TD NEWS+VIEWS
VOLUME 21 • MARCH 2026

Patient-Forward Approaches for Tardive Dyskinesia: From Differential Diagnosis to Appropriate Treatment

DIFFERENTIAL DIAGNOSIS

Differentiating Tardive Dyskinesia From Other Drug-Induced Movement Disorders: Key Distinctions and Guideline-Recommended Treatments

Review essential diagnostic differences that help ensure proper identification and treatment of tardive dyskinesia.

NEUROBIOLOGY SIDEBAR

Considerations Regarding the Mechanism of Action of Vesicular Monoamine Transporter 2 Inhibitors and Anticholinergics in Tardive Dyskinesia and Drug-Induced Parkinsonism

Explore why the distinct MOAs in these disorders are important and how that should inform treatment.

TREATMENT

Understanding AUSTEDO XR®: A Once-Daily Treatment Option for Adult Patients With Tardive Dyskinesia

Examine data from the clinical trials of AUSTEDO® (deutetrabenazine) tablets, including efficacy, subgroup analyses, and safety profile, followed by information on dosing.

EXPERT COMMENTARY

Expert Commentary With Henry Nasrallah, MD, and Daniel Dees, MD

Henry Nasrallah, MD
Professor of Psychiatry,
Neurology and Neuroscience
Cincinnati, Ohio

Daniel Dees, MD
Movement Disorder Specialist
Mobile, Alabama

This newsletter is produced by Teva Pharmaceuticals. Drs Henry Nasrallah and Daniel Dees 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 for full Prescribing Information, including Boxed Warning.

DIFFERENTIAL DIAGNOSIS

Differentiating Tardive Dyskinesia From Other Drug-Induced Movement Disorders: Key Distinctions and Guideline-Recommended Treatments

Tardive dyskinesia (TD) is one of several movement disorders caused by exposure to antipsychotics and other dopamine receptor blocking agents (DRBAs). It is critical to differentiate TD from other drug-induced movement disorders (DIMDs), particularly drug-induced parkinsonism (DIP), because anticholinergics which may be used to treat it can worsen TD. Through proper identification of TD, adequate and effective therapy can be provided to improve outcomes for patients.[1]

An Overview on DIMDs and Differential Diagnosis

DRBAs, including both atypical and typical antipsychotics, are an important treatment option for potentially devastating psychiatric disorders like schizophrenia, bipolar disorder, and major depressive disorder.[1] While these medications can be effective, they can also result in DIMDs.[2]

The term extrapyramidal symptoms (EPS) has been used broadly to describe all drug-induced abnormal movements and is still used by the US Food and Drug Administration (FDA) and among psychiatry providers. As our understanding of these conditions has evolved, **the EPS term is now considered outdated as it fails to capture the distinct clinical presentations associated with individual DIMDs**.[1,3-5]

Understanding the clinical presentation of common DIMDs can aid in the differential diagnosis **(Videos 1.1-1.4)**.[1]

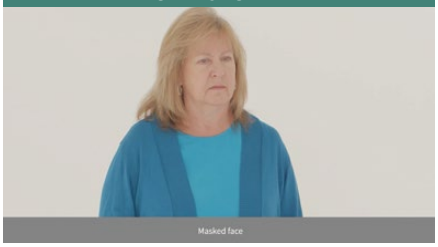
- TD is characterized by excessive and irregular movements, often affecting the face
- DIP is characterized by an overall paucity of movement but may also be accompanied by tremor
- Acute dystonia is characterized by pulling, twisting, sustained, and repetitive movements or postures
- Acute akathisia is characterized by a feeling of restlessness with an urge to move

Videos 1.1-1.4. Distinguishing Movements of TD, DIP, Acute Dystonia, and Acute Akathisia[6-9]

TD
ICD-10: G24.01*

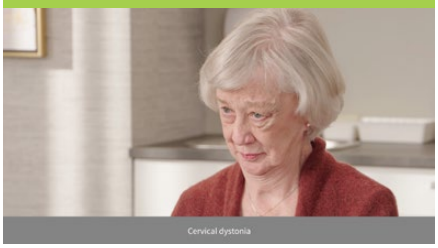
Click here to view video

DIP
ICD-10: G21.1



Click here to view video

Acute Dystonia
ICD-10: G24.02



Click here to view video

*The ICD-10 code G24.01 is for drug-induced subacute dyskinesia and is applicable to TD.

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 for full Prescribing Information, including Boxed Warning.

TD is distinct and must be distinguished from other DIMDs, particularly DIP, to ensure appropriate treatment.

The Widespread and Inappropriate Use of Anticholinergics for DIMDs

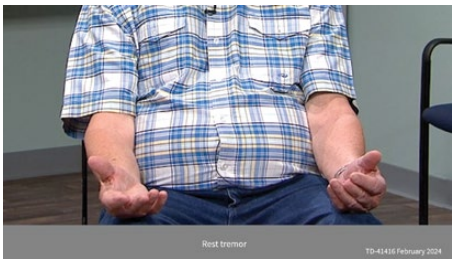
Because the EPS term is used broadly to describe motor symptoms linked with the use of DRBAs, anticholinergic medications, such as benztropine, were commonly prescribed to treat any abnormal movements regardless of the underlying DIMD.[1,3,4] While benztropine is indicated to treat DIP, it is not recommended for patients with TD because it can worsen symptoms.[5,10,11] **Despite this warning, misuse of anticholinergics for treating TD persists. Approximately 40% of healthcare professionals (HCPs) in psychiatry report prescribing benztropine to treat or prevent TD.**[12]

Anticholinergics are not an appropriate treatment for TD because they can worsen symptoms.

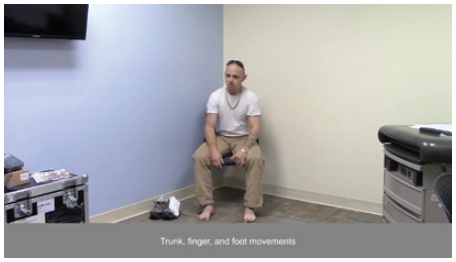
Keys to Differentiating Between TD and DIP

It is critical to differentiate between TD and DIP because the wrong treatment could lead to a worsening of symptoms.[5,11] By understanding the key features that differ between TD and DIP, such as the timing of onset and the nature and frequency of movements, these disorders can be accurately identified **(Videos 1.5-1.6)**.[5,13] DIP typically develops within a few weeks to months of starting or after a dose increase of an antipsychotic and is characterized by a paucity or slowness of movements. When present, movements are rhythmic, and DIP may also be associated with rigidity.[5,11,13,14] In contrast, TD typically develops after months to years of antipsychotic use. The minimum exposure history required for the diagnosis of TD is at least 3 months (or 1 month in patients aged ≥60 years). It is characterized by irregular movements that are jerky and unpredictable, without associated rigidity.[5,11,13,15] Through careful assessment and differential diagnosis based on clinical presentation of the movements, HCPs can identify TD and ensure appropriate treatment is provided.[1,16]

Videos 1.5-1.6. Clinical Presentation of DIP vs TD Movements



Click here to view video



Click here to view video

	Drug-Induced Parkinsonism (DIP)	Tardive Dyskinesia (TD)
Onset of symptoms	Within a few **weeks to months** of • Starting an antipsychotic • Increasing the dosage of an antipsychotic • Reducing the dosage of an anticholinergic medication used to treat DIP	After using an antipsychotic for at least a few **months to years** • Elderly persons may develop TD symptoms in a shorter period of time • Movements may appear after discontinuation or after a reduction in dosage of the antipsychotic
Types of symptoms	• **Paucity or slowness** of movement (akinesia/bradykinesia) • Movements, when present, are **rhythmic** (tremor) • **Rigidity,** assessed during a physical exam, may be present	• **Excessive and continuous** movements • Movements are **irregular, unpredictable, jerky, twitchy** (choreoathetosis) • Not associated with rigidity

