

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 medication such as tetrabenazine and deutetrabenazine may be useful for controlling chorea in the setting of Huntington's disease, especially milder forms of chorea. Tetrabenazine, deutetrabenazine and valbenazine block transport of dopamine into vesicles in the presynaptic terminal, depleting dopamine in the vesicles and reducing dopamine transmission. Other treatment options include atypical and typical neuroleptics, amantadine, and riluzole.

Tarditive 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 tarditive 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 tarditive dyskinesia.

Mechanism of Action

The VMAT transporter transports and packages catecholamine neurotransmitters for reuse. By inhibiting the VMAT transporter, less neurotransmitter is available for release at the synaptic junction. Dopamine is a catecholamine that promotes movement when released at most motor synapses. By inhibiting VMAT and reducing dopamine, uncontrolled involuntary movements can be attenuated.

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:

A. Chorea associated with Huntington's disease

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

- A. Used for the treatment of chorea associated with Huntington's disease; and
- B. Prescribed by or in consultation with a neurologist
- C. Inadequate response or inability to tolerate generic tetrabenazine (for Xenazine® requests only)

B. Tardive Dyskinesia

INITIAL CRITERIA

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

- A. Diagnosis of moderate to severe tardive dyskinesia; and
- B. One of the following:
 - 1. Persistent symptoms of tardive dyskinesia despite a trial of dose reduction, tapering, or discontinuation of the offending medication; or
 - 2. Member is not a candidate for a trial of dose reduction, tapering, or discontinuation of the offending medication

AND

- C. Prescribed by or in consultation with one of the following:
 - 1. Neurologist; or
 - 2. Psychiatrist

AND

D. Documentation of baseline AIMS

REAUTHORIZATION CRITERIA

Valbenazine (Ingrezza®) or deutetrabenazine (Austedo®) is reapproved with documentation of positive clinical response to therapy, as demonstrated by improvement in AIMS.

Authorization duration: Initial criteria-3 months; Reauthorization criteria-Indefinite.

▶ **Black Box Warning:**

**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. Anyone considering the use of tetrabenazine or deutetrabenazine must balance the risks of depression and suicidality with the clinical need for control of choreiform movements. Closely observe patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior. Inform patients, caregivers, and families of the risk of depression and suicidality, and instruct them to report behaviors of concern promptly to the treating health care provider.

Exercise particular 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. April 2017. Revised 9/2017. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=7ea3c60a-45c7-44cc-afc2-d87fa53993c0&type=display>. Accessed November 14 2018

Ingrezza® (valbenazine) [package insert]. San Diego, CA: Neurocrine Biosciences. July 2018. Available at: <https://ingrezza.com/HCP/PI>. Accessed November 27, 2018.

Suchowersky O. Overview of chorea. UpToDate. June 2018. Available at: <https://www.uptodate.com/contents/overview-of->

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Suchowersky O. Huntington's disease: management. UpToDate. August 2018. Available at: https://www.uptodate.com/contents/huntington-disease-management?source=search_result&search=huntingtons&selectedTitle=2~50. Accessed November 27, 2018.

Xenazine® (tetrabenazine) [package insert]. Deerfield, IL. Lundbeck. June 2015. Revised 9/2017. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ac768bab-8afa-4446-bc7f-caeeffec0cda&type=display>. Accessed November 14 2018

Tardive Dyskinesia. National Alliance on Mental Illness Web Site. <https://www.nami.org/Learn-More/Mental-Health-Conditions/Related-Conditions/Tardive-Dyskinesia>. Accessed November 27, 2018.

What is Huntington's Disease? Huntington's Disease Society of America Web Site. <http://hdsa.org/what-is-hd/>. Accessed November 27, 2018.

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®	Deutetrabenzine
Ingrezza®	Valbenazine

Cross References:

N/A

Policy Version Number:	10.00
P&T Approval Date:	October 11, 2018
Policy Effective Date:	January 01, 2019
Next Required Review Date:	October 11, 2019

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.