MEDICAL MUTUAL®

Drug Policy

Policy:	Xenazine (tetrabenazine)	Annual Review Date: 06/22/2023 Last Revised Date: 06/22/2023

OVERVIEW

Tetrabenazine reversibly depletes monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals.[1] Tetrabenazine, and its major circulating metabolites (α-dihydrotetrabenazine [HTBZ] and β-HTBZ), reversibly inhibits vesicular monoamine transporter type 2 (VMAT2), resulting in decreased uptake of monoamines into synaptic vesicles and depletion of monoamine stores. Tetrabenazine is indicated for the treatment of chorea associated with Huntington's disease (HD). There are several other published studies which have assessed the efficacy and safety of tetrabenazine for the treatment of other hyperkinetic movement disorders.

In 2013, The American Academy of Neurology (AAN) released guidelines for the treatment of tardive syndromes and listed Tetrabenazine as a treatment for Tardive Dyskinesia Sydrome (Level C evidence). Up-to-date lists VMAT2 inhibitors, such as tetrabenazine, as second-line therapy for adults with Hyperkinetic Dystonia that have failed a Levodopa trial and a clonazepam trial (2021). The AAN, in 2019, released guidelines for the treatment of tics in patients with Tourette's syndrome and other tic disorders, which stated that there is limited evidence for the effective use of Tetrabenazine to treat these tics but that Tetrabenazine is increasingly being prescribed off-label for this indication.

Beginning in September 2015, tetrabenazine has been available as an AB-rated generic to brand Xenazine. Generic tetrabenazine is FDA-approved and is available in the same tablet dosage form and the same 12.5 mg and 25 mg strengths as brand Xenazine. Discontinue if patient develops Neuroleptic Malignant Syndrome.

POLICY STATEMENT

This policy involves the use of Xenazine and generic tetrabenazine. Prior authorization is recommended for pharmacy benefit coverage of Xenazine and generic tetrabenazine. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Xenazine as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Xenazine be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

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RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Xenazine is recommended in those who meet the following criteria:

1. **Chorea Associated with Huntington's Disease (HD)**
   Criteria. *Patient must meet the following criteria*
   - **A.** Xenazine is prescribed by or in consultation with a neurologist; AND
   - **B.** Patient is ≥ 18 years old; AND
   - **C.** Patient has been diagnosed with chorea associated with HD confirmed by genetic testing (for example, an expanded HTT CAG repeat sequence of at least 36); AND
   - **D.** The patient does not have hepatic impairment; AND
   - **E.** The patient is not concomitantly taking reserpine, monoamine oxidase inhibitors (MAOIs; selegiline, phenelzine, tranylcypromine), Ingrezza, Austedo; AND
   - **F.** If brand Xenazine is requested, the patient has tried and cannot take generic tetrabenazine tablets (due to formulation differences in the inactive ingredients between brand and generic tablets) as identified by the prescribing physician [documentation required]

2. **Hyperkinetic Dystonia**
   Criteria. *Patient must meet the following criteria*
   - **A.** Xenazine is prescribed by or in consultation with a neurologist; AND
   - **B.** Patient is ≥ 18 years old; AND
   - **C.** The patient does not have hepatic impairment; AND
   - **D.** The patient is not concomitantly taking reserpine, monoamine oxidase inhibitors (MAOIs; selegiline, phenelzine, tranylcypromine), Ingrezza, or Austedo; AND
   - **E.** If brand Xenazine is requested, the patient has tried and cannot take generic tetrabenazine tablets (due to formulation differences in the inactive ingredients between brand and generic tablets) as identified by the prescribing physician [documentation required]

3. **Tardive Dyskinesia (TD)**
   Criteria. *Patient must meet the following criteria*
   - **A.** Xenazine is prescribed by or in consultation with a neurologist; AND
   - **B.** Patient is ≥ 18 years old; AND
   - **C.** The patient does not have hepatic impairment; AND
   - **D.** The patient is not concomitantly taking reserpine, monoamine oxidase inhibitors (MAOIs; selegiline, phenelzine, tranylcypromine), Ingrezza, Austedo; AND
   - **E.** The patient has been clinically diagnosed with TD according to the DSM V criteria [documentation required]:
     - **i.** Involuntary athetoid or choreiform movements; AND
     - **ii.** History of treatment with a neuroleptic agent (i.e. antipsychotics); AND
     - **iii.** Symptoms lasting longer than 4-8 weeks; AND
   - **F.** Adjustments to possible offending medication (such as dose reduction or discontinuation) were attempted but ineffective in resolving TD symptoms OR patient is not a candidate for dose reduction or discontinuation of the offending medication; AND

G. If a patient is using the offending medication for a behavioral health indication, the use of a second generation (atypical) antipsychotic has been attempted unless contraindicated; AND
H. If brand Xenazine is requested, the patient has tried and cannot take generic tetrabenazine tablets (due to formulation differences in the inactive ingredients between brand and generic tablets) as identified by the prescribing physician [documentation required]

