| Pharmacy Policy Bulletin: J-0523 Xenazine (tetrabenazine) – Commercial and Healthcare Reform | |
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| **Number:** J-0523 | **Category:** Prior Authorization |
| **Line(s) of Business:**<br>☒ Commercial<br>☒ Healthcare Reform<br>☐ Medicare | **Benefit(s):**<br>**Commercial:**<br>**Prior Authorization (1.):**<br>**1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization<br><br>**Healthcare Reform:** Not Applicable |
| **Region(s):**<br>☒ All<br>☐ Delaware<br>☐ New York<br>☐ Pennsylvania<br>☐ West Virginia | **Additional Restriction(s):**<br>None |
| **Version:** J-0523-012 | **Original Date:** 05/10/2017 |
| **Effective Date: 07/18/2025** | **Review Date:** 06/25/2025 |

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| **Drugs Product(s):** | • Xenazine (tetrabenazine) |
| **FDA-Approved Indication(s):** | • Treatment of chorea associated with Huntington's Disease (Huntington's Chorea) |

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| **Background:** | • Xenazine (tetrabenazine) is a selective and reversible centrally acting monoamine depleting agent. Specifically, tetrabenazine inhibits the transporter protein, vesicular monoamine transporter type 2 (VMAT2) resulting in depletion of monoamines (for example dopamine, serotonin, norepinephrine, and histamine) from nerve terminals. Tetrabenazine preferentially depletes dopamine over norepinephrine and serotonin. Decreased levels of monoamines result in fewer choreiform movements.<br>• Huntington's disease is a hereditary progressive neurodegenerative disorder. One hallmark of the condition is involuntary movements, which include akathisia (restlessness), dystonia (muscle spasms in the arms, head, or trunk), and chorea. Chorea is the most common involuntary movement in Huntington's disease and is characterized by brief and abrupt movements that are irregular and unpredictable.<br>• The 2019 International Guidelines for the Treatment of Huntington's Disease states that tetrabenazine is one of the first-line treatments for chorea (grade A) unless the patient suffers from not well-managed depression or suicidal thoughts. Second generation neuroleptics (grade B) are first-line treatments for chorea when the patient has associated personality and/or behavioral or psychotic disorders. Deutetrabenazine (grade A) may be proposed as an alternative to tetrabenazine in countries where it is available.<br>• Patients requiring doses of Xenazine above 50 mg per day should be genotyped for the drug metabolizing enzyme CYP2D6 to determine appropriate dosing. Doses above 50 mg per day should be titrated up slowly at weekly intervals by 12.5 mg daily, to allow the identification of a tolerated dose that reduces chorea. Doses above 50 mg per day should be given in a three times a day regimen. |

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| | ○ The maximum daily dose for a poor metabolizer (PM) is 50 mg with a maximum single dose of 25 mg.<br>○ The maximum daily dose for an extensive metabolizer (EM) or intermediate metabolizer (IM) is 100 mg with a maximum single dose of 37.5 mg.<br>○ The CYP2D6 genetic type is correlated with the following CYP2D6 enzyme activity: PM = no CYP2D6 activity; IM = low CYP2D6 activity; EM = normal CYP2D6 activity; ultra-rapid metabolizers = high CYP2D6 activity.<br>• Prescribing Considerations:<br>○ Xenazine carries a black box warning for increased risk of depression and suicidal thoughts and behavior (suicidality) in patients with HD.<br>○ Use is contraindicated in those who are actively suicidal or with inadequately treated depression, those with hepatic impairment or on a concomitant MAOI or reserpine.<br>○ Due to the risk of clinically relevant QT prolongation, the use of Xenazine should be avoided in combination with other drugs known to prolong QTc in those with congenital long QT syndrome, and in patients with a history of cardiac arrhythmias.<br>○ Patients should be monitored for possible adverse events, particularly Parkinsonism, depression/suicidality, and unusual behavior.<br>○ Xenazine should be prescribed by or under the supervision of a neurologist.<br>○ Patients should not be concurrently prescribed Austedo (deutetrabenazine) or Ingrezza (valbenazine) with Xenazine. |

## Approval Criteria

**I. Initial Authorization**

When a benefit, coverage of Xenazine (tetrabenazine) may be approved when all of the following criteria are met **(A., B., and C.)**:

**A.** The member is 18 years of age or older.

**B.** The member has a diagnosis of chorea associated with Huntington's disease. (ICD-10: G10)

**C.** If the request is for brand Xenazine, the member has experienced therapeutic failure or intolerance to generic tetrabenazine.

**II. Reauthorization**

When a benefit, reauthorization of Xenazine (tetrabenazine) may be approved when all of the following criteria are met **(A. and B.):**

**A.** The prescriber attests that the member has experienced positive clinical response to therapy.

**B.** If the request is for brand Xenazine, the member has experienced therapeutic failure or intolerance to generic tetrabenazine.

**III. Quantity Limitations**

When a benefit, coverage of doses above 50 mg/day may be approved up to 100 mg/day when all of the following criteria are met **(A. and B.)**:

**A.** The member has experienced therapeutic failure or intolerance to a dose of 50 mg/day.

**B.** The member is not a poor CYP2D6 metabolizer.

**IV.** An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

## Limitations of Coverage

**I.** The member should not be actively suicidal.
**II.** If the member has a diagnosis of depression, the prescriber attests the member is receiving adequate treatment (for example cognitive behavioral therapy, pharmacotherapy).
**III.** Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support its effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
**IV.** For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

## Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

## Automatic Approval Criteria

None

**References:**


1. Xenazine [package insert]. Deerfield, IL: Lundbeck; November 2019.
2. Austedo [package insert]. Deerfield, IL: Teva Pharmaceuticals USA, Inc.; September 2023.
3. Wild EJ, Tabrizi SJ. The differential diagnosis of chorea. *Practical Neurology.* 2007;7:360-373.
4. Get to Know an Enzyme: CYP2D6. Pharmacy Times. Available at: https://www.pharmacytimes.com/publications/issue/2008/2008-07/2008-07-8624. Accessed May 02, 2025.
5. Bachoud-Lévi AC, Ferreira J, Massart R, et al. International Guidelines for the Treatment of Huntington's Disease. Front Neurol. 2019;10:710.