTC) setting?
Tiffany Nelson: The use of antipsychotics in the LTC setting differs significantly from the community setting because of distinct patient demographics, risks, and regulatory rules. In the community setting, these medications are used for a wider range of conditions, while LTC facilities largely limit them to specific diseases such as schizophrenia, schizoaffective disorder, and Huntington's. LTC facilities also follow protocols for gradual dose reduction (GDR) if antipsychotics are deemed unnecessary, and require justifications if residents continue to be on antipsychotics either at the original or reduced dose.

Dr Mohamed: I would like to add that many antipsychotic prescriptions in LTC are carried over from treatments started in hospitals or community settings, which might not always be appropriate. For example, antipsychotics are often used for major depressive disorder, even though this condition usually needs combined treatment with antidepressants like selective serotonin reuptake inhibitors (SSRIs). Therefore, effective management requires coordinated efforts among pharmacists, practitioners, administrators, and nurses to ensure resident well-being.

Q: What best practices are in place to assess the appropriate use of antipsychotics for residents entering the facility?
Tiffany Nelson: First, it is crucial to establish the accuracy of the resident's diagnosis, to see if they truly warrant these medications. A comprehensive history should be taken. To accomplish this, caregivers can be a valuable resource for insights into previous management strategies and the effectiveness of past treatments. Unnecessary medications should be carefully discontinued, and medications that are needed but have safety concerns should be substituted with safer options.

Dr Mohamed: The decision to use antipsychotic medications involves weighing the benefits against the risks. In our facility, we have a consulting pharmacist who reviews the drug regimen of each resident, ensuring antipsychotics are prescribed within the appropriate clinical and regulatory frameworks and are medically necessary. **If antipsychotic use is not justified, a GDR is attempted to discontinue the medication.** We make an exception and allow continued use if GDR attempts worsen a resident's condition or affects their safety.

Q: How do F-tags that are related to inappropriate and unnecessary medication use affect the Centers for Medicare & Medicaid Services (CMS) star rating of LTC facilities?
Tiffany Nelson: **The unnecessary use of medications can lead to**

IMPORTANT SAFETY INFORMATION (CONTINUED)

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 XR and AUSTEDO.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

F-tag violations and negatively impact a facility's star rating. For instance, the off-label use of antipsychotics, even when it may be medically justified, or using benztropine to treat tardive dyskinesia (TD), can negatively affect the facility's rating. To avoid this, it is essential to demonstrate appropriate medication use with proper documentation. As residents age, their health conditions and medication needs can change, which requires careful monitoring. Ultimately, preventing F-tag violations relies on accurate clinical assessment, appropriate medication use and dosing, and ongoing evaluation.

Dr Mohamed: Misdiagnosis and inadequate education can result in high rates of inappropriate antipsychotic use. To address this, F-tag 757 requires facilities to avoid unnecessary medications and maintain thorough documentation to justify their use. Additionally, F-tag 605 ensures freedom from chemical restraints and F-tag 841 mandates medical director oversight, highlighting the importance of precise prescribing. Preventing unnecessary antipsychotic medication requires enhanced education, comprehensive assessments, and coordinated efforts among staff.

Q: How does the risk of developing a movement disorder compare between residents versus the general population?

Tiffany Nelson: Age and female sex are well-established risk factors for developing movement disorders in individuals exposed to dopamine receptor blocking agents. Keeping these risk factors in mind and maintaining a high level of suspicion is essential for identifying and addressing movement disorders in these high-risk groups.

Dr Mohamed: I would like to further emphasize Tiffany's point that older residents are at a significantly increased risk for developing TD. Therefore, residents at risk should be assessed for TD at every encounter.

Q: How familiar are LTC staff with the various movement disorders caused by antipsychotic drugs?

Tiffany Nelson: LTC staff often lack the necessary education and training to recognize and distinguish between the various movement disorders caused by antipsychotics. These disorders are often incorrectly generalized as extrapyramidal symptoms (EPS), despite having distinct symptoms and requiring different treatments. This lack of understanding is often seen in the frequent recording of an Abnormal Involuntary Movement Scale (AIMS) score of 0, even in residents with observable movements. This highlights a significant need for improved education in LTC facilities about the distinctions between different movement disorders and accurately conducting an AIMS examination every 6 months for residents on antipsychotic drugs.

Dr Mohamed: Distinguishing between the various movement disorders is key to proper intervention. Most staff in LTC are unable to distinguish between the 2 most common movement disorders, TD and drug-induced parkinsonism (DIP), which are caused by the same offending agent but have opposite clinical features and completely different treatments, with treatment for one exacerbating the other.

