Clinical Policy: Tetrabenazine (Xenazine)

Reference Number: CP.PHAR.92
Effective Date: 12.01.11
Last Review Date: 08.20
Line of Business: HIM, Medicaid

Revision Log

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)**:**

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):
  - Actively suicidal, or who have depression which is untreated or undertreated
  - Hepatic impairment
  - Taking monoamine oxidase inhibitors (MAOIs) or reserpine
  - Taking deutetrabenazine or valbenazine
- Boxed warning(s):
  - 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.

(AAN Guidelines 2012, Huntington Study Group 1996, Mestre 2018)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chorea associated with Huntington's disease	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	50 mg/day (max single dose of 25 mg) Extensive or intermediate CYP2D6 metabolizer: 100 mg/day (max single dose of 37.5 mg)

VI. Product Availability

Tablets: 12.5 mg, 25 mg

VII. References

1. Xenazine Prescribing Information. Deerfield, IL: Lundbeck; November 2019. Available at: http://www.xenazineusa.com. Accessed February 6, 2020.
2. Potter NT, Spector EB, Prior TW. Technical standards and guidelines for Huntington disease testing. Genet Med. 2004:6(1):61-65.
3. ACMG/ASHG STATEMENT. Laboratory guidelines for Huntington disease genetic testing. The American College of Medical Genetics/American Society of Human Genetics Huntington Disease Genetic Testing Working Group. Am. J. Hum. Genet. 1998; 62:000–000.
4. Kremer B, Goldberg P, Andrew SE. A worldwide study of the Huntington's disease mutation: the sensitivity and specificity of measure CAG repeats. NEJM. May 19, 1994; 330(20):1401-1406.
5. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. August 7, 2012;79:598-603.
6. Unified Huntington's disease rating scale: reliability and consistency. Movement Disorder Society. Movement Disorders. 1996;11(2):136-143.
7. Mestre TA, Forjaz MJ, Mahlknecht P, et al. Rating scales for motor symptoms and signs in Huntington's disease: Critque and recommendation. International Parkinson and Movement Disorders Society. Movement Disorders Clinical Practice. 2018;5(2):111-117. DOI:10.1002/mdc3.1257.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added safety and efficacy information to Background	01.15	02.15
Policy converted to new template. Criteria: Neurologist and age requirement added. Renamed to Tetrabenazine	01.16	01.16
Policy converted to new template. Age removed; max dose added. Definition of hepatic impairment is added as Child-Pugh A, B or C.	12.16	01.17
Policy converted to new template. Added age limit as safety and efficacy has not been established in pediatric populations. 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]). Modified DDI contraindication to include acceptable time of last use (MAOI > 14 days ago, reserpine > 20 days ago). Removed reasons to discontinue per new safety strategy. Increased approval durations from 3/6 months to 6/12 months.	06.28.17	11.17
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.	02.05.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.11.20	05.20
Genetic testing and UHDRS scoring added to chorea criteria; Appendix D added; references reviewed and updated.	07.07.20	08.20

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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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.