Xenazine®
(tetrabenazine) Tablets

Xenazine is the only FDA-approved therapy to treat chorea associated with Huntington’s disease (HD).\(^1\) The word chorea comes from the Greek word for “dance”.\(^2\) HD affects an estimated 25,000 people in the U.S.\(^3\) and chorea occurs in an estimated 90 percent of people with HD at some point in their disease.\(^4\) Xenazine was approved by the U.S. Food and Drug Administration in August 2008.

Please see Important Safety Information, including Boxed Warning about the increased risk of depression and suicidality, on following page.

About Xenazine

- Xenazine is the only FDA-approved therapy for chorea associated with Huntington’s disease,\(^1\) a rare, inherited neurological disorder that may be passed from parent to child through a gene mutation.\(^5\) Each child of a parent with HD has a 50% chance of inheriting the disease.\(^5\)
  - HD causes a degeneration of specific brain cells.\(^5\)
  - Chorea is the most visible and often the first presenting symptom of HD.\(^6\)
- While the precise mechanism of action by which tetrabenazine exerts its effect on chorea is unknown, Xenazine binds to a molecule known as VMAT2 (vesicular monoamine transporter 2), depleting dopamine from neuronal stores.\(^7\)
- Xenazine has been clinically proven to provide significant reduction in chorea associated with HD when compared to placebo.\(^7\)
- Xenazine has an FDA-mandated Risk Evaluation and Mitigation Strategy (REMS) to inform healthcare professionals of the increased risk of drug-associated depression and suicidality, proper titration and dosing, and the risk of drug-drug interactions with strong CYP2D6 inhibitors in patients taking Xenazine.\(^1\)

Clinical Study Highlights

- The pivotal trial was a 12-week U.S. multi-center, prospective, double-blind, placebo-controlled study of 84 patients with HD chorea.\(^7\)
  - The Unified Huntington’s Disease Rating Scale (UHDRS) is used to assess outcomes associated with treatment for HD symptoms, including chorea.\(^8\)
  - Xenazine showed significant improvement, defined as a ≥ 3.0 point change in UHDRS Total Chorea Score (TCS) (average of weeks 9 and 12) as compared to baseline, in HD chorea. This change was noted in 69% of patients (37 out of 54) taking Xenazine versus 23% (7 out of 30) taking placebo\(^6\) (\(P<0.0001\)).\(^7,10\)
  - The most commonly reported adverse events (AEs) were sedation/somnolence, fatigue, insomnia, depression, akathisia, anxiety, and nausea.\(^7\)
  - The withdrawal of Xenazine therapy at week 13 led to a recurrence of HD chorea, with total chorea scores returning to baseline levels.\(^10\)
- In an open-label continuation study, the safety and efficacy profiles of Xenazine reported in the controlled clinical trial were supported over 80 weeks for treatment of HD chorea.\(^9\) Of 75 patients enrolled, 45 completed the study.\(^9\)
In the open-label 80-week study, the most commonly reported moderate to severe adverse events (AEs) were sedation/somnolence, depressed mood, anxiety, insomnia, and akathisia. Parkinsonism and dysarthria scores were significantly increased at week 80 compared to baseline.

Data from the long-term extension study demonstrate a statistically significant reduction in TCS in patients compared to baseline who completed 80 weeks of Xenazine treatment (n=45), with a mean reduction in the TCS of 4.6 UHDRS units ($P<0.001$). At week 81, following a one-week washout period, the mean TCS of patients increased 5.3 UHDRS units compared to week 80 ($P<0.001$). This result is similar to the controlled clinical trial where TCS returned to baseline after discontinuation.

**Indications and Usage:**

XENAZINE is a medicine that is used to treat the involuntary movements (chorea) of Huntington’s disease. XENAZINE does not cure the cause of the involuntary movements, and it does not treat other symptoms of Huntington’s disease, such as problems with thinking or emotions.

It is not known whether XENAZINE is safe and effective in children.

**Important Safety Information:**

- **XENAZINE can cause serious side effects, including:**
  - depression
  - suicidal thoughts
  - suicidal actions
- You should not start taking XENAZINE if you are depressed (have untreated depression or depression that is not well controlled by medicine) or have suicidal thoughts.
- Pay close attention to any changes, especially sudden changes, in mood, behaviors, thoughts or feelings, or worsening depression. This is especially important when XENAZINE is started and when the dose is changed.

- Do not take XENAZINE if you have liver problems or are taking monoamine oxidase inhibitors or reserpine.

Ask your doctor or pharmacist if you are not sure. At least 20 days should pass after stopping reserpine before starting XENAZINE.

- Tell your doctor if you are pregnant, breast-feeding or have breast cancer. **Do not start any new medicines while taking XENAZINE without talking to your doctor first.**
- The need for therapy should be evaluated on an ongoing basis with your doctor. The dose of XENAZINE should be adjusted slowly over several weeks for a dose that is appropriate for you. Tell your doctor if you stop taking XENAZINE for more than 5 days. **Do not take another dose until you talk to your doctor. If your doctor thinks you need to take more than 50 mg of XENAZINE each day, you will need to have a blood test to see if a higher dose is right for you.**
- Neuroleptic Malignant Syndrome (NMS) is a potentially fatal side effect reported with XENAZINE. Call your doctor right away and go to the nearest emergency room if you develop these signs and symptoms that do not have another obvious cause: high fever, stiff muscles, problems thinking, very fast or uneven heartbeat, or increased sweating. XENAZINE should be stopped immediately if NMS is diagnosed.
- XENAZINE can also cause other serious side effects, including: parkinsonism (slight shaking, body stiffness, trouble moving or keeping your balance), restlessness (akathisia), trouble swallowing, irregular heartbeat, and dizziness due to blood pressure changes when you change position (orthostatic hypotension). Trouble swallowing may increase the risk of pneumonia. Uncontrolled movements called tardive dyskinesia (TD) may also develop in patients treated with XENAZINE. It is possible that the TD will not go away.
- Side effects such as irregular heartbeat, NMS, and parkinsonism, may be increased when using XENAZINE with other drugs (e.g., dopamine antagonists).
- Sleepiness is a common side effect of XENAZINE; **do not drive a car or operate dangerous machinery until you know how XENAZINE affects you.** Alcohol and other drugs may increase sleepiness caused by XENAZINE.
• Some side effects, such as depression, tiredness, trouble sleeping, sleepiness, parkinsonism, agitation, and restlessness (akathisia), may be dose-dependent. If the side effects don’t stop or lessen, your doctor should consider lowering the dose or stopping your XENAZINE. The most commonly reported side effects in studies with XENAZINE were sleepiness, trouble sleeping, depression, tiredness, anxiety, restlessness, agitation and nausea.

For more information, please see the full Prescribing Information, including Boxed Warning, the Medication Guide, or go to www.xenazineusa.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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SOURCES


7 Xenazine® (tetrabenazine) Full Prescribing Information. Deerfield, IL: Lundbeck.

