Clinical Policy: Tetrabenazine (Xenazine)
Reference Number: CP.PHAR.92
Effective Date: 12.01.11
Last Review Date: 08.20
Line of Business: HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Tetrabenazine (Xenazine®) is a vesicular monoamine transporter 2 (VMAT) inhibitor.

FDA Approved Indication(s)
Xenazine is indicated for the treatment of chorea associated with Huntington’s disease.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Xenazine is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Chorea Associated with Huntington Disease (must meet all):
      1. Diagnosis of chorea associated with Huntington disease;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 18 years;
      4. Targeted mutation analysis demonstrates a cytosine-adenine-guanine (CAG) trinucleotide expansion of ≥ 36 repeats in the huntingtin (HTT) gene;
      5. Evidence of chorea is supported by a Unified Huntington Disease Rating Scale (UHDRS) score ranging from 1 to 4 on any one of chorea items 1 through 7 (see Appendix D);
      6. Tetrabenazine is not prescribed concurrently with Austedo® or Ingrezza®;
      7. Dose does not exceed 50 mg per day (100 mg per day if genotype testing confirms extensive or intermediate CYP2D6 metabolizer status).

   Approval duration: 6 months

   B. Other diagnoses/indications
      1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Chorea Associated with Huntington Disease (must meet all):
CLINICAL POLICY
Tetrabenazine

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by a reduction since baseline in any one of UHDRS chorea items 1 through 7 (see Appendix D);
3. Tetrabenazine is not prescribed concurrently with Austedo or Ingrezza;
4. If request is for a dose increase, new dose does not exceed 50 mg per day (100 mg per day if genotype testing confirms extensive or intermediate CYP2D6 metabolizer status).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   AAN: American Academy of Neurology
   FDA: Food and Drug Administration
   HTT: huntingtin
   MAOI: monoamine oxidase inhibitors
   UHDRS: Unified Huntington Disease Rating Scale
   VMAT2: vesicular monoamine transporter 2

   Appendix B: Therapeutic Alternatives
   Not applicable

   Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s):
     o Actively suicidal, or who have depression which is untreated or undertreated
     o Hepatic impairment
     o Taking monoamine oxidase inhibitors (MAOIs) or reserpine
     o Taking deutetabenazine or valbenazine
   • Boxed warning(s):
     o Depression and suicidality
Appendix D: The Unified Huntington Disease Rating Scale (UHDRS)

- The UHDRS encompasses motor, behavioral, cognitive, and functional components for use in evaluating patients with Huntington disease and is commonly used in both research and clinical practice.
- The American Academy of Neurology (AAN) guidelines evaluating pharmacologic therapies for chorea associated with Huntington disease describe the chorea subscore of the UHDRS motor component as a rating of 7 body regions (facial, bucco-oral-lingual, trunk, extremities) on a five-point scale from 0 to 4 with 0 representing no chorea.
- See Huntington Study Group 1996 and Mestre et al. 2018 for additional information about the UHDRS.


V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chorea associated with Huntington’s disease</td>
<td>12.5 mg PO QD for first week, then 12.5 mg PO BID for second week, then titrate by 12.5 mg weekly thereafter to tolerated dose that reduces chorea; doses of 37.5 mg and up to 50 mg/day should be administered in 3 divided doses per day</td>
<td>50 mg/day (max single dose of 25 mg)</td>
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<tr>
<td></td>
<td>Extensive or intermediate CYP2D6 metabolizer: 100 mg/day (max single dose of 37.5 mg)</td>
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</tbody>
</table>

VI. Product Availability

Tablets: 12.5 mg, 25 mg

VII. References
Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Change Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Added safety and efficacy information to Background</td>
<td>01.15</td>
<td>02.15</td>
</tr>
<tr>
<td>Policy converted to new template.</td>
<td>01.16</td>
<td>01.16</td>
</tr>
<tr>
<td>Criteria: Neurologist and age requirement added.</td>
<td></td>
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<tr>
<td>Renamed to Tetrabenazine</td>
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<tr>
<td>Policy converted to new template.</td>
<td>12.16</td>
<td>01.17</td>
</tr>
<tr>
<td>Age removed; max dose added.</td>
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<tr>
<td>Definition of hepatic impairment is added as Child-Pugh A, B or C.</td>
<td></td>
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</tr>
<tr>
<td>Policy converted to new template.</td>
<td>06.28.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Added age limit as safety and efficacy has not been established in pediatric</td>
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<td>populations.</td>
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<tr>
<td>Removed the following contraindications: actively suicidal or untreated/inadequately treated depression (cannot be objectively confirmed and hepatic impairment (requires clinical judgment; adverse reaction is not predictable per PI [safety and efficacy of increased exposure to Xenazine is unknown]).</td>
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<tr>
<td>Modified DDI contraindication to include acceptable time of last use (MAOI &gt; 14 days ago, reserpine &gt; 20 days ago).</td>
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<td>Removed reasons to discontinue per new safety strategy.</td>
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<td>Increased approval durations from 3/6 months to 6/12 months.</td>
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<tr>
<td>2Q 2018 annual review: no significant changes; added HIM line of business; Removed DDI requirements from Section I (information added to Appendix C); added caution to prevent duplicate therapy with similar agents references reviewed and updated.</td>
<td>02.05.18</td>
<td>05.18</td>
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<td>2Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>02.26.19</td>
<td>05.19</td>
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<tr>
<td>2Q 2020 annual review: no significant changes; references reviewed and updated.</td>
<td>02.11.20</td>
<td>05.20</td>
</tr>
<tr>
<td>Genetic testing and UHDRS scoring added to chorea criteria; Appendix D added; references reviewed and updated.</td>
<td>07.07.20</td>
<td>08.20</td>
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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.
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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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