

Xenazine® (*Tetrabenazine*)

FDA-APPROVED INDICATION

Xenazine® is indicated for the treatment of chorea associated with Huntington's disease.

NOTE: Xenazine has a FDA Black Box Warning: Xenazine may increase risk of depression, suicidal thoughts, and suicidal actions.

COVERAGE POLICY

Xenazine® is covered for members who meet the following criteria:

- A. Documented diagnosis of Huntington's Disease with chorea, and
- B. Prescribed by specialist (neurologist) properly monitoring the disease progression and making necessary dosing adjustments, and
- C. Compliant with REMS* (Risk Evaluation and Mitigation Strategy) (see Appendix A)

DOSE

Normal: The recommended starting dose is 12.5 mg orally once daily in the morning. After 1 week, the dose may be increased to 12.5 mg twice daily and titrated slowly at weekly intervals by 12.5 mg. If a dose of 37.5 mg to 50 mg per day is required, it should be given in divided doses 3 times a day. The maximum recommended single dose is 25 mg and the maximum daily dose is 100 mg.

CYP2D6 extensive and intermediate metabolizers: Titrate doses up slowly at weekly intervals by 12.5 mg. Doses greater than 50 mg/day should be given in divided doses 3 times a day. The maximum recommended single dose is 37.5 mg and the maximum recommended daily dose is 100 mg.

CYP2D6 poor metabolizers: Titrate doses up slowly at weekly intervals by 12.5 mg. The maximum recommended single dose is 25 mg and the maximum recommended daily dose is 50 mg.

CYP2D6 Inhibitors: When a concomitant strong CYP2D6 inhibitor, such as fluoxetine, paroxetine, or quinidine, is being added to a patient already receiving a stable dose of tetrabenazine, the daily dose of tetrabenazine should be cut in half. To initiate treatment with tetrabenazine in patients on a stable dose of a strong CYP2D6 inhibitor, titrate tetrabenazine doses up slowly at weekly intervals by 12.5 mg. The maximum recommended single dose is 25 mg and the maximum recommended daily dose is 50 mg.

Quantity limit: 8 tablets/day for 12.5 mg and 4 tablets/day for 25 mg

AUTHORIZATION PERIOD

Initial Approval: 3 months

Extended Approval: Annual review based on continued therapeutic response

NON COVERAGE

Xenazine® is NOT covered for members with the following:

- A. Patients who are actively suicidal, or patients with untreated or inadequately treated depression
- B. Patients with impaired hepatic function
- C. Patients currently taking monoamine oxidase inhibitors
- D. Patients currently taking reserpine
- E. Any non FDA-approved indications
- F. Diagnosis of other movement disorders, such as, but not limited to, tardive dyskinesia, dystonia, Tourette's Syndrome and other drug induced movement.

REFERENCES

1. Xenazine® (tetrabenazine) prescribing information. Ovation Pharmaceuticals; September 2008.
2. Huntington Study Group. Tetrabenazine as antichorea therapy in Huntington disease: a randomized controlled trial. *Neurology* 2006;66:366-372.
3. Jankovic J, Beach J. Long-term effects of tetrabenazine in hyperkinetic movement disorders. *Neurology* 1997;48:358-362.
4. Xenazine, Formulary Dossier, Ovation Pharmaceuticals. October, 2008.
5. Frank, S. Et al. A study of chorea after terabenazine withdrawal in patients with Huntington's disease. *Clin Neuropharmacol.* 2008; 31: 127-33.
6. Huntington Study Group. Unified Huntington's disease rating scale: reliability and consistency. *Mov Disorder.* 1996; 11: 136-142.

Appendix A

Risk Evaluation and Mitigation Strategy (REMS)* summary for Xenazine

The goals of the REMS are to reduce the risk of drug-associated depression and suicidality in patients receiving Xenazine, to promote informed prescribing along with proper titration and dosing, and to minimize the risk of drug-drug interactions with strong CYP2D6 inhibitors.

DEPRESSION AND SUICIDALITY

XENAZINE can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease. Anyone considering the use of XENAZINE must balance the risks of depression and suicidality with the clinical need for control of choreiform movements. Close observation of patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior should accompany therapy. Patients, their caregivers, and families should be informed of the risk of depression and suicidality and should be instructed to report behaviors of concern promptly to the treating physician.

Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in Huntington's disease. XENAZINE is contraindicated in patients who are actively suicidal, and in patients with untreated or inadequately treated depression. (see CONTRAINDICATIONS; WARNINGS - Risk of Depression and Suicidality, and PRECAUTIONS - Information for Patients).

Elements for the REMS will include:

1) Patient Medication Guide

- A medication guide will be dispensed with each Xenazine prescription
- Each Xenazine unit-of-use shipped to pharmacies will have 3 medication guides attached to the bottle
- Each Xenazine bottle will have a prominent notice on the bottle label to dispense a medication guide with each prescription
- Each “Dear Pharmacist” letter will include 10 medication guides and instructions to include a medication guide with each prescription
- Medication Guides will be made available through sales/clinical reps, on the Company website, or available through a toll-free number

2) Communication Plan for physicians and pharmacists at the time of launch and annually thereafter

- Physician materials include:
 - Xenazine package insert (PI)
 - Dear Healthcare Professional Letter
 - Xenazine Medication guide
 - Prescribing Xenazine: A Healthcare Professional Guide
 - Patient/Caregiver Counseling Guide
 - Initial Dosing Plan
- Pharmacist materials include:
 - Dear Pharmacist Letter
 - Xenazine Package Insert (PI)
 - Xenazine Medication Guide
 - Prescribing Xenazine: A Healthcare Professional Guide

3) Pharmacy Management Systems

- To ensure the proper clinical data is available in drug compendia and pharmacy benefit manager (PBM) databases

4) Ongoing Healthcare Professional Education that includes REMS messaging

- Trained Speaker’s Bureau
- Major Professional meetings (e.g. American Neurology Association (ANA), Movement Disorder Society (MDS))
- Continuing Education (CE) formats via product website

5) Ongoing formal evaluations of REMS elements