Accurate Diagnosis for Appropriate Treatment

TD is a chronic and irreversible condition.[1] Although discontinuing the antipsychotic may improve or resolve the symptoms associated with DIP, antipsychotic reduction or complete withdrawal may fail to improve the symptoms of TD or might even induce withdrawal dyskinesia.[5,11] Similarly, while anticholinergic medications, such as benztropine, are an appropriate treatment for DIP, they should not be used to treat or prevent TD because it may lead to worsening movements.[5,11]

The American Psychiatric Association (APA) recommends treatment with a VMAT2 inhibitor for TD that impacts patients' lives, but it should be noted that these agents can worsen parkinsonism.[1,13] **For patients with TD who are taking an anticholinergic, consider gradually reducing and discontinuing it and initiate treatment with a VMAT2 inhibitor when appropriate.**[5,17]

VMAT2 inhibitors are the only FDA-approved treatment for TD.

Key Takeaways

- DIMDs have distinct clinical presentations and should have different approaches to treatment. This makes differentiating between movements essential for determining the appropriate treatment[1]
- Anticholinergics are not an appropriate treatment for TD and may exacerbate movements[5,11]
- TD and DIP differ in clinical presentation, timing of onset, and the nature and frequency of movements[5,13]
  - DIP typically develops within a few weeks to months of starting or increasing the dose of an antipsychotic and is characterized by a paucity or slowness of movements. When present, movements are rhythmic, and DIP is often associated with rigidity[5,11,13,14]
  - TD typically develops after at least a few months of antipsychotic use. It is characterized by irregular movements that are jerky and unpredictable[5,11,13,15]
- The APA recommends VMAT2 inhibitors for the treatment of TD that is impacting the patient[17] ■

NEUROBIOLOGY SIDEBAR

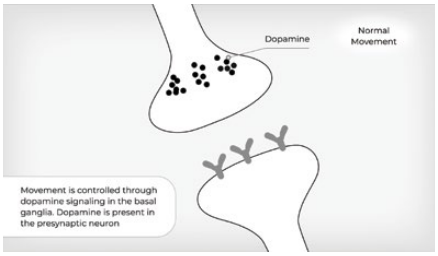
Considerations Regarding the Mechanism of Action of Vesicular Monoamine Transporter 2 Inhibitors and Anticholinergics in Tardive Dyskinesia and Drug-Induced Parkinsonism

Tardive Dyskinesia (TD) and Drug-Induced Parkinsonism (DIP) Are Different Disorders With Opposite Mechanisms

TD and DIP are common movement disorders caused by exposure to dopamine receptor blocking agents such as antipsychotics, antiemetics, and prokinetics. However, the symptoms associated with each disorder **require different treatment approaches**, as they result from **opposite pathophysiological mechanisms (Video 2)**.[1,2]

- **DIP is a hypodopaminergic disorder:** the acute blockade of dopamine receptors by typical and atypical antipsychotics leads to a reduction in postsynaptic dopamine signaling. Reduced signaling results in the **hypokinetic movements** associated with DIP[1,3]
- **TD is a hyperdopaminergic disorder:** it is thought that chronic blockade of dopamine receptors results in an increase of receptor function, which is partly theorized to result from receptor hypersensitivity or upregulation. This results in increased dopamine signaling, manifesting as the **hyperkinetic movements** that are characteristic of TD[1,2]

Video 2. TD and DIP Are Different Disorders With Distinct Underlying Causes



Click here to view video

Understanding the Impact of Medications on TD and DIP

Differentiating between DIP and TD is crucial as **the wrong treatment could lead to a worsening of symptoms.**[1,4] In DIP, a decrease in dopamine signaling amplifies cholinergic activity. Thus, **anticholinergics can be effective in treating DIP** because they inhibit acetylcholine and therefore restore the dopamine-acetylcholine balance. In contrast, in TD, an increase in dopamine signaling dampens cholinergic activity.[5] Thus, **anticholinergic medications** such as benztropine **are not effective in treating TD and may even worsen hyperkinetic symptoms** because they increase acetylcholine signaling **(Figure 2)**.[1,4,6]

Vesicular monoamine transporter 2 (VMAT2) inhibitors are the **only US Food and Drug Administration (FDA)-approved treatment for TD** and are

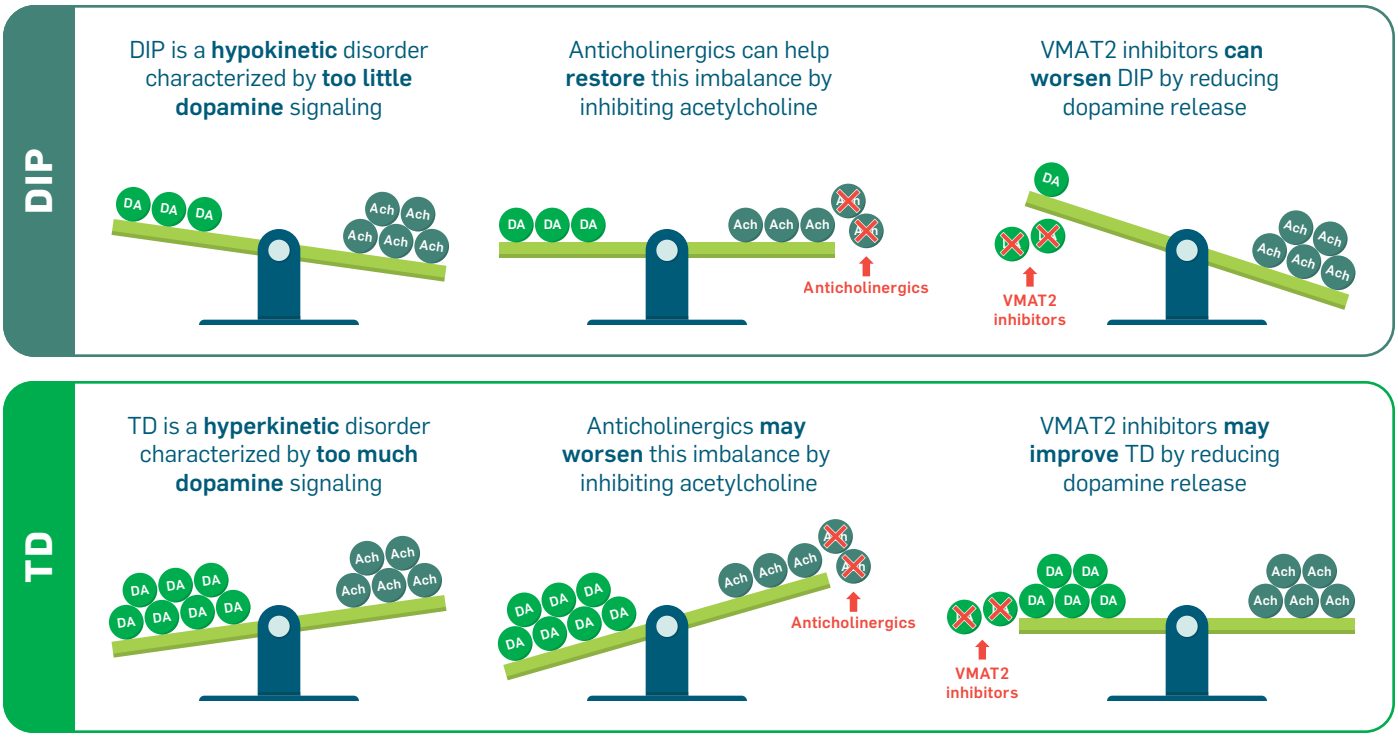
TD and DIP are distinct disorders with opposite underlying mechanisms; DIP arises from reduced dopamine signaling, whereas TD results from an excess of dopamine activity.

