PRIOR AUTHORIZATION POLICY

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

DATE REVIEWED: 06/10/2020

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 (e.g., tics in Tourette Syndrome and tardive dyskinesia).

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.

Clinical Efficacy

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.

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

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]

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, deutetrabenazine, 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.

Safety
The prescribing information for tetrabenazine includes a contraindication in patients who are actively suicidal or who have depression which is untreated or undertreated.[1] Of note, tetrabenazine is only FDA-approved for use in patients with Huntington's disease. Tetrabenazine also has a Boxed Warning regarding depression and suicidality in patients with Huntington's disease. Patients with Huntington's disease are at increased risk for depression and suicidal ideation or behaviors (suicidality), and tetrabenazine may increase the risk for suicidality in these patients. When considering the use of tetrabenazine, the risk of suicidality should be balanced against the need for treatment of chorea. All patients treated with tetrabenazine should be observed for new or worsening depression or suicidality. If depression or suicidality does not resolve, consider discontinuing treatment with tetrabenazine.

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.

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.** 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.

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

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

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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