**Tetrabenazine**

**Medical Necessity Criteria**

Tetrabenazine (Xenazine®) is considered medically necessary when BOTH of the following criteria are met:

- Treatment of ONE on the following:
  - Documented diagnosis of Huntington's disease when ALL of the following criteria are met:
    - Confirmed by genetic testing (for example, an expanded HTT CAG repeat sequence of at least 36)
    - Presence of chorea
    - Prescribed by or in consultation with a neurologist
  - Documented diagnosis of Hyperkinetic Dystonia when prescribed by or in consultation with a neurologist
  - Documented diagnosis of Hyperkinetic movement disorder associated with Tourette’s syndrome when prescribed by or in consultation with a neurologist or a psychiatrist
  - Documented diagnosis of Tardive Dyskinesia when BOTH of the following criteria are met:
    - Individual has a history of treatment with a dopamine receptor blocking agent (for example, antipsychotics, metoclopramide, prochlorperazine)
    - Prescribed by or in consultation with a neurologist or a psychiatrist
- Documented intolerance to 1 generic formulation of Xenazine

**Initial authorization is up to 12 months.**
EFFECTIVE 7/01/2020

Tetrabenazine (Xenazine) is considered medically necessary for continued use when the following are met:
• Individual continues to meet the initial criteria
• Attestation of beneficial clinical response

Reauthorization for up to 12 months.

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.

Tetrabenazine (Xenazine®) is considered experimental, investigational or unproven for ANY other use.

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

*If you’re a Cigna provider, please log in to the Cigna for Health Care Professionals website and search for specific patients to view their covered medications.

FDA Approved Indications

FDA Approved Indication
Xenazine is indicated for the treatment of chorea associated with Huntington’s disease.

Recommended Dosing

FDA Recommended Dosing
The dose of Xenazine should be individualized.

Dosing Recommendations Up to 50 mg per day
The starting dose should be 12.5 mg per day given once in the morning. After one week, the dose should be increased to 25 mg per day given as 12.5 mg twice a day. Xenazine should be titrated up slowly at weekly intervals by 12.5 mg daily, to allow the identification of a tolerated dose that reduces chorea. If a dose of 37.5 to 50 mg per day is needed, it should be given in a three times a day regimen. The maximum recommended single dose is 25 mg. If adverse reactions such as akathisia, restlessness, parkinsonism, depression, insomnia, anxiety or sedation occur, titration should be stopped and the dose should be reduced. If the adverse reaction does not resolve, consideration should be given to withdrawing Xenazine treatment or initiating other specific treatment (e.g., antidepressants).

Dosing Recommendations Above 50 mg per day
Patients who require doses of Xenazine greater than 50 mg per day should be first tested and genotyped to determine if they are poor metabolizers (PMs) or extensive metabolizers (EMs) by their ability to express the drug metabolizing enzyme, CYP2D6. The dose of Xenazine should then be individualized accordingly to their status as PMs or EMs.

Extensive and Intermediate CYP2D6 Metabolizers
Genotyped patients who are identified as extensive (EMs) or intermediate metabolizers (IMs) of CYP2D6, who need doses of Xenazine above 50 mg per day, should be titrated up slowly at weekly intervals by 12.5 mg daily, to allow the identification of a tolerated dose that reduces chorea. Doses above 50 mg per day should be given in a three times a day regimen. The maximum recommended daily dose is 100 mg and the maximum recommended single dose is 37.5 mg. If adverse reactions such as akathisia, parkinsonism, depression, insomnia, anxiety or sedation occur, titration should be stopped and the dose should be reduced. If the adverse reaction does not resolve, consideration should be given to withdrawing Xenazine treatment or initiating other specific treatment (e.g., antidepressants).

Poor CYP2D6 Metabolizers
In PMs, the initial dose and titration is similar to EMs except that the recommended maximum single dose is 25 mg, and the recommended daily dose should not exceed a maximum of 50 mg.

Drug Availability
Xenazine is available as oral tablets containing 12.5 mg or 25 mg of tetrabenazine.

Background

Therapeutic Alternatives
Xenazine has an FDA approved generic therapeutic equivalent.

Professional Societies/Organizations

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

American Academy of Neurology (AAN) guidelines for the treatment of tardive syndromes (TDS) were updated in 2018 and define TDS as disorders that meet the following three criteria: (1) A history of at least 3 months' total cumulative neuroleptic exposure. (2) The presence of at least “moderate” abnormal involuntary movements in one or more body areas or at least “mild” movements in 2 or more body areas. And (3), the absence of other conditions that might produce abnormal involuntary movements. The AAN states tardive dyskinesia (TD) symptoms include various involuntary movements, including lingual-facial-buccal movements. In comparison, the AAN states TDS includes not only lingual-facial-buccal dyskinesia but also the variant forms, collectively termed tardive syndromes. The guideline recommends valbenazine and deutetebenazine, as first-line treatment options. The updated guideline also states tetrabenazine should be used only if valbenazine and deutetebenazine are unavailable and second-line agents, such as gingko biloba or clonazepam, do not provide adequate relief. (Bhidayasiri, 2013 and 2018)

American Academy of Neurology (AAN) practice guideline recommendations for the treatment of tics in people with Tourette syndrome and chronic tic disorders state that the dopamine depleters, tetrabenazine, deutetebenazine, 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. (Pringsheim, 2019)

There are multiple controlled and uncontrolled trials conducted with tetrabenazine that included patients with dystonias. In retrospective trials, an overall moderate clinical improvement or better was seen in 161 out of 163 patients with dystonia treated with tetrabenazine. (Guay, 2010) 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. In adults, tetrabenazine can be tried (alone of as combination therapy) following a low-dose trial of anticholinergic. (Dressler, 2011)

Off Label Uses
AHFS Drug Information 2019 Edition supports the following off-label uses: Hyperkinetic movement disorder associated with Tourette’s syndrome and Tardive dyskinesia.

Comparative Studies
There are no clinical studies comparing Xenazine with other therapeutic alternatives.

Generics
The FDA’s generic drug approval process does not require the drug sponsor to repeat costly animal and clinical research on ingredients or dosage forms already approved for safety and effectiveness. Generic drugs must establish the following for approval:
- contain the same active ingredients as the innovator drug (inactive ingredients may vary)
- be identical in strength, dosage form, and route of administration
A generic drug is the same as a brand-name drug in dosage, safety, strength, quality, the way it works, the way it is taken and the way it should be used. FDA requires generic drugs have the same high quality, strength, purity and stability as brand-name drugs. Not every brand-name drug has a generic drug. When new drugs are first made they have drug patents. Most drug patents are protected for 20 years. The patent, which protects the company that made the drug first, doesn’t allow anyone else to make and sell the drug. When the patent expires, other drug companies can start selling a generic version of the drug. But, first, they must test the drug and the FDA must approve it.

References