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 for full Prescribing Information, including Boxed Warning.

Figure 2. Unlike Anticholinergics, VMAT2 Inhibitors May Improve TD by Reducing Excessive Dopamine Signaling[1,3,5]



recommended by the American Psychiatric Association (APA) Guidelines if TD has an impact on the patient, regardless of severity of movements.[7] These agents have been shown to be effective in **improving TD symptoms** by reducing dopamine signaling and helping to restore the dopamine-acetylcholine balance.[1] On the other hand, they **can worsen DIP** by further reducing dopamine signaling and amplifying cholinergic activity **(Figure 2)**.[1]

For patients with TD who are taking an anticholinergic, gradually reduce and discontinue anticholinergic therapy and initiate treatment with a VMAT2 inhibitor as appropriate.[1,5,7]

Differentiating between DIP and TD is crucial as the wrong treatment could lead to a worsening of symptoms.

Summary

- TD and DIP are different disorders with opposite pathophysiological mechanisms; DIP is a hypodopaminergic disorder while TD is a hyperdopaminergic disorder[1-3]
- Differentiating between DIP and TD is crucial as the wrong treatment could lead to a worsening of symptoms[1,4]
  - Anticholinergic medications are indicated for the treatment of DIP but can exacerbate TD symptoms[1,4]
  - VMAT2 inhibitors are indicated for TD but worsen parkinsonism[1]
- APA Guidelines recommend VMAT2 inhibitors for TD that has an impact on the patient, regardless of severity of movements[7] ■

IMPORTANT SAFETY INFORMATION (CONTINUED)

Akathisia, Agitation, and Restlessness: AUSTEDO XR® (deutetrabenazine) extended-release tablets and AUSTEDO® (deutetrabenazine) tablets 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 for full Prescribing Information, including Boxed Warning.

ONCE-DAILY
Austedo XR®
(deutetrabenazine)
extended-release
6 mg, 12 mg, 18 mg, 24 mg, 30 mg,
36 mg, 42 mg, and 48 mg tablets

TREATMENT

Understanding AUSTEDO XR: A Once-Daily Treatment Option for Adult Patients With Tardive Dyskinesia

Tardive dyskinesia (TD) and drug-induced parkinsonism (DIP) are movement disorders resulting from exposure to dopamine receptor blocking agents, such as antipsychotic medications. However, **each disorder has distinct underlying pathophysiology and specific clinical presentation and requires different treatment approaches**.[1,2] While anticholinergic medications can be used to treat the symptoms of DIP, they are not effective in treating TD and may even worsen hyperkinetic symptoms.[1] **Vesicular monoamine transporter 2 (VMAT2)** inhibitors, such as AUSTEDO XR, are the **only US Food and Drug Administration (FDA)-approved treatment for adult patients with TD**.[3]

This article reviews key efficacy and safety data from the pivotal clinical trials of AUSTEDO and dives into the range of available dosing options, including recommendations for specific populations and patients taking concomitant medications. Also included are data from real-world surveys of patient-reported experiences on AUSTEDO XR.

Understanding the Mechanism of Action of AUSTEDO XR

The precise mechanism by which deutetrabenazine exerts its activity is unknown but is believed to be related to its effect as a **reversible depletor of monoamines, including dopamine, from nerve terminals (Video 3)**.[4]

Findings From Pivotal Clinical Trials for AUSTEDO: ARM-TD, AIM-TD, and RIM-TD

The efficacy and safety of AUSTEDO in the treatment of TD was evaluated in **2 pivotal clinical trials, ARM-TD** (Aim to Reduce Movements in Tardive Dyskinesia) and **AIM-TD** (Addressing Involuntary Movements in Tardive Dyskinesia)[5,6]:

- **ARM-TD – Flexible-dose study (N=113):** 12-week, randomized, double-blind, placebo-controlled phase 2/3 trial in which doses were titrated to an individualized dose that reduced abnormal movements and was tolerated. After screening, patients were randomized 1:1 to receive AUSTEDO twice daily (BID) or placebo[6]
- **AIM-TD – Fixed-dose study (N=222):** 12-week, randomized, double-blind, placebo-controlled phase 3 trial in which patients were randomized to receive placebo or AUSTEDO (12 mg, 24 mg, or 36 mg)[4,5]

Video 3. Mechanism of Action of AUSTEDO XR

Click here to view video

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.

PPlease see additional Important Safety Information throughout and click here for full Prescribing Information, including Boxed Warning.

The primary efficacy endpoint in both trials was the change in Abnormal Involuntary Movement Scale (AIMS) total score from baseline to Week 12.[4-7]

AUSTEDO® (deutetrabenazine) tablets was not studied in patients currently taking or who had recently (within 30 days) received anticholinergic medications. However, patients with prior anticholinergic use were not excluded from the study.[7] Excluding patients currently taking anticholinergics aligns with TD treatment guidelines and warnings in the label of benztropine, a common anticholinergic, which states that it does not alleviate TD symptoms and may aggravate them.[3,8]

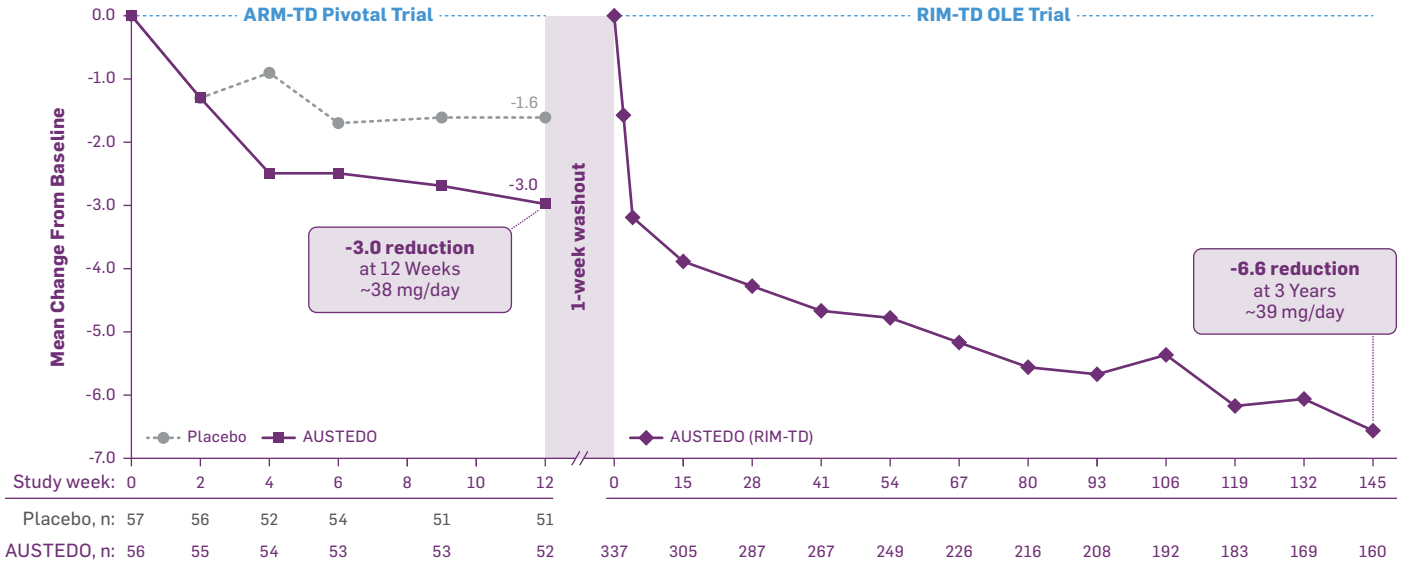
In these placebo-controlled trials, patients who received AUSTEDO demonstrated **a rapid response as early as Week 2** and **achieved a significant and meaningful reduction in TD severity at Week 12**.[4,6,7]