Q: What clinical features can help clinicians distinguish between TD and DIP?

Tiffany Nelson: TD is characterized by involuntary hyperkinetic movements commonly affecting the perioral region, hands, and fingers. In contrast, DIP is associated with slower, rhythmic movements such as bradykinesia, where patients exhibit a slow gait, masked facial expressions, and fine motor tremors, especially noticeable during actions like reaching or grasping. These observable differences can guide nursing staff to identify the correct disorder and initiate proper treatment interventions.

Dr Mohamed: To distinguish TD from DIP, clinicians can also assess the timeline of antipsychotic drug use and the onset of symptoms. DIP typically develops within weeks to months of starting treatment with antipsychotics, whereas TD often emerges at least after a few months. In elderly patients, TD may develop more rapidly, sometimes within a month.

Q: What is currently recommended regarding the use of anticholinergics such as benztropine for treatment of DIP?

Dr Mohamed: While anticholinergics are indicated for DIP, their use must be weighed against potential adverse effects, particularly in older adults who may experience cognitive impairment, dry mouth, constipation, and confusion. These risks can lead to hospitalizations or injuries, making the safety profile of anticholinergics a critical consideration.

Tiffany Nelson: When managing DIP, particularly in older adults, it is important to remember that DIP is reversible. Therefore, instead of resorting to anticholinergics, reducing the offending agent can often work. For residents who do not show improvement when antipsychotics are reduced, it is important to also evaluate them for Parkinson's disease, a condition common in older adults and often misidentified as DIP. Moreover, if the movement symptoms are not troublesome for the resident, treatment can sometimes be avoided. However, if these initial approaches are ineffective and treatment becomes necessary, it is important to choose the safest option available. I always start at the lowest possible dose of the anticholinergic and titrate slowly to reach the appropriate therapeutic level. In addition, residents should be reevaluated every 4 to 6 weeks to assess whether ongoing treatment continues to be required.

Q: Once TD is diagnosed, what is your approach to initiating treatment? What has been your experience with AUSTEDO XR® (deutetrabenazine) extended-release tablets?

Tiffany Nelson: Once TD is diagnosed, I use both the AIMS and the ImpactTD scale to assess the severity and impact of movements on the resident. Up to 98% of patients with TD experience its impact on some aspect of their life. **It is essential to remember that the impact of TD can be significant, regardless of how severe the movements are. In my residents, I typically initiate treatment with AUSTEDO XR if the TD symptoms are impacting them.**

The titration begins at 12 mg, with weekly increments of 6 mg/day, up to a maximum of 48 mg/day, while regularly evaluating improvements in both movement and overall patient outcome. The dosing flexibility offered by AUSTEDO XR allows for dose adjustment at any point during the treatment.

Dr Mohamed: I agree with Tiffany's approach to treating residents with TD using AUSTEDO XR, ensuring it is titrated to an effective and well-tolerated dose. I also make it a point to review and eliminate unnecessary medications, like benztropine, that may have been initiated for TD symptoms. Additionally, LTC residents often take multiple medications, which increases the risk of drug-drug interactions. **A key advantage of AUSTEDO XR is that it has no dose restrictions when used with CYP3A4 inducers and inhibitors and can be used up to 36 mg/day with CYP2D6 inhibitors and metabolizers.**

Key Learning Points

- In LTC facilities, antipsychotics are used for specific conditions, like schizophrenia, schizoaffective disorder, and Huntington's, following strict regulations, while their use in the community is broader
- Thorough patient assessments and collaborative management are vital in LTC to justify antipsychotic use and to avoid unnecessary prescriptions
- Inappropriate medication use can lead to F-tag violations, which adversely affect a facility's star rating
- LTC staff often need better training to distinguish between movement disorders like TD and DIP
- Identifying and appropriately treating TD symptoms can enhance nursing care by minimizing time needed to help residents with daily activities like bathing, feeding, and dressing
- AUSTEDO XR offers flexible dosing from 12 mg/day up to 48 mg/day for TD treatment in adults ■

IMPORTANT SAFETY INFORMATION (CONTINUED)

Common Adverse Reactions: The most common adverse reactions for AUSTEDO® (deutetrabenazine) tablets (>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. Adverse reactions with AUSTEDO XR extended-release tablets are expected to be similar to AUSTEDO tablets.

