

PHARMACY COVERAGE GUIDELINE

AUSTEDO® (deutetrabenazine) oral
AUSTEDO XR® (deutetrabenazine extended-release) oral
INGREZZA® (valbenazine) oral
INGREZZA SPRINKLE® (valbenazine) oral
Tetrabenazine oral
XENAZINE® (tetrabenazine) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for AUSTEDO (deutetrabenazine), AUSTEDO XR (deutetrabenazine extended-release), INGREZZA (valbenazine), INGREZZA SPRINKLE (valbenazine), XENAZINE (tetrabenazine), and Tetrabenazine generic

Criteria for Initial Therapy:

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Prescriber Qualifications

- Prescribed by a Psychiatrist or Neurologist or is in consultation with a Psychiatrist or Neurologist

Indication

- **ONE** of the following:
 - Chorea associated with Huntington's disease
 - Tardive dyskinesia

Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- **For Huntington's Disease:** Family history of the disease (if known), typical clinical features characterized by chorea, psychiatric illness, dementia, and genetic testing for pathogenic disease causing trinucleotide (cytosine adenine guanine (CAG)) repeat expansion in the huntingtin (*HTT*) gene
- **For Tardive Dyskinesia:** Presence of typical dyskinetic or dystonic involuntary movements, a history of at least one month of ongoing or previous dopamine receptor blocking agent exposure, and the exclusion of other causes of abnormal movements

Alternative Therapies

- **For Huntington's disease chorea BOTH** of the following:
 - Failure (trial of at least three months duration), contraindication, intolerance, or is not a candidate for **tetrabenazine** (generic)
 - Failure (trial of at least three months duration), contraindication, intolerance, or is not a candidate for **ONE** of the following:
 1. aripiprazole
 2. olanzapine
 3. risperidone
- **For tardive dyskinesia ALL** of the following:
 - Discontinue offending drug if clinically appropriate
 - Switch from first to second generation antipsychotic drug if clinically appropriate
 - Failure (trial of at least three months duration), contraindication, intolerance, or is not a candidate for **ONE** of the following:
 1. clonazepam
 2. amantadine
 - Failure (trial of at least three months duration), contraindication, intolerance, or is not a candidate for **tetrabenazine** (generic)
 - For localized forms of severe tardive dystonia (e.g., cervical dystonia, blepharospasm): Failure (trial of at least three months duration), contraindication, intolerance, or is not a candidate for botulinum toxin injections

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Brand Specific Criteria

- **For brand Xenazine (tetrabenazine):** Failure (trial of at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for **generic tetrabenazine** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
- **For brands Austedo, Austedo XR, Ingrezza, or Ingrezza Sprinkle if available:** Failure (trial of at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))

Safety

- There is **NONE** of the following:
 - Suicidal or untreated/inadequately treated depression
 - Hepatic impairment (**Does not apply for Ingrezza and Ingrezza Sprinkle**)
 - Congenital long QT syndrome or history of cardiac arrhythmias associated with QT prolongation
 - Concomitant use with:
 1. Reserpine or within 20 days of stopping reserpine
 2. Monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping MAOI
 3. Other vesicle monoamine transporter type 2 (VMAT 2) inhibitors
 4. Drugs that prolong QTc interval such as:
 - a. Antipsychotic medications (chlorpromazine haloperidol thioridazine ziprasidone)
 - b. Antibiotics (moxifloxacin)
 - c. Class 1A antiarrhythmic medications (quinidine procainamide)
 - d. Class III antiarrhythmic medications (amiodarone sotalol)
 - e. **Additionally for Ingrezza and Ingrezza Sprinkle:** Strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort)

Documentation Requirements

- A completed request form must be submitted including:
 - Chart notes
 - Lab results
 - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

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Prescriber Qualification

- Continues to be seen by a Psychiatrist or Neurologist or in consultation with a Psychiatrist or Neurologist

Clinical Response

- **For Huntington's disease:** Reduction in chorea
- **For tardive dyskinesia:** Improvement in symptoms compared to baseline such as:
 - Protruding and twisting movements of the tongue
 - Pouting, puckering, or smacking movements of the lips
 - Retraction of the corners of the mouth
 - Bulging of the cheeks
 - Chewing movements
 - Blepharospasm
 - Twisting, spreading, and piano playing finger movements
 - Tapping foot movements
 - Dystonic extensor postures of the toes