- In ARM-TD, patients receiving **AUSTEDO** had an **AIMS score reduction of 3.0 points from baseline** to Week 12, compared with **1.6 points in the placebo** group (treatment effect of -1.4 points, *P*=0.019) **(Figure 3.1, left graph)**.[6,7] At Week 12, 94% of patients were taking a dose of ≥30 mg/day, and the average daily dose was ~38 mg[6,7]
- In AIM-TD, **AUSTEDO** led to an **AIMS total score reduction of 3.3 points** from baseline in the 36 mg/day arm compared with a **reduction of 1.4 points with placebo at Week 12** (treatment effect of -1.9 points, *P*=0.001).[4,5]

Patients on a stable dose of an antipsychotic maintained that medication while on AUSTEDO.[5,6]

A rapid response as early as Week 2 and movement improvement at Week 12 were observed in patients who received AUSTEDO.

Figure 3.1. AIMS Score Reduction in Pivotal and OLE Studies[4,6,7,9]



Patients in the ARM-TD and RIM-TD studies received the AUSTEDO BID formulation.
Baseline AIMS score: ARM-TD (placebo: 9.6 [SD, 3.8]; AUSTEDO: 9.6 [SD, 4.1]) and RIM-TD (AUSTEDO: 10.7 [SD, 4.7]).
ARM-TD, Aim to Reduce Movements in Tardive Dyskinesia; OLE, open-label extension; RIM-TD, Reducing Involuntary Movements in Participants With TD.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Sedation and Somnolence: Sedation is a common dose-limiting adverse reaction of AUSTEDO XR® (deutetrabenazine) extended-release tablets and AUSTEDO tablets. 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.

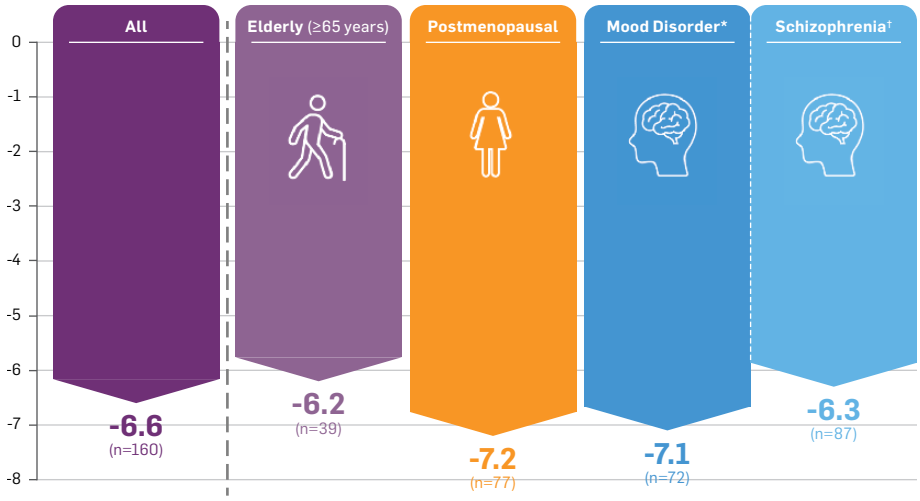
Please see additional Important Safety Information throughout and click here for full Prescribing Information, including Boxed Warning.

RIM-TD (Reducing Involuntary Movements in Participants With TD), a single-arm, open-label extension (OLE), long-term maintenance study, was designed to evaluate **long-term treatment with AUSTEDO for up to 3 years**.[9] Following completion of ARM-TD or AIM-TD, patients were eligible to enter the RIM-TD study.[9] Among the patients evaluated, 337 patients were in treatment at baseline and 160 patients remained on treatment through the end of Week 145.[9] The mean overall compliance rate, assessed by pill counts, was nearly **90% at 3 years**.[7]

Increased improvement in AIMS total score was observed over 3 years in the longest TD clinical trial to date (OLE), with **71% of patients at Week 145 seeing improvement relative to Week 15 (Figure 3.1, right graph)**. At Week 145, 87% of patients were taking a dose of ≥30 mg/day and the average daily dose was ~39 mg.[7,9]

Increased improvement in AIMS total score was observed over 3 years, even in patients at increased risk for TD, in the longest TD clinical trial to date (OLE).

Figure 3.2. Mean Change From Baseline in AIMS Total Score at Week 145[9-12]



Patients in the ARM-TD and RIM-TD studies received the AUSTEDO BID formulation.
*Includes patients with bipolar disorder and depression.
†Includes schizophrenia or schizoaffective disorder.
AIMS, Abnormal Involuntary Movements Scale.

AUSTEDO is the **only VMAT2 inhibitor** demonstrating 3-year results in patients at **increased risk of TD**, including in **(Figure 3.2)**[10-12]

- Patients ≥65 years
- Postmenopausal women
- Patients with mood disorders and schizophrenia

Demonstrated Safety and Tolerability Profile in Pivotal and 3-Year Studies: Studied Across a Diverse Population

The most common adverse reactions reported across both placebo-controlled studies in patients with TD treated with AUSTEDO (>3% and greater than placebo) were nasopharyngitis and insomnia.[4] Adverse reactions occurring in patients treated with AUSTEDO (12-48 mg/day) (≥2%) are summarized in **Figure 3.3**.

Discontinuation due to adverse events (AEs) occurred in 4% of patients taking AUSTEDO compared with 3% of patients treated with placebo.[5] Four percent of patients required dose reduction of AUSTEDO due to AEs compared with 2% of patients taking placebo.[4] Once patients were titrated to their maintenance dose, several AEs were no longer reported, including dry mouth and nausea in AIM-TD

The safety and tolerability profile of AUSTEDO in the OLE study was comparable to the ARM-TD and AIM-TD studies.

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 for full Prescribing Information, including Boxed Warning.

Figure 3.3. Placebo-Controlled TD Studies: Adverse Reactions Reported in ≥2% of Patients With TD Treated With AUSTEDO® (deutetrabenazine) tablets[4,7]

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%

and somnolence and dry mouth in ARM-TD.[7]

No new safety signals were identified in RIM-TD, and AEs were comparable with those in the 12-week clinical trials.[9]

It is important to highlight that the safety and tolerability of AUSTEDO was consistent in older and younger patients, in postmenopausal women, and in patients with underlying psychotic or mood disorders.[10-12]

Adverse reactions with AUSTEDO XR are expected to be similar to AUSTEDO BID.[4]

Dosing Options for AUSTEDO XR: A One Pill, Once-Daily Approved Treatment for Adult Patients With TD

AUSTEDO XR is available in 12 mg, 18 mg, 24 mg, 30 mg, 36 mg, 42 mg, and 48 mg extended-release tablets, providing **dosing flexibility for effective and tolerable symptom control**.[4] The recommended starting dose of AUSTEDO XR for patients with TD is 12 mg/day, which may be increased at weekly intervals by 6 mg/day.[4] The average daily dose in

With 7 different dosing options, AUSTEDO XR® (deutetrabenazine) extended-release tablets provides patients with the flexibility to reach effective symptom control while maintaining tolerability.

clinical trials was >36 mg/day, and 52% of patients were taking 36 mg/day, 42 mg/day, or 48 mg/day at Week 145 in the long-term study.[5,9] Additionally, in pharmacokinetic studies, increased plasma levels of AUSTEDO correlated with higher potential for treatment success, but not AEs.[13,14]

AUSTEDO XR should be swallowed whole. Tablets should not be chewed, crushed, or broken. AUSTEDO XR may be taken with or without food **(Figure 3.4)**.[4] If a patient misses a dose for less than 1 week, they can restart at the same dose of AUSTEDO XR or AUSTEDO.[4]

Dosage Recommendations and Metabolic Considerations for VMAT2 Inhibitors

Patients with TD often take medications for both nonpsychiatric comorbidities and mental health

IMPORTANT SAFETY INFORMATION (CONTINUED)

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 additional Important Safety Information throughout and click here for full Prescribing Information, including Boxed Warning.