Please see additional Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

References

OVERVIEW OF TD AND DIP: Distinguishing Between Tardive Dyskinesia (TD) and Drug-Induced Parkinsonism (DIP): Why Accurate Diagnosis Matters

1. Ward KM, Citrome L. Antipsychotic-related movement disorders: drug-induced parkinsonism vs. tardive dyskinesia—key differences in pathophysiology and clinical management. *Neurol Ther.* 2018;7(2):233-248. **2.** Hauser RA, Meyer JM, Factor SA, et al. Differentiating tardive dyskinesia: a video-based review of antipsychotic-induced movement disorders in clinical practice. *CNS Spectr.* 2022;27(2):208-217. **3.** Lenka A, Jankovic J. Extrapyramidal system/symptoms/signs should be retired. *Neurol Clin Pract.* 2024;14(4):e200308. **4.** Miller JJ. Everyone please stop (EPS). *Psychiatric Times.* 2022;39(8). Accessed May 22, 2025. https://www.psychiatrictimes.com/view/everyone-please-stop-eps- **5.** Ogino S, Miyamoto S, Miyake N, Yamaguchi N. Benefits and limits of anticholinergic use in schizophrenia: focusing on its effect on cognitive function. *Psychiatry Clin Neurosci.* 2014;68(1):37-49. **6.** Carbon M, Hsieh C-H, Kane JM, Correll CU. Tardive dyskinesia prevalence in the period of second-generation antipsychotic use: a meta-analysis. *J Clin Psychiatry.* 2017;78(3):e264-e278. **7.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed, Text Revision. Washington, DC: American Psychiatric Association; 2022. **8.** Psychiatry & Behavioral Health Learning Network. Q&A: updates from Dr Rakesh Jain on managing tardive dyskinesia. Updated June 15, 2021. Accessed May 22, 2025. https://www.hmpgloballearningnetwork.com/site/psychbehav/qas/qa-updates-dr-rakesh-jain-managing-tardive-dyskinesia **9.** Patel T, Chang F. Practice recommendations for Parkinson's disease: assessment and management by community pharmacists. *Can Pharm J (Ott).* 2015;148(3):142-149. **10.** American Psychiatric Association. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia.* 3rd ed. Washington, DC: American Psychiatric Association; 2021. Accessed May 22, 2025. **11.** Data on file. Teva Neuroscience, Inc. Parsippany, NJ. **12.** Chepke C, Benning B, Cicero S, et al. Investigating real-world benztropine usage patterns in movement disorders: claims analysis and health care provider survey results. *Prim Care Companion CNS Disord.* 2023;25(4):22m03472. **13.** 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2019;67(4):674-694. **14.** Cogentin® (benztropine mesylate injection). Prescribing Information. Lake Forest, IL: Oak Pharmaceuticals, Inc. **15.** Design for *Care Compare* nursing home five-star quality rating system: technical users' guide. Department of Health and Human Services, Centers for Medicare & Medicaid Services. January 2025. Accessed May 22, 2025. https://www.cms.gov/medicare/provider-enrollment-and-certification/certificationandcomplianc/downloads/usersguide.pdf **16.** Center for clinical standards and quality/quality, safety and oversight group. Department of Health and Human Services, Centers for Medicare & Medicaid Services. November 2024. Accessed May 25, 2025. https://www.cms.gov/files/document/revised-long-term-care-ltc-surveyor-guidance-significant-revisions-enhance-quality-and-oversight-ltc.pdf **17.** Benztropine mesylate tablet. Prescribing Information. Warren, NJ: Cipla USA, Inc. **18.** Vanegas-Arroyave N, Caroff SN, Citrome L, et al. An evidence-based update on anticholinergic use for drug-induced movement disorders. *CNS Drugs.* 2024;38(4):239-254.

TREATMENT: AUSTEDO XR®—A Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor for the Treatment of Tardive Dyskinesia (TD)