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- **For brand Xenazine (tetrabenazine):** Failure (trial of at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for **generic tetrabenazine** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
- **For brands Austedo, Austedo XR, Ingrezza, or Ingrezza Sprinkle if available:** Failure (trial of at least three months duration), contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))

Safety

- There is **NONE** of the following:
 - Suicidal or untreated/inadequately treated depression
 - Hepatic impairment (**Does not apply for Ingrezza and Ingrezza Sprinkle**)
 - Congenital long QT syndrome or history of cardiac arrhythmias associated with QT prolongation
 - Concomitant use with:
 1. Reserpine or within 20 days of stopping reserpine
 2. Monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping MAOI
 3. Other vesicle monoamine transporter type 2 (VMAT 2) inhibitors
 4. Drugs that prolong QTc interval such as:
 - a. Antipsychotic medications (chlorpromazine haloperidol thioridazine ziprasidone)
 - b. Antibiotics (moxifloxacin)

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- c. Class 1A antiarrhythmic medications (quinidine procainamide)
 - d. Class III antiarrhythmic medications (amiodarone sotalol)
 - e. **Additionally for Ingrezza and Ingrezza Sprinkle:** Strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort)
- Significant adverse effects such as:
1. QT prolongation
 2. Neuroleptic malignant syndrome
 3. Akathisia, agitation, restlessness, parkinsonism not resolved with dose adjustment
 4. Emerging or worsening depression, suicidality, or behavioral changes
 5. Symptomatic hyperprolactinemia (**Does not apply for Ingrezza and Ingrezza Sprinkle**)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year
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Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
 2. Off-Label Use of Cancer Medications
-

Description:

Austedo (deutetrabenazine), Austedo XR (deutetrabenazine extended release), tetrabenazine (brand Xenazine and generic), Ingrezza (valbenazine), and Ingrezza Sprinkle (valbenazine) are indicated for the treatment of chorea associated with Huntington's disease (HD). The mechanism of the anti-chorea action is unknown, but it is believed to be related to depletion of monoamines from nerve terminals. Austedo (deutetrabenazine), Austedo XR (deutetrabenazine extended release), Ingrezza (valbenazine), and Ingrezza Sprinkle (valbenazine) are indicated for the treatment of adults with tardive dyskinesia (TD). The mechanism of action of deutetrabenazine and valbenazine in the treatment of TD is unknown but is thought to be due to regulation of monoamine uptake from the cytoplasm into the synaptic vesicle for storage and release.

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Deutetrabenazine, tetrabenazine, and valbenazine are reversible inhibitors of the vesicle monoamine transporter type 2 (VMAT-2). They inhibit uptake of the neurotransmitter's serotonin, norepinephrine, histamine, and, especially, dopamine into the granular vesicles of presynaptic neurons and ultimately lead to depletion of monoamine stores. Dopamine is a chemical that communicates between certain nerve cells in the brain. In patients with HD, this system is overactive and results in abnormal movements of chorea. The pathophysiology of TD remains poorly understood, but it is believed to be the result of chronic blockade of dopamine receptors, particularly D2 and possibly D3, by dopamine receptor blocking agents (DRBA). In addition to dopamine, other neurotransmitter receptors may be important, especially 5-hydroxytryptamine 2 (5-HT₂) receptors that modulate motor activity. One of the most prominent theories about TD pathogenesis is that chronic exposure to the neuroleptics results in D2 receptor upregulation with postsynaptic dopamine receptor super-sensitivity.

HD is a rare, inherited neurological disorder affecting about 1 in 10,000 people in the United States. The disease results from degeneration and deterioration of brain cells. The deterioration causes uncontrolled movements (chorea), cognitive decline, and psychiatric/behavioral changes. Cognitive symptoms include confusion on time and place, loss of judgment, memory loss, and personality changes. Movement problems include restless leg, fidgeting, facial movements, head turning to shift eye position, jerking of arms, legs, face and other body parts, speech problems, slow uncontrolled movements, swallowing problems, and unsteady gait. As chorea worsens the individual is at risk for falls. Due to swallowing difficulties, HD individuals also have difficulty in maintaining nutrition leading to further declines in functional capacity.