Figure 3.4. AUSTEDO XR Dosing Options Allow to Titrate Weekly Until Effective and Tolerable Symptom Control Is Reached[4]

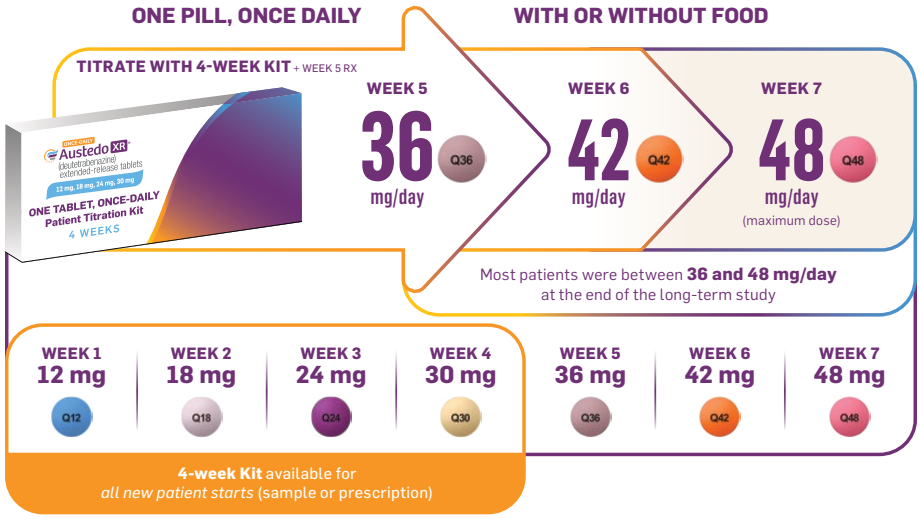


Image shown is not the actual 4-week Titration Kit. Tablets not shown to actual size.

Figure 3.5. Consider Metabolic Pathways When Choosing a VMAT2 Inhibitor for TD[4,15,16]

	AUSTEDO XR	Ingrezza® (valbenazine)
Strong CYP3A4/5 inducer	No dose restriction	Concomitant use is not recommended
Strong CYP3A4/5 inhibitor	No dose restriction	40 mg/day (lowest available dose)
Strong CYP2D6 inducer (or if a patient is a poor CYP2D6 metabolizer)	Up to 36 mg/day	40 mg/day (lowest available dose)
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.

stabilization. Therefore, it is critical for clinicians to be aware of these regimens and consider metabolic pathways to reduce the risk of drug-drug interactions (DDIs) when choosing a VMAT2 inhibitor for TD. AUSTEDO XR is primarily metabolized by CYP2D6, with minor contributions from CYP3A4/5 and other enzymes to form several minor metabolites.[4] The metabolic profile of AUSTEDO XR allows for few restrictions related to DDIs.[4] In patients taking concomitant strong CYP2D6 inhibitors or who are poor CYP2D6 metabolizers, there are 5 available dosing options with a maximum dosage of 36 mg/day.[4] Only AUSTEDO XR allows for the ability to increase once-daily dose in patients taking strong CYP inhibitors and inducers.[4,15]

ONLY AUSTEDO XR allows for the ability to increase once-daily dose in patients taking strong CYP inhibitors and inducers.

Moreover, no dose adjustments to P-glycoprotein (P-gp) substrates (eg, calcium channel blockers, statins, antimicrobials, and digoxin) are required when taking AUSTEDO XR **(Figure 3.5)**.[4,16] It is important to highlight that there are no specified restrictions on the use of AUSTEDO XR® (deutetrabenazine) tablets in patients taking concomitant anticholinergic medications.[4]

Patient-Reported Experiences With AUSTEDO XR: Insights From Real-World Surveys

Alongside clinical data, real-world evidence derived from patients' self-reported experiences can provide valuable insights to support discussions about treatment options

IMPORTANT SAFETY INFORMATION (CONTINUED)

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. 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 for full Prescribing Information, including Boxed Warning.

with patients. A prospective, cross-sectional survey involving 209 patients with TD, which assessed patients' experiences, found that more than 90% of patients reported movement reduction with AUSTEDO XR, resulting in improvements in daily living.[17] Patients also noted improved emotional, social, and physical well-being **(Figure 3.6)**.[17]

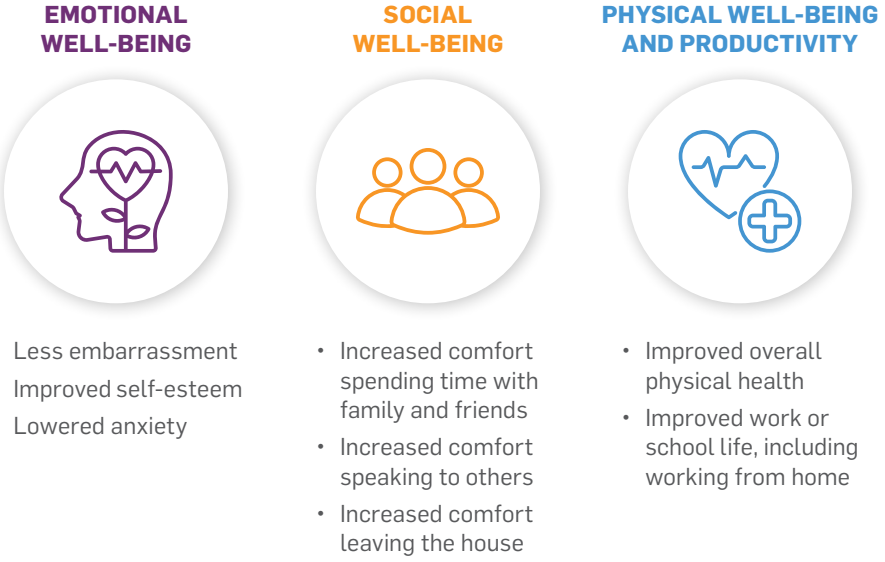
97% of patients planned to continue taking AUSTEDO XR. In addition, 60% reported taking it in the morning, and 42% reported usually taking it without food.[17]

As a result of movement reduction with AUSTEDO XR, >90% of patients reported improvement in well-being and daily living activities.

