Drug Coverage Policy

Effective Date……06/15/2025
Coverage Policy Number……IP0208
Policy Title……Tetrabenazine

Vesicular Monoamine Transporter Type 2 Inhibitors – Tetrabenazine

- Xenazine® (tetrabenazine tablets - Lundbeck, generic)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Tetrabenazine, a vesicular monoamine transporter type 2 inhibitor, is indicated for the treatment of **chorea associated with Huntington's disease** in adults.[1]

Clinical Efficacy
There are several published studies which have assessed the efficacy and safety of tetrabenazine for the treatment of other hyperkinetic movement disorders (e.g., tics in Tourette syndrome and tardive dyskinesia).[2-4] While most of the data for treatment of Tourette syndrome indicate that antipsychotic medications, both typical and atypical, are most effective, other medications (including tetrabenazine) may be used first to avoid the potential side effects of dopamine blockade.[5]

Guidelines
The American Academy of Neurology (AAN) evidence-based guidelines on pharmacologic treatment of chorea in Huntington's disease (2012; retired) state that if chorea in Huntington's disease requires treatment, clinicians should prescribe tetrabenazine, amantadine, or Rilutek® (riluzole tablets) [Level B].[6]

The AAN published an evidence-based guideline for the treatment of tardive syndromes (2013; retired).[7] The authors found that tetrabenazine possibly reduces tardive syndrome symptoms (based on two consistent Class III studies). Therefore, tetrabenazine may be considered in treating tardive syndromes (Level C).

The AAN published practice guideline recommendations for the treatment of tics in patients with Tourette syndrome and chronic tic disorders (2019).[8] The guidelines state that the dopamine depleters, tetrabenazine, deutetrabenazine, and valbenazine, are lacking published, randomized, controlled trials in the treatment of tics but note that these drugs are increasingly used off-label for this indication. When appropriately dosed, these drugs are generally well-tolerated but may be associated with drowsiness, depression, and parkinsonism.

Coverage Policy

Policy Statement
Prior Authorization is required for prescription benefit coverage of tetrabenazine. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with tetrabenazine as well as the monitoring required for adverse events and long-term efficacy, approval requires tetrabenazine to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Tetrabenazine (Xenazine, generics) is considered medically necessary when ONE of the following is met (1, 2, 3, or 4):

FDA-Approved Indication

1. **Chorea Associated with Huntington's Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Diagnosis of Huntington's disease is confirmed by genetic testing (for example, an expanded HTT CAG repeat sequence of at least 36); AND
   - **C)** The medication is prescribed by or in consultation with a neurologist; AND
   - **D)** Preferred product criteria is met for the product(s) as listed in the below table(s)

Other Uses with Supportive Evidence

2. **Hyperkinetic Dystonia.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is prescribed by or in consultation with a neurologist; AND
   C) Preferred product criteria is met for the product(s) as listed in the below table(s)

3. **Tardive Dyskinesia.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has a history of use of dopamine receptor blocking agent;
   Note: Examples of dopamine receptor blocking agents include dopamine agonists (e.g., pramipexole, ropinirole), antipsychotics, metoclopramide, prochlorperazine.
   C) The medication is prescribed by or in consultation with a neurologist or psychiatrist.
   D) Preferred product criteria is met for the product(s) as listed in the below table(s)

4. **Tourette Syndrome and Related Tic Disorders.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is prescribed by or in consultation with a neurologist.
   C) Preferred product criteria is met for the product(s) as listed in the below table(s)

Employer Plans:

Product	Criteria
Xenazine	**1.** Patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient tried generic tetrabenazine tablets; AND **ii.** Patient cannot continue to use generic tetrabenazine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction.

Individual and Family Plans:

Product	Criteria
Xenazine	**1.** Patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient tried generic tetrabenazine tablets; AND **ii.** Patient cannot continue to use generic tetrabenazine tablets due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based

literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Tetrabenazine (Xenazine, generics) for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Xenazine® tablets [prescribing information]. Deerfield, IL: Lundbeck; November 2019.
2. Merative Micromedex®. Merative US. Available at: https://www.micromedexsolutions.com/. Accessed on March 26, 2025. Search terms: tetrabenazine.
3. Chen JJ, Ondo WG, Dashtipour K, et al. Tetrabenazine for the treatment of hyperkinetic movement disorders: a review of the literature. *Clin Ther*. 2012;34(7):1487-504.
4. Guay DR. Tetrabenazine, a monoamine-depleting drug used in the treatment of hyperkinetic movement disorders. *Am J Geriatr Pharmacother*. 2010;8(4):331-373.
5. Quezada J, Coffman KA. Current Approaches and New Developments in the Pharmacological Management of Tourette Syndrome. *CNS Drugs*. 2018; 32(1):33–45.
6. 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.* 2012;79:597-603.
7. Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology.* 2013;81(5):463-469.
8. Pringsheim T, Okun MS, Müller-Vahl K, et al. Practice guideline recommendations summary: treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology*. 2019;92:896-906.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	Updated the title of the policy from Tetrabenazine to Vesicular Monoamine Transporter Type 2 Inhibitors – Tetrabenazine. **Tardive Dyskinesia.** Updated "Individual has a history of treatment with a dopamine receptor blocking agent (for example, antipsychotics, metoclopramide, prochlorperazine)" to now be "Patient has a history of use of dopamine receptor blocking agent" with the examples moved to a Note.	09/01/2024
Annual Revision	The Conditions Not Covered statement was reworded.	06/15/2025

The policy effective date is in force until updated or retired.