Chorea is an abnormal involuntary movement caused by overactivity of the neurotransmitter dopamine in the areas of the brain that control movement. It is characterized by brief, irregular contractions that are not repetitive or rhythmic, but appear to flow from one muscle to the next. The full spectrum of motor impairment in HD includes eye movement abnormalities, Parkinsonian features and dystonia, myoclonus, tics, ataxia, dysarthria, dysphagia, spasticity with hyperreflexia and extensor plantar responses.

The underlying pathology and neurochemical bases of HD are complex and not fully understood. It is thought that dopamine and glutamate transmission and their interaction with receptors at various sites in the brain are affected.

A recent guideline on the treatment of HD published in 2012 from the American Academy of Neurology (AAN) stated that amantadine, tetrabenazine, or riluzole (although its effect is dose dependent) may be used for chorea. Nabilone may have a weak or a slight effect on chorea, but long-term information is lacking. Data on use of clozapine, other neuroleptics, or donepezil were not sufficient to make a recommendation for or against their use in the management of chorea. Evidence from four small, randomized, double-blind, placebo-controlled trials is conflicting for amantadine. However, based upon results from two of these trials, guidelines from the American Academy of Neurology conclude that amantadine is likely effective in decreasing HD chorea, though the degree of benefit is unknown.

Tardive dyskinesia (TD) is one of the most well-known types of tardive syndromes (TDS). TD is estimated to affect 500,000 people in the United States. TDS are movement disorders that affect voluntary muscles. In TDS, abnormal body movements occur, and these movements cannot be controlled voluntarily. Classic TD usually

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involves random rhythmic involuntary movements of the face; affecting the tongue, lips, or jaw where abnormal movement of the jaw is seen as a chewing motion and facial grimacing. Other affected body parts include the hands, arms, legs, fingers, toes, or hips. TDS includes other types of abnormal movements besides TD and includes tardive akathisia, tardive dystonia, tardive myoclonus, tardive tremor, and tardive tics (also known as tardive tourettism).

TD results from chronic (three or more months) exposure to DRBA, some neuroleptics or antipsychotics (typical and atypical agents), tricyclic antidepressants (amoxapine), and antiemetics or other medications used for gastrointestinal disorders (promethazine and metoclopramide). Not all individuals who are using DRBA go on to develop TD. Factors that may contribute to the development of TD include duration of treatment, type of DRBA used, age, alcohol use or use of other substances of abuse, HIV/AIDS, and female gender. The diagnosis of TD is based on the patient's history of exposure to DRBA, characteristic clinical presentation, and exclusion or other conditions such as Huntington's disease.

In 2013 the American Academy of Neurology evidence-based guideline on the treatment of TDS stated that clonazepam or ginkgo biloba probably improves TDS, and both should be considered as treatment. The guideline also stated that amantadine and tetrabenazine might be considered as treatment for TDS.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
[MedWatch Forms for FDA Safety Reporting | FDA](#)

Resources:

Austedo (deutetrabenazine) tab and Austedo XR (deutetrabenazine) extended-release tab product information, revised by Teva Neuroscience, Inc. 02-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 30, 2025.

Ingrezza (valbenazine) cap and Ingrezza Sprinkle cap product information, revised by Neurocrine Biosciences, Inc. 02-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 30, 2025.

Xenazine (tetrabenazine) tab product information, revised by Lundbeck Pharmaceuticals, LLC. 11-2019. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 30, 2025.

Tetrabenazine tab product information, revised by Ajanta Pharma USA, Inc. 11-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 30, 2025.

Suchowersky O. Huntington disease: Management. In: UpToDate, Hurlig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Literature current through November 2025. Topic last updated October 16, 2025. Accessed January 01, 2026.

Suchowersky O. Huntington disease: Clinical features and diagnosis. In: UpToDate, Hurlig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Literature current through November 2025. Topic last updated January 23, 2025. Accessed January 01, 2026.

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Liang TW. Tardive dyskinesia: Prevention, treatment, and prognosis. In: UpToDate, Hurtig HI, Marder S, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Literature current through November 2025. Topic last updated October 06, 2025. Accessed January 01, 2026.

Deik A. Tardive dyskinesia: Etiology, risk factors, clinical features, and diagnosis. In: UpToDate, Hurtig HI, Marder S, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Literature current through November 2025. Topic last updated November 06, 2025. Accessed January 01, 2026.

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