Summary

- TD and DIP have distinct underlying pathophysiology and specific clinical presentation that require different treatment approaches[1,2]
- AUSTEDO XR is a VMAT2 inhibitor approved in the US for the treatment of adults with TD[4]
- Established efficacy and safety profile with AUSTEDO
  - In placebo-controlled clinical trials, patients who received AUSTEDO BID demonstrated a rapid response as early as Week 2 and achieved a significant and meaningful reduction in TD severity at Week 12[4-6]
  - AUSTEDO demonstrated a significant improvement in AIMS reduction with a proven safety and tolerability profile across a diverse population over 3 years[9-12]
  - Adverse reactions with AUSTEDO XR are expected to be similar to AUSTEDO[4]
- The flexible, once-daily AUSTEDO XR options enable patients to titrate as needed to achieve effective dosing and tolerable symptom control[4]
- Only AUSTEDO XR allows for the ability to increase once-daily dose in patients taking strong CYP inhibitors and inducers[4,15]
- Results from real-world surveys of patients with TD found improvements in daily living across several areas of their lives as a result of movement reduction with AUSTEDO XR.[17] ■

Figure 3.6. As a Result of Movement Reduction With AUSTEDO XR, Patients Reported Improvements in Well-Being and Daily Living Activities[17]



IMPORTANT SAFETY INFORMATION (CONTINUED)

Depression and Suicidality in Patients with Huntington's Disease: AUSTEDO XR and AUSTEDO® (deutetrabenazine) tablets 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 for full Prescribing Information, including Boxed Warning.

Expert Commentary With Henry Nasrallah, MD, and Daniel Dees, MD

Henry Nasrallah, MD
Professor of Psychiatry,
Neurology and Neuroscience
Cincinnati, Ohio

Daniel Dees, MD
Movement Disorder Specialist
Mobile, Alabama

This newsletter is produced by Teva Pharmaceuticals. Drs Henry Nasrallah and Daniel Dees were compensated by Teva for their insights.

Antipsychotics are an essential treatment option for patients with psychotic and/or mood disorders, but it is equally important to recognize that these medications and other dopamine receptor blocking agents (DRBAs) can cause drug-induced movement disorders (DIMDs), including acute dystonia, acute akathisia, drug-induced parkinsonism (DIP), and tardive dyskinesia (TD). In this conversation, Drs Nasrallah and Dees discuss the nuances of recognizing and treating DIMDs and their experience with TD diagnosis, assessment, and treatment.

Q: How do you differentiate TD from other DIMDs?

Dr Dees: Put simply, TD is a hyperkinetic movement disorder—too much movement; DIP is a hypokinetic movement disorder—too little movement. However, it is also critical to understand the phenomenology associated with different movement disorders. Let's consider TD and DIP, the most common DIMDs, as an example.

TD can be associated with chorea, athetosis and, in some cases, dystonia. So, let's define those phenomenologies. Chorea is randomly flowing movements from one body part to another. Athetosis is slow, writhing movements also flowing from one body part to another. Dystonia is defined as sustained involuntary muscle contractions. TD most often affects the orofacial region, but in greater than half of all patients affects all extremities and even the trunk as well. Common symptoms include lip puckering, facial grimacing, tongue protrusions, excessive blinking, and "piano playing" in the fingers or toes. TD movements are irregular, nonpredictable, and constantly flowing.

DIP, on the other hand, is characterized by an overall paucity of movement and associated with bradykinesia and rigidity. Bradykinesia is a primary symptom of DIP and is defined as small, slow movements. The patient will feel as if they are trying to make big movements but are unable to do so, resulting in difficulty with common activities such as standing from a chair with no armrests. Rigidity is muscle stiffness resulting in resistance to movement. Additionally, 75% of patients with DIP will have tremor at rest, although 25% of patients with DIP will have no tremor. Tremor typically occurs in the jaw, hands, and feet. These

IMPORTANT SAFETY INFORMATION (CONTINUED)

Contraindications: AUSTEDO XR and AUSTEDO 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 for full Prescribing Information, including Boxed Warning.

3 phenomenologies are indicative of DIP; however, more advanced DIP may have postural instability and falls. Common additional symptoms include "masked face" with reduced blinking, shuffling gait, and lack of arm swing.

We can determine whether our patient's symptoms are due to TD, DIP, or both by defining these phenomenologies.

Dr Nasrallah: TD and DIP can also be differentiated based on the onset of symptoms. DIP has acute onset, often starting days to weeks after initiating treatment with or increasing the dose of an antipsychotic. TD, on the other hand, is a late-onset movement disorder, occurring after long-term exposure to an antipsychotic. That's why we refer to it as "tardive."

Q: Why is it important to distinguish TD from other DIMDs—particularly DIP?

Dr Dees: Learning to make the distinction between TD and DIP is essential because they require different treatments. DIP can be treated with anticholinergics, but these medications don't help with the flowing movements associated with TD and can actually make movement worse, especially in older patients. A correct diagnosis determines the appropriate course of treatment.

DIP can be treated with anticholinergics, but these medications don't help with TD and can actually make movements worse.

Dr Nasrallah: I agree. These movements have different underlying causes. Acute DIP results from hypodopaminergic state in the brain while TD results from hyperdopaminergic state. Anticholinergics increase dopamine activity and thus help reduce the severity of DIP, but will worsen TD movements. The American Psychiatric Association (APA) recommends vesicular monoamine transporter 2 (VMAT2) inhibitors, which are the only US Food and Drug Administration (FDA)-approved treatment for TD that has an impact on the patient.

Q: Less than 6% of patients with TD are treated with VMAT2 inhibitors, and ~40% of psychiatry healthcare professionals prescribe benztropine, a common anticholinergic, to treat TD. What explains the persistent use of anticholinergics for TD despite warnings that it worsens symptoms?

Dr Nasrallah: The challenge we encounter in psychiatry is the continued use of terms like extrapyramidal symptoms (EPS) to describe any DIMD experienced by a patient taking antipsychotics. This umbrella term doesn't adequately differentiate between the movement disorders, like TD and DIP, that require different treatments.

In the 1950s, antipsychotic medications were discovered as a treatment option for various psychiatric conditions. However, some patients receiving these medications developed abnormal movements that were reminiscent of parkinsonism. At the time, anticholinergic medications were commonly used to treat parkinsonism, and clinicians began using them to alleviate the drug-induced movements experienced by patients on antipsychotics. It became common practice to prescribe anticholinergics alongside antipsychotics to address these side effects.

When TD was recognized as a distinct movement disorder associated with long-term antipsychotic use, it was initially grouped together with DIP under the broader classification of EPS. As a result, both conditions were treated with anticholinergics despite the differences in their underlying mechanisms.

For many years, no effective treatment existed for TD, leading to

the continued use of the term EPS and the reliance on anticholinergics. This practice has become entrenched in clinical settings despite the approval of VMAT2 inhibitors for the treatment of TD in 2017, and it remains a significant barrier to overcome.

Q: How would you discuss discontinuing an anticholinergic with a patient?

Dr Dees: This can be a challenging conversation to have with patients, but it is extremely important. I've encountered patients who do not want to discontinue their anticholinergic medication, especially if they have been taking it for a long period of time. This scenario is where I think that patient education is absolutely critical. I want the patient to understand why we are discontinuing the anticholinergic—namely, that it may be making their symptoms worse. I want to engage in a conversation to develop a treatment plan that addresses all of their concerns, including their TD. For my patients with TD, I will explain that anticholinergics are not an appropriate treatment, but VMAT2 inhibitors have been approved by the FDA for the treatment of TD.

I want the patient to understand why we are discontinuing the anticholinergic—namely, that it may be making their TD symptoms worse.

Q: How do clinical practice guidelines inform the way you manage patients on antipsychotics and at risk of developing TD?

