

Pharmacy Policy Bulletin

Title: VMAT2 Inhibitors

Policy #: Rx.01.88

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **tetrabenazine (Xenazine®)**, **deutetrabenazine (Austedo®)** and **Valbenazine (Ingrezza®)** as provided under the member's prescription drug benefit.

Description:

Huntington's disease (HD) is an inherited, progressive, neurodegenerative disease with no cure or disease modifying therapies currently available. The disease is characterized by choreiform movements, psychiatric problems, and dementia. Therapy focuses on management of symptoms and supportive care. There are approximately 30,000 Americans with symptomatic HD. Symptoms usually appear between the ages of 30 and 50 and progressively worsen.

Chorea is a hyperkinetic movement disorder that may manifest in association with Huntington's Disease. Chorea is characterized by involuntary brief, random, and irregular contractions. Anti-chorea medications such as tetrabenazine, deutetrabenazine and Valbenazine may be useful for controlling chorea in the setting of Huntington's disease, especially milder forms of chorea. Other treatment options include atypical and typical neuroleptics, amantadine, and riluzole.

Tardive dyskinesia is a movement disorder that is characterized by random movement of various facial muscles, including the tongue and jaw. In more severe cases, it may also involve movements of the arms, legs, fingers, toes, trunk or hips. A common risk factor for developing tardive dyskinesia is long-term treatment with antipsychotic medications. It has particularly been associated with first-generation antipsychotic treatment, but there are reports of patients receiving second-generation antipsychotics developing tardive dyskinesia.

Tourette syndrome (TS) is a neurological disorder manifested by motor and phonic tics with onset during childhood. Tics are the clinical hallmark of TS. Tics are sudden, brief, intermittent movements (motor tics) or utterances (phonic tics). Tics have been considered involuntary, but tics can temporarily be voluntarily suppressed.

Mechanism of Action

Tetrabenazine, deutetrabenazine, and Valbenazine reversibly inhibit the human vesicular monoamine transporter type 2 (VMAT2) resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores.

Tetrabenazine (Xenazine®) and **deutetrabenazine (Austedo®)** are indicated for the treatment of chorea associated with Huntington's disease.

Deutetrabenazine (Austedo®) and **Valbenazine (Ingrezza®)** are indicated for the treatment of adults with tardive dyskinesia.

Policy:

Chorea associated with Huntington's disease

INITIAL CRITERIA: Tetrabenazine (Xenazine®) or deutetrabenazine (Austedo®) is approved when ALL of the following are met:

1. Used for the treatment of chorea associated with Huntington's disease; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a neurologist; and
4. For brand Xenazine® only, inadequate response or inability to tolerate generic tetrabenazine

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Tetrabenazine (Xenazine®) or deutetrabenazine (Austedo®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Tardive Dyskinesia

INITIAL CRITERIA: Valbenazine (Ingrezza®) or deutetrabenazine (Austedo®) is approved when ALL of the following are met:

1. Diagnosis of moderate to severe tardive dyskinesia; and
2. Member is 18 years of age or older; and
3. One of the following:
 - a. Persistent symptoms of tardive dyskinesia despite a trial of dose reduction, tapering, or discontinuation of the offending medication; or
 - b. Member is not a candidate for a trial of dose reduction, tapering, or discontinuation of the offending medication; and
4. Prescribed by or in consultation with one of the following:
 - a. Neurologist; or
 - b. Psychiatrist

Initial Authorization duration: 3 months

REAUTHORIZATION CRITERIA: Valbenazine (Ingrezza®) or deutetrabenazine (Austedo®) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Tourette's syndrome

INITIAL CRITERIA: Tetrabenazine (Xenazine®) is approved when ALL of the following are met:

1. Diagnosis of Tourette's Syndrome; and
2. Member has tics associated with Tourette's syndrome; and
3. Inadequate response or inability to tolerate haloperidol or risperidone; and
4. Prescribed by or on consultation with a neurologist or a psychiatrist

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Tetrabenazine (Xenazine®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

**TETRABENAZINE (Xenazine®) and DEUTETRABENAZINE (Austedo®):
DEPRESSION AND SUICIDALITY**

Tetrabenazine and deutetrabenazine can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease. Balance risks of depression and suicidality with the clinical need for control of chorea when considering the use of tetrabenazine and deutetrabenazine. Close observation of patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior should accompany therapy. Inform patients, 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 in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in Huntington disease. Tetrabenazine and deutetrabenazine are contraindicated in patients who are actively suicidal, and in patients with untreated or inadequately treated depression.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Austedo® (deutetrabenazine) [package insert]. North Wales, PA. Teva Pharmaceuticals. February 2023. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=7ea3c60a-45c7-44cc-afc2-d87fa53993c0&type=display>. Accessed April 20, 2023.

Ingrezza® (valbenazine) [package insert]. San Diego, CA: Neurocrine Biosciences. August 2022. Available at: <https://ingrezza.com/HCP/PI>. Accessed April 20, 2023.

Jankovic, J. Tourette Syndrome: Pathogenesis, clinical features, and diagnosis. UpToDate. December 2022. Available at: https://www.uptodate.com/contents/tourette-syndrome-pathogenesis-clinical-features-and-diagnosis?search=tourette%20syndrome&source=search_result&selectedTitle=1~23&usage_type=default&display_rank=1. Assessed April 20, 2023.

Suchowersky O. Overview of chorea. UpToDate. September 2022. Available at: <https://www.uptodate.com/contents/overview-of-chorea?source=machineLearning&search=chorea&selectedTitle=1~102§ionRank=2&anchor=H29672870#H29672870>. Accessed April 20, 2023.

Suchowersky O. Huntington's disease: management. UpToDate. February 2023. Available at: https://www.uptodate.com/contents/huntington-disease-management?source=search_result&search=huntingtons&selectedTitle=2~50. Accessed April 20, 2023.

Xenazine® (tetrabenazine) [package insert]. Deerfield, IL. Lundbeck. November 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ac768bab-8afa-4446-bc7f-caeeffec0cda&type=display>. Accessed April 20, 2023.

Tardive Dyskinesia. National Alliance on Mental Illness Web Site. <https://www.nami.org/About-Mental-Illness/Treatments/Mental-Health-Medications/Tardive-Dyskinesia>. Accessed April 20, 2023.

What is Huntington's Disease? Huntington's Disease Society of America Web Site. <https://hdsa.org/what-is-hd/overview-of-huntingtons-disease/>. Accessed April 20, 2023.

Wimalasena K. Vesicular monoamine transporters: Structure-function, pharmacology, and medicinal chemistry. *Med Res Rev.* 2010;31(4):483-519. doi:10.1002/med.20187

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Xenazine®	Tetrabenazine
Austedo®	Deutetrabenazine
Ingrezza®	Valbenazine

Cross References:

Off-Label Use Rx.01.33

Policy Version Number:	15.00
P&T Approval Date:	March 16, 2023
Policy Effective Date:	July 01, 2023
Next Required Review Date:	March 16, 2024

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.