EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Xenazine® (tetrabenazine tablets – Lundbeck, generics)

TAC APPROVAL DATE: 07/01/2015; selected revision 02/10/2016 and 02/24/2016

LAY CRITERIA EFFECTIVE DATE: 03/01/2016

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 [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.

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. Additionally, due to the availability of generic tetrabenazine tablets, approval of brand Xenazine requires a previous trial of the generic. All approvals are provided for 3 years in duration.

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 (HD).** Approve for 3 years if the patient meets BOTH of the following criteria (A and B):
   - **A)** Tetrabenazine is prescribed by or after consultation with a neurologist; AND
   - **B)** 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].

Tetrabenazine is indicated for the treatment of chorea associated with HD.[1] In addition, the 2012 American Academy of Neurology (AAN) evidence-based guidelines on pharmacologic treatment of chorea in HD states that if HD chorea requires treatment, clinicians should prescribe tetrabenazine, amantadine, or Rilutek® (riluzole tablets) [Level B].[2]

Other Uses with Supportive Evidence

2. **Hemiballism.** Approve for 3 years if the patient meets BOTH of the following criteria (A and B):
   A) Tetrabenazine is prescribed by or after consultation with a neurologist; AND
   B) 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].

   In case reports, tetrabenazine has been effective at treating various involuntary movement disorders, including hemiballism.[12,18]

3. **Hyperkinetic Dystonia.** Approve for 3 years if the patient meets BOTH of the following criteria (A and B):
   A) Tetrabenazine is prescribed by or after consultation with a neurologist; AND
   B) 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].

   There are multiple controlled and uncontrolled trials conducted with tetrabenazine that included patients with dystonias.[4-8,10-11,15,18,23-24] In retrospective trials, an overall moderate clinical improvement or better was seen in 161 out of 163 patients with dystonia treated with tetrabenazine.[23] 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.[24] In adults, tetrabenazine can be tried (alone or as combination therapy) following a low-dose trial of anticholinergic.

4. **Tardive Dyskinesia (TD).** Approve for 3 years if the patient meets BOTH of the following criteria (A and B):
   A) Tetrabenazine is prescribed by or after consultation with a neurologist or psychiatrist; AND
   B) 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].

   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).[3-13] Indirect comparisons suggest tetrabenazine may be the most effective agent available for this disorder[4], although further studies assessing long-term benefit and the propensity of the drug to aggravate TD are needed. In 2013, the AAN published an evidence-based guideline for the treatment of tardive syndromes (TDS).[14] 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).

5. **Tourette Syndrome and Related Tic Disorders.** Approve for 3 years if the patient meets BOTH of the following criteria (A and B):

A) Tetrabenazine is prescribed by or after consultation with a neurologist; AND
B) 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].

Improvement has been observed in some patients with Tourette syndrome treated with tetrabenazine after poor response to prior therapy (e.g., haloperidol), in uncontrolled studies.[3-8,10,15-17]

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. Rationale for non-coverage for these specific conditions is provided below. (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	Lay Criteria Effective Date
Annual revision	No changes to criteria.	06/13/2012	--
Annual revision	No changes to criteria.	06/12/2013	--
Annual revision	No changes to criteria.	06/18/2014	Previously in effect
Selected revision	Approval duration increased to 3 years from 1 year,	08/06/2014	08/26/2014
Annual revision	No changes to criteria.	07/01/2015	Previously in Effect
DEU revision	9/16/2015: Addition of generics to Xenazine to the policy. No changes to criteria.	--	Previously in Effect
Selected revision	Additional criteria requiring prior trial of generic tetrabenazine tablets if brand Xenazine if requested.	02/10/2016	02/12/2016
Selected revision	Additional requirement ("AND cannot take") added to trial of generic tetrabenazine prior to approval of brand Xenazine. This requirement will require documentation.	02/24/2016	03/01/2016

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.