



EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Vesicular Monoamine Transporter Type 2 Inhibitors – Tetrabenazine tablets (Xenazine® – Lundbeck, generics)

TAC APPROVAL DATE: 05/22/2019

OVERVIEW

Tetrabenazine reversibly depletes monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals.¹ Tetrabenazine, and its major circulating metabolites (α -dihydroxytetrabenazine [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 (e.g., tics in Tourette Syndrome and tardive dyskinesia [TD]).

Beginning in September 2015, tetrabenazine has been available as an AB-rated generic to brand Xenazine. Generic tetrabenazine is Food and Drug Administration (FDA)-approved and is available in the same tablet dosage form and the same 12.5 mg and 25 mg strengths as brand Xenazine.

Guidelines

The American Academy of Neurology (AAN) evidence-based guidelines on pharmacologic treatment of chorea in HD (2012) states that if chorea in HD requires treatment, clinicians should prescribe tetrabenazine, amantadine, or Rilutek® (riluzole tablets) [Level B].²

The AAN published an evidence-based guideline for the treatment of tardive syndromes (TDS) [2013].³ The authors found that tetrabenazine possibly reduces TDS symptoms (based on two consistent Class III studies). Therefore, tetrabenazine may be considered in treating TDS (Level C).

The AAN published practice guideline recommendations for the treatment of tics in people with Tourette syndrome and chronic tic disorders (2019).⁴ The guidelines state that the dopamine depleters, tetrabenazine, deutetabenazine, and valbenazine, are lacking published, randomized, controlled trials in the treatment of tics but note that these drugs are increasingly used off-label. When appropriately dosed, these drugs are generally well-tolerated but may be associated with drowsiness, depression, and parkinsonism.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of tetrabenazine. 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. All approvals are provided for the duration noted below.

Automation: None.

05/22/2019

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RECOMMENDED AUTHORIZATION CRITERIA

Coverage of tetrabenazine is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Chorea Associated with Huntington's Disease (HD).** Approve for 1 year if tetrabenazine is prescribed by or in consultation with a neurologist.

Other Uses with Supportive Evidence

2. **Hyperkinetic Dystonia.** Approve for 1 year if tetrabenazine is prescribed by or in consultation with a neurologist.

There are multiple controlled and uncontrolled trials conducted with tetrabenazine that included patients with dystonias.^{6-10,12,13,16,19,21,22} In retrospective trials, an overall moderate clinical improvement or better was seen in 161 out of 163 patients with dystonia treated with tetrabenazine.²¹ A treatment algorithm for secondary dystonias was developed that notes tetrabenazine can be tried following a trial of an anticholinergic in children with severe secondary dystonias.²² In adults, tetrabenazine can be tried (alone or as combination therapy) following a low-dose trial of anticholinergic.

3. **Tardive Dyskinesia (TD).** Approve for 1 year if tetrabenazine is prescribed by or in consultation with a neurologist or psychiatrist.

Tetrabenazine has been studied for the treatment of TD, either as initial therapy or in patients who have responded poorly to other agents (e.g., reserpine, bromocriptine, clozapine).⁵⁻¹⁵

4. **Tourette Syndrome and Related Tic Disorders.** Approve for 1 year if tetrabenazine is prescribed by or in consultation with a neurologist.

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.¹⁸

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tetrabenazine 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.

REFERENCES

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OTHER REFERENCES UTILIZED

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Early annual revision	Removal of Hemiballism from Other Uses with Supportive Evidence. Change to the policy name: now Vesicular Monoamine Transporter Type 2 (VMAT2) Inhibitors – Tetrabenazine.	4/26/2017
Annual revision	No changes to criteria.	04/25/2018
Selected revision	Removal of the requirement for a previous trial of generic tetrabenazine if brand Xenazine is requested. This is due to a new VMAT2 Inhibitor Preferred Specialty Management policy.	08/29/2018
Annual revision	No change to criteria.	05/22/2019

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.