Dr Nasrallah: The APA guidelines, which contribute to the standard of care, state that patients taking antipsychotics should be assessed for movements during a clinical evaluation at every visit. Further, a structured assessment should be conducted annually or every 6 months in high-risk patients, such as elderly patients, postmenopausal females, patients with a mood disorder, and those with a previous movement disorder.

The Abnormal Involuntary Movement Scale (AIMS) is the standard scale for systematically assessing and quantifying the severity of TD movements. It assesses 7 items—4 regions of the face, where TD most often occurs, upper extremities, lower extremities, and trunk.

By adhering to clinical practice guidelines and the standard of care, we can ensure that TD is identified and treated appropriately. It is worth noting that patients may score a 0 on the AIMS for years while taking an antipsychotic before developing movements. We want to identify and document when a patient's score jumps plus 1 or plus 2. If movements are detected, we should then ask about impact.

AIMS is the standard scale for systematically assessing and quantifying the severity of TD movements.

At every clinical encounter, I ask my patients taking antipsychotics if they have noticed movements that they don't like in their face or body. If they mention or have movements, I ask about impact. Does it bother or embarrass them? And then, importantly, I will ask about treatment. Are they willing to take medication to address it? The APA guidelines recommend treatment for TD that has an impact on the patient, regardless of the severity of movements.

Q: Why is it important to recognize TD and its impact on patients and address the abnormal movements?

Dr Nasrallah: TD can have a profound impact on patients physically, socially, and

IMPORTANT SAFETY INFORMATION (CONTINUED)

QTc Prolongation: AUSTEDO XR and AUSTEDO may prolong the QT interval, but the degree of QT prolongation is not clinically significant when AUSTEDO XR or AUSTEDO is administered within the recommended dosage range. AUSTEDO XR and AUSTEDO should be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias.

Please see additional Important Safety Information throughout and click here for full Prescribing Information, including Boxed Warning.

psychologically. Patients may not be able to properly use their hands, chew their food, or button their shirts. They may isolate themselves from others, and TD can also make it more difficult to manage the patient's underlying mental health condition. The biopsychosocial impact of TD can be distressing for patients.

Dr Dees: I'd add that nobody wants to be the person that the other people on the bus don't want to sit next to. It's an instinct probably ingrained into us since childhood. TD can make you feel socially ostracized. And for many patients, these movements have an added impact to an already distressing mental health condition. So, the impetus to treat is impact. Does this bother you enough to start taking a pill every day to make it better?

Dr Nasrallah: In my clinical experience, I have found that it is important to initiate treatment for TD, regardless of severity of movements, as soon as possible once a diagnosis has been made if it has an impact on the patient. In fact, the FDA trials for both VMAT2 inhibitors in the market included patients with mild, moderate, or severe TD.

Even mild movements can have a substantial impact, depending on the individual patient's circumstances. My brief advice to my colleagues would be to be vigilant for DIMDs in patients taking antipsychotics, diagnose TD early and understand the impact of movements on your patient's life, and consider clinical practice guidelines, which recommend treatment with a VMAT2 inhibitor for TD that impacts the patient.

In my clinical experience, I have found that it is important to initiate treatment for TD, regardless of severity of movements, as soon as possible once a diagnosis has been made if it has an impact on the patient.

Q: What are the features of AUSTEDO XR that are most important to you or to your patients?

Dr Nasrallah: First, AUSTEDO has a demonstrated efficacy and safety profile, which was established in 2 randomized, placebo-controlled clinical trials. The most common adverse reactions reported in patients with TD treated with AUSTEDO (>3% and greater than placebo) were nasopharyngitis and insomnia. Second, increasing improvement in AIMS total score was observed through 3 years in an open-label extension (OLE) study, with 71% of patients at Week 145 seeing improvement relative to Week 15.

A very important factor for my patients is a reduction in movements and the resulting improvement in their social and emotional well-being. Teva conducted a survey to assess satisfaction among patients taking AUSTEDO XR. Patients reported greater self-esteem and feeling more comfortable with social activities, including spending time with family or working. When discussing treatments, my goal is to help patients understand how reduction of their movements could subsequently help to reduce the impact of TD on their lives.

AUSTEDO has a demonstrated efficacy and safety profile, which was established in 2 randomized, placebo-controlled clinical trials.

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® (deutetrabenazine) extended-release tablets and AUSTEDO® (deutetrabenazine) tablets; intensive symptomatic treatment and medical monitoring; and treatment of any concomitant serious medical problems.

Please see additional Important Safety Information throughout and click here for full Prescribing Information, including Boxed Warning.

Dr Dees: When starting AUSTEDO XR® (deutetrabenazine) extended-release tablets, all patients with TD begin with a 12-mg dose, which may be increased at weekly intervals by 6 mg/day until the desired symptom control is tolerably achieved. It is important that we find that reasonable dose to achieve therapeutic effect. That is why we increase the dose until we are able to see symptom control. AUSTEDO XR is available in doses from 12 mg to 48 mg, which allows providers to individualize the treatment to the patient's needs.

Q: How has management of TD changed over time, and what do you see as the most important challenge for clinicians today?

Dr Nasrallah: I would like to reiterate that using outdated terms like EPS that do not differentiate between movement disorders doesn't just delay diagnosis, but it can really impact the patient. We know that TD can lead to biopsychosocial repercussions for our patients, so it's really important to understand that TD is distinct from other DIMDs and to identify TD early and treat it with a VMAT2 inhibitor.

Dr Dees: I agree. There used to be nothing we, as providers, could do to effectively treat TD. Now, we are equipped with VMAT2 inhibitors, such as once-daily AUSTEDO XR, that can help control the symptoms of TD, and I find that really inspiring. What we need to remain focused on is accurately identifying TD from other DIMDs, like DIP, to ensure that appropriate treatment can be prescribed, and the patient can see the benefit. ■

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.

Parkinsonism: AUSTEDO XR and AUSTEDO® (deutetrabenazine) tablets 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.

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

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 for full Prescribing Information, including Boxed Warning.

Select References

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed, Text Revision. Washington, DC: American Psychiatric Association; 2022.

American Psychiatric Association. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. 3rd ed. American Psychiatric Association; 2021. Accessed November 12, 2025. https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841

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.

AUSTEDO XR® (deutetrabenazine) extended-release tablets/ AUSTEDO® current Prescribing Information. Parsippany, NJ: Teva Neuroscience, Inc.

Bhidayasiri R, Jitkritsadakul O, Friedman JH, Fahn S. Updating the recommendations for treatment of tardive syndromes: a systematic review of new evidence and practical treatment algorithm. *J Neurol Sci*. 2018;389:67-75.

Caroff SN. Overcoming barriers to effective management of tardive dyskinesia. *Neuropsychiatr Dis Treat*. 2019;15:785-794.

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.

Caroff SN, Yeomans K, Lenderking WR, et al. RE-KINECT: a prospective study of the presence and healthcare burden of tardive dyskinesia in clinical practice settings. *J Clin Psychopharmacol*. 2020;40(3):259-268.

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.

Data on file. Teva Neuroscience, Inc. Parsippany, NJ.

Duma SR, Fung VSC. Drug-induced movement disorders. *Aust Prescr*. 2019;42(2):56-61.

Fahn S, Jankovic J, Hallet M, eds. *Principles and Practice of Movement Disorders*. 2nd ed. Elsevier, Inc; 2011.

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.

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: Psych Congress Elevate; May 30-June 2, 2024; Las Vegas, NV.

Guy W. *ECDEU Assessment Manual for Psychopharmacology*: Revised. Rockville, MD: US Department of Health, Education and Welfare, Public Health Service, Alcohol, Drug Abuse and Mental Health Administration, NIMH Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976:534-537. DHEW publication number ADM 76-338.

