[XENAZINE® (tetrabenazine) Tablets]

Indications and Usage:

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

Important Safety Information:

WARNING: DEPRESSION AND SUICIDALITY

***See full prescribing information for complete boxed warning*.**

- **Increases the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease.**
- **Balance risks of depression and suicidality with the clinical need for control of chorea when considering the use of XENAZINE.**
- **Monitor patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior.**
- **Inform patients, caregivers, and families of the risk of depression and suicidality and instruct to report behaviors of concern promptly to the treating physician.**
- **Exercise caution when treating patients with a history of depression or prior suicide attempts or ideation.**
- **XENAZINE is contraindicated in patients who are actively suicidal, and in patients with untreated or inadequately treated depression.**

- XENAZINE is also contraindicated in patients who have impaired hepatic function or are taking monoamine oxidase inhibitors (MAOIs) or reserpine. XENAZINE should not be used in combination with an MAOI, or within a minimum of 14 days of discontinuing therapy with an MAOI. At least 20 days should elapse after stopping reserpine before starting XENAZINE.

- Prescribers should periodically re-evaluate the need for XENAZINE in their patients by assessing the beneficial effect on chorea and possible adverse effects, including worsening mood, cognition, rigidity, and functional capacity. XENAZINE should be titrated slowly over several weeks for a dose that is appropriate for each patient.

- Before a dose greater than 50 mg/day is administered, the patient's CYP2D6 metabolizer status should be determined. Do not exceed 50 mg/day or 25 mg/dose if XENAZINE is administered with a strong CYP2D6 inhibitor.

- XENAZINE therapy should be re-titrated if there is a treatment interruption of greater than 5 days, or a treatment interruption occurring due to a change in the patient's medical condition or concomitant medications.

- A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with XENAZINE. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria, rhabdomyolysis, and acute renal failure. The management of NMS should include immediate discontinuation of XENAZINE and other drugs not essential to concurrent therapy.

- XENAZINE can also cause other serious side effects, including: akathisia, restlessness, agitation, parkinsonism, and sedation/somnolence. These side effects may require a dose reduction or discontinuation of XENAZINE. Monitoring of vital signs on standing should be considered in patients who are vulnerable to hypotension. Dysphagia has also been reported with use of XENAZINE; some cases of dysphagia were associated with aspiration pneumonia.

- QT prolongation–related arrhythmias have been reported with use of XENAZINE. XENAZINE should not be used in combination with drugs known to prolong QTc (which in certain circumstances can lead to torsades de pointes and/or sudden death), in patients with congenital long QT syndrome, or in patients with a history of cardiac arrhythmias. A potentially irreversible syndrome of involuntary, dyskinetic movements called tardive

dyskinesia (TD) may develop in patients treated with neuroleptic drugs. If signs and symptoms of TD appear in a patient treated with XENAZINE, drug discontinuation should be considered. The risk of parkinsonism, NMS, and akathisia may be increased by concomitant use of XENAZINE and dopamine antagonists or antipsychotics.

- XENAZINE elevates serum prolactin concentrations. XENAZINE may induce sedation/somnolence which may impair the ability to drive or operate dangerous machinery. Alcohol or other sedating drugs can worsen sedation/somnolence.

- Some adverse events, such as depression, fatigue, insomnia, sedation/somnolence, parkinsonism, and akathisia, may be dose-dependent. If the adverse effect does not resolve or decrease, consideration should be given to lowering or discontinuing XENAZINE. The most commonly reported adverse events with XENAZINE compared to placebo were sedation/somnolence (31% vs 3%), fatigue (22% vs 13%), insomnia (22% vs 0%), depression (19% vs 0%), akathisia (19% vs 0%), anxiety (15% vs 3%), and nausea (13% vs 7%).

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

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