4. Tourette Syndrome and Related Tic Disorders
Criteria. *Patient must meet the following criteria*

A. Xenazine is prescribed by or in consultation with a neurologist; AND
B. Patient is ≥ 18 years of age; AND
C. The patient does not have hepatic impairment; AND
D. The patient is not concomitantly taking reserpine, monoamine oxidase inhibitors (MAOIs; selegiline, phenelzine, tranylcypromine), Ingrezza, Austedo; AND
E. The patient has tried or is not a candidate for habit reversal training with Comprehensive Behavioral Intervention for Tics (CBIT); AND
F. If brand Xenazine is requested, the patient has tried and cannot take generic tetrabenazine tablets (due to formulation differences in the inactive ingredients between brand and generic tablets) as identified by the prescribing physician

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Xenazine has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation

supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Xenazine® tablets [prescribing information]. Deerfield, IL: Lundbeck; November 2019.
2. 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.
3. Kenney C, Jankovic J. Tetrabenazine in the treatment of hyperkinetic movement disorders. *Expert Rev Neurotherapeutics.* 2006;6:7-17.
4. Jankovic J, Orman J. Tetrabenazine therapy of dystonia, chorea, tics, and other dyskinesias. *Neurology.* 1988;38:391-394.
5. Kenney C, Hunter C, Jankovic J. Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders. *Mov Disord.* 2007;22:193-197.
6. Jankovic J, Beach J. Long-term effects of tetrabenazine in hyperkinetic movement disorders. *Neurology.* 1997;48:358-362.
7. Paleacu D, Giladi N, Moore O, et al. Tetrabenazine treatment in movement disorders. *Clin Neuropharmacol.* 2004;27:230-233.
8. Ondo WG, Hanna PA, Jankovic J. Tetrabenazine treatment for tardive dyskinesia: assessment by randomized videotape protocol. *Am J Psychiatry*. 1999;156:1279-1281.
9. Jankovic J. Treatment of hyperkinetic movement disorders with tetrabenazine: a double-blind crossover study. *Ann Neurol*. 1982;11(1):41-47.
10. Asher SW, Aminoff MJ. Tetrabenazine and movement disorders. *Neurology*. 1981;31(8):1051-1053.
11. Kingston D. Tetrabenazine for involuntary movement disorders. *Med J Aust*. 1979;1(13):628-630.
12. Kazamatsuri H, Chien C, Cole JO. Treatment of tardive dyskinesia: clinical efficacy of a dopamine-depleting agent, tetrabenazine. *Arch Gen Psychiat*. 1972;27:95-99.
13. 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.
14. Jain S, Greene PE, Frucht SJ. Tetrabenazine therapy of pediatric hyperkinetic movement disorders. *Mov Disord.* 2006;21:1966-1972.
15. Ondo WG, Jong D, Davis A. Comparison of weight gain in treatments for Tourette syndrome: tetrabenazine versus neuroleptic drugs. *J Child Neurol.* 2008;23:435-437.
16. Sweet RD, Bruun R, Shapiro E, Shapiro AK. Presynaptic catecholamine antagonists as treatment for Tourette syndrome. *Arch Gen Psychiatry*. 1974;31:857-861.
17. Swash M, Roberts AH, Zakko H, Heathfield KWG. Treatment of involuntary movement disorders with tetrabenazine. *J Neurol Neurosurg Psychiatry*. 1972;35(2):186-191.
18. Pakkenberg H, Fog R. Spontaneous oral dyskinesia. Results of treatment with tetrabenazine, pimozide, or both. *Arch Neurol.* 1974;31(5):352-353.
19. Heggarty H, Wright T. Tetrabenazine in athetoid cerebral palsy. *Develop Med Child Neurol.* 1974;16:137-142.
20. Gilligan BS, Wodak J, Veale J, Munro OR. Tetrabenazine in the treatment of extrapyramidal dyskinesias. *Med J Aust*. 1972;2(19):1054-1056.
21. Kenney C, Hunter C, Mejia N, Jankovic J. Is history of depression a contraindication to treatment with tetrabenazine. *Clin Neuropharmacol*. 2006;29(5):259-264.
22. Guay DR. Tetrabenazine, a monoamine-depleting drug used in the treatment of hyperkinetic movement disorders. *Am J Geriatr Pharmacother*. 2010;8(4):331-373.
23. Dressler D. Nonprimary dystonias. *Handb Clin Neurol*. 2011;100:513-538.
24. Tetrabenazine. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 16 April 2019. Accessed on 17 June 2019.
25. Quezada J, Coffman KA. Current Approaches and New Developments in the Pharmacological Management of Tourette Syndrome. CNS Drugs. 2018; 32(1):33–45.
26. Tetrabenazine. Accessdata.fda.gov [online database] accessed on 11 June 2020
27. Kluwer W. [online database] Huntington disease: Management. 2020. Accessed 11 June 2020.