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.

Ingrezza® (valbenazine) capsules. Prescribing Information. San Diego, CA: Neurocrine Biosciences, Inc.

Jain R, Konings M, Thompson S, et al. Real-world evidence of patient experience with once-daily deutetrabenazine extended-release tablets for tardive dyskinesia and chorea in Huntington disease in the United States. Poster presented at: The Annual Psych Congress; October 29-November 2, 2024; Boston, MA.

Miller JJ. Everyone please stop (EPS). *Psychiatric Times*. 2022;39(8). Accessed November 12, 2025. https://www.psychiatrictimes.com/view/everyone-please-stop-eps-

Mushlin S, Green H. *Decision Making in Medicine: An Algorithmic Approach*. 3rd ed. Elsevier, Inc; 2010.

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.

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.

Vasan S, Padhy RK. Tardive Dyskinesia. In: StatPearls [Internet]. StatPearls Publishing; 2025. Accessed November 12, 2025. https://www.ncbi.nlm.nih.gov/books/NBK448207/

IMPORTANT SAFETY INFORMATION (CONTINUED)

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.

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. 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 for full Prescribing Information, including Boxed Warning.

References

DIFFERENTIAL DIAGNOSIS: Differentiating Tardive Dyskinesia From Other Drug-Induced Movement Disorders: Key Distinctions and Guideline-Recommended Treatments

1. 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*. 2020;27(2):208-217. **2.** Duma SR, Fung VS. Drug-induced movement disorders. *Aust Prescr*. 2019;42(2):56-61. **3.** Miller JJ. Everyone please stop (EPS). *Psychiatric Times*. 2022;39(8). Accessed November 15, 2025. https://www.psychiatrictimes.com/view/everyone-please-stop-eps- **4.** 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. **5.** 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. **6.** ICD-10 Data. 2025 ICD-10-CM Diagnosis Code G24.01. Accessed November 12, 2025. https://www.icd10data.com/ICD10CM/Codes/G00-G99/G20-G26/G24-/G24.01 **7.** ICD-10 Data. 2025 ICD-10-CM Diagnosis Code G21.1. Accessed November 12, 2025. https://www.icd10data.com/ICD10CM/Codes/G00-G99/G20-G26/G21-/G21.1 **8.** ICD-10 Data. 2025 ICD-10-CM Diagnosis Code G24.02. Accessed November 12, 2025. https://www.icd10data.com/ICD10CM/Codes/G00-G99/G20-G26/G24-/G24.02 **9.** ICD-10 Data. 2025 ICD-10-CM Diagnosis Code G25.71. Accessed November 12, 2025. https://www.icd10data.com/ICD10CM/Codes/G00-G99/G20-G26/G25-/G25.71 **10.** Benztropine mesylate tablet. Prescribing Information. Warren, NJ: Cipla USA, Inc. **11.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed, Text Revision. Washington, DC: American Psychiatric Association; 2022. **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.** Psychiatry & Behavioral Health Learning Network. July 20, 2020. Q&A: updates from Dr Rakesh Jain on managing tardive dyskinesia. Accessed October 31, 2025. hmpgloballearningnetwork.com/site/pcn/article/qa-updates-dr-rakesh-jain-managing-tardive-dyskinesia **14.** 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. **15.** Caroff SN. Overcoming barriers to effective management of tardive dyskinesia. *Neuropsychiatr Dis Treat*. 2019;15:785-794. **16.** Guy W. *ECDEU Assessment Manual for Psychopharmacology: Revised*. Rockville, MD: US Department of Health, Education and Welfare, Public Health Service, Alcohol, Drug Abuse and Mental Health Administration, NIMH Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976:534-537. DHEW publication number ADM 76-338. **17.** American Psychiatric Association. *The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*. 3rd ed. Washington, DC: American Psychiatric Association; 2021.

NEUROBIOLOGY SIDEBAR: Considerations Regarding the Mechanism of Action of Vesicular Monoamine Transporter 2 Inhibitors and Anticholinergics in Tardive Dyskinesia and Drug-Induced Parkinsonism

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.** Conn H, Jankovic J. Drug-induced parkinsonism: diagnosis and treatment. *Expert Opin Drug Saf*. 2024;23(12):1503-1513. **4.** American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed, Text Revision. Washington, DC: American Psychiatric Association; 2022. **5.** 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. **6.** Benztropine mesylate tablet. Prescribing Information. Warren, NJ: Cipla USA Inc. **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.

TREATMENT: Understanding AUSTEDO XR®: A Once-Daily Treatment Option for Adult Patients With Tardive Dyskinesia

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.** 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 November 4, 2025. https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841 **4.** AUSTEDO XR® (deutetrabenazine) extended-release tablets/AUSTEDO® current Prescribing Information. Parsippany, NJ: Teva Neuroscience, Inc. **5.** 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. **6.** 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. **7.** Data on file. Teva Neuroscience, Inc. Parsippany, NJ. **8.** Benztropine mesylate tablet. Prescribing Information. Warren, NJ: Cipla USA, Inc. **9.** 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. **10.** Nasrallah H, Chen M, Barkay H, Gordon MF, Finkbeiner S. Long-term efficacy and safety of deutetrabenazine in postmenopausal women with tardive dyskinesia. Presented at: 35th Annual Psych Congress 2022; September 17-20, 2022; New Orleans, LA. **11.** Sajatovic M, Gandhi P, Konings M, Barash S, Finkbeiner S. Long-term safety and efficacy of deutetrabenazine in patients aged ≥65 years with tardive dyskinesia. Presented at: American Association for Geriatric Psychiatry; March 14-17, 2025; Phoenix, AZ. **12.** Hauser RA, Barkay H, Fernandez HH, et al. Deutetrabenazine provides long-term benefit for tardive dyskinesia regardless of underlying condition and dopamine receptor antagonist use: a post hoc analysis of the 3-year, open-label extension study. *J Clin Psychopharmacol*. 2024;44(4):386-396. **13.** Levi M, Schneider F, Gosselin NH, et al. Population pharmacokinetic and exposure safety analyses of deutetrabenazine in patients with moderate to severe tardive dyskinesia. Presented at: American Conference on Pharmacometrics; October 20-23, 2019; Orlando, FL. **14.** Singh R, Sunzel EM, Dongwoo K, et al. Assessment of the deutetrabenazine exposure-response relationships for patients with moderate-to-severe tardive dyskinesia. Presented at: Psych Congress; September 17-20, 2022; New Orleans, LA. **15.** Ingrezza® (valbenazine) capsules. Prescribing Information. San Diego, CA: Neurocrine Biosciences, Inc. **16.** DrugBank Online. P-glycoprotein substrates. Accessed November 4, 2025. https://go.drugbank.com/categories/DBCAT002668 **17.** Jain R, Konings M, Thompson S, et al. Real-world evidence of patient experience with once-daily deutetrabenazine extended-release tablets for the treatment of tardive dyskinesia in the United States. Presented at: Annual Psych Congress Elevate; May 28-31, 2025; Las Vegas, NV.

connecTD™

More Questions About TD? Find Answers at ConnecTD

The TD journey can be complex for patients—and for the healthcare professionals who help them. ConnecTD is filled with interactive learning experiences about the assessment of abnormal movements, their impact, and the appropriate treatment of TD.

On ConnecTD, you'll find the following comprehensive modules:

- Screening for and Assessing TD
- Differentiating Drug-Induced Parkinsonism (DIP) and TD
- The Impact of TD
- Patient Journeys With TD

Visit ConnecTD to deepen your understanding of TD.

Click Here To Explore ConnecTD