1. AUSTEDO® XR (deutetrabenazine) extended-release tablets/AUSTEDO® current Prescribing Information. Parsippany, NJ: Teva Neuroscience, Inc. **2.** Hauser RA, Meyer JM, Factor SA, et al. Differentiating tardive dyskinesia: a video-based review of antipsychotic-induced movement disorders in clinical practice. *CNS Spectr.* 2022;27(2):208-217. **3.** Rao AS, Camilleri M. Review article: metoclopramide and tardive dyskinesia. *Aliment Pharmacol Ther.* 2010;31(1):11-19. **4.** Data on file. Parsippany, NJ: Teva Neuroscience, Inc. **5.** Benztropine mesylate tablets. Prescribing Information. Warren, NJ: Cipla USA, Inc. **6.** Vanegas-Arroyave N, Caroff SN, Citrome L, et al. An evidence-based update on anticholinergic use for drug-induced movement disorders. *CNS Drugs.* 2024;38(4):239-254. **7.** American Psychiatric Association. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia.* 3rd ed. Washington, DC: American Psychiatric Association; 2021. **8.** Caroff SN, Davis VG, Miller DD, et al. Treatment outcomes of patients with tardive dyskinesia and chronic schizophrenia. *J Clin Psychiatry.* 2011;72(3):295-303. **9.** Citrome L, Isaacson SH, Larson D, Kremens D. Tardive dyskinesia in older persons taking antipsychotics. *Neuropsychiatr Dis Treat.* 2021;17:3127-3134. **10.** Anderson KE, Stamler D, Davis MD, et al. Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Psychiatry.* 2017;4(8):595-604. **11.** Fernandez HH, Factor SA, Hauser RA, et al. Randomized controlled trial of deutetrabenazine for tardive dyskinesia: the ARM-TD study. *Neurology.* 2017;88(21):2003-2010. **12.** Hauser RA, Barkay H, Fernandez HH, et al. Long-term deutetrabenazine treatment for tardive dyskinesia is associated with sustained benefits and safety: a 3-year, open-label extension study. *Front Neurol.* 2022;13:773999. **13.** Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. *J Am Med Dir Assoc.* 2015;16(6):535.e1-e12. **14.** Ingrezza® (valbenazine) capsules. Prescribing Information. San Diego, CA: Neurocrine Biosciences, Inc.

Suggested Reading

EXPERT COMMENTARY: Expert Commentary With Hany Mohamed and Tiffany Nelson

1. 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2019;67(4):674-694. **2.** American Psychiatric Association. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia.* 3rd ed. American Psychiatric Association; 2021. https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841 **3.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed, Text Revision. Washington, DC: American Psychiatric Association; 2022. **4.** AUSTEDO XR® (deutetrabenazine) extended-release tablets/AUSTEDO® current Prescribing Information. Parsippany, NJ: Teva Neuroscience, Inc. **5.** Center for clinical standards and quality/quality, safety and oversight group. Department of Health and Human Services, Centers for Medicare & Medicaid Services. November 2024. Accessed April 3, 2025. https://www.cms.gov/files/document/revised-long-term-care-ltc-surveyor-guidance-significant-revisions-enhance-quality-and-oversight-ltc.pdf **6.** Cogentin® (benztropine mesylate injection). Prescribing Information. Lake Forest, IL: Oak Pharmaceuticals, Inc. **7.** Data on file. Teva Neuroscience, Inc. Parsippany, NJ. **8.** Design for *Care Compare* nursing home five-star quality rating system: technical users' guide. Department of Health and Human Services, Centers for Medicare & Medicaid Services. January 2025. Accessed June 17, 2025. https://www.cms.gov/medicare/provider-enrollment-and-certification/certificationandcomplianc/downloads/usersguide.pdf **9.** Duma SR, Fung VS. Drug-induced movement disorders. *Aust Prescr.* 2019;42(2):56-61. **10.** Finkbeiner S, Konings M, Henegar M, et al. Multidimensional impact of tardive dyskinesia: interim analysis of clinician-reported measures in the IMPACT-TD registry. Presented at: Annual Psych Congress Elevate; May 30-June 2, 2024; Las Vegas, NV. **11.** Hauser RA, Meyer JM, Factor SA, et al. Differentiating tardive dyskinesia: a video-based review of antipsychotic-induced movement disorders in clinical practice. *CNS Spectr.* 2022;27(2):208-217. **12.** Karrouri R, Hammani Z, Benjelloun R, Otheman Y. Major depressive disorder: validated treatments and future challenges. *World J Clin Cases.* 2021;9(31):9350-9367. **13.** Rothschild AJ. Treatment for major depression with psychotic features (psychotic depression). *Focus (Am Psychiatr Publ).* 2016;14(2):207-209. **14.** Spielmans GI, Berman MI, Linardatos E, Rosenlicht NZ, Perry A, Tsai AC. Adjunctive atypical antipsychotic treatment for major depressive disorder: a meta-analysis of depression, quality of life, and safety outcomes. *PLoS Med.* 2013;10(3):e1001403. **15.** Ward KM, Citrome L. Antipsychotic-related movement disorders: drug-induced parkinsonism vs. tardive dyskinesia—key differences in pathophysiology and clinical management. *Neurol Ther.* 2018;7(2):233-248.

Please see Important Safety Information throughout and click here or visit www.AUSTEDOhcp.com to read/print the full Prescribing Information, including Boxed Warning, for AUSTEDO XR.

You may choose to have your name removed from our mailing list at any time by writing us at:
Teva/Privacy Officer • 400 Interpace Parkway • Parsippany, NJ 07054