Tetrabenazine: Drug information

Brand Names: US

- Xenazine

Brand Names: Canada

- Nitoman

Pharmacologic Category

- Central Monoamine-Depleting Agent;
- Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, Oral:

- Xenazine: 12.5 mg [contains corn starch]
- Xenazine: 25 mg [scored; contains corn starch]

Generic: 12.5 mg, 25 mg

Generic Equivalent Available (US): Yes

Pricing: US

Tablets (Tetrabenazine Oral)

12.5 mg (per each): $75.59 - $78.81

25 mg (per each): $151.18 - $157.62

Tablets (Xenazine Oral)

12.5 mg (per each): $137.46

25 mg (per each): $274.91

Dosage Forms: Canada

Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet:

- Nitoman: 25 mg

Dosing: Adult

Dose should be individualized; titrate slowly

Chorea associated with Huntington disease: Oral:

Initial: 12.5 mg once daily in the morning, may increase to 12.5 mg twice daily after 1 week. Dosage may be increased by 12.5 mg daily at weekly intervals; daily doses >37.5 mg should be divided into 3 doses (maximum single dose: 25 mg)

Patients requiring doses >50 mg/day: Genotype for CYP2D6:

Extensive/intermediate metabolizers: Maximum: 100 mg/day; 37.5 mg/dose

Poor metabolizers: Maximum: 50 mg/day; 25 mg/dose

Concomitant use with strong CYP2D6 inhibitors (eg, fluoxetine, paroxetine, quinidine): Maximum: 50 mg/day; 25 mg/dose.

Note: If treatment is interrupted for >5 days, retitration is recommended. If treatment is interrupted for <5 days resume at previous maintenance dose.

Tardive dyskinesia (off-label use): Oral: **Note:** Dose is individualized based on efficacy and tolerance. Initial: 50 mg/day in divided doses; if needed, may increase daily dose by 50 mg every two weeks up to maximum of 150 mg/day in divided doses. Additional data may be necessary to further define the role of tetrabenazine in this condition (Kazamatsuri 1972; Godwin-Austen 1971; Ondo 1999).

Alternatively, an initial dose of 25 to 37.5 mg/day in 2 or 3 divided doses has been recommended with increases or decreases in increments of 12.5 mg/day at weekly intervals. Usual maximum tolerated dose: 75 mg/day in 3 divided doses; in very rare cases, doses up to 200 mg/day have been used (Nitoman Canadian product labeling 2014).

Tourette syndrome (Canadian labeling): Initial: 12.5 mg 2 to 3 times daily; may be increased by 12.5 mg daily at weekly intervals; should be increased to maximal tolerated and effective dose. Usual maximum tolerated dosage: 25 mg 3 times daily; maximum recommended dose: 200 mg/day

Dosing: Renal Impairment: Adult

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment: Adult

Use is contraindicated.

Dosing: Pediatric

Tourette syndrome (Canadian labeling): Children and Adolescents: Oral: Administer 50% of adult dose. Initial: 6.25 mg 2 to 3 times daily; may be increased by 6.25 mg daily at weekly intervals; should be titrated slowly to maximal tolerated and effective dose (dose is individualized).

Dosing: Renal Impairment: Pediatric

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment: Pediatric

Use is contraindicated.

Prescribing and Access Restrictions

Xenazine is available only through specialty pharmacies. For more information regarding the procurement of Xenazine, healthcare providers, patients, and caregivers may contact the Xenazine Information Center (XIC) at 1-888-882-6013 or at:

Health care providers:
http://www.xenazineusa.com/HCP/PrescribingXenazine/Default.aspx

Patients and caregivers: http://www.xenazineusa.com/AboutXenazine/Getting-Your-Prescription.aspx

Administration

Oral: May administer without regard to meals.

Use

Chorea associated with Huntington disease: Treatment of chorea associated with Huntington disease

Canadian labeling: Additional use (not in US labeling):Treatment of chronic tic disorders, including Tourette syndrome

Use: Off-Label

Tardive dyskinesia

Adverse Reactions

Note: Many adverse effects are dose-related and may resolve at lower dosages. Adverse effects reported for adults with chorea associated with Huntington disease.

>10%:

Central nervous system: Drowsiness (≤17% to ≤57%), sedation (≤17% to ≤57%), depression (19% to 35%), extrapyramidal reaction (15% to 33%), fatigue (22%), insomnia (22%), akathisia (19% to 20%), anxiety (15%), falling (15%)

Gastrointestinal: Nausea (13%)

Respiratory: Upper respiratory tract infection (11%)

1% to 10%:

Central nervous system: Drug-induced Parkinson's disease (3% to 10%), equilibrium disturbance (9%), irritability (9%), abnormal gait (4%), dizziness (4%), dysarthria (4%), headache (4%), obsessive rumination (4%)

Gastrointestinal: Dysphagia (4% to 10%), vomiting (6%), decreased appetite (4%), diarrhea (2%)

Genitourinary: Dysuria (4%)

Hematologic & oncologic: Bruise (6%)

Neuromuscular & skeletal: Bradykinesia (9%)

Respiratory: Bronchitis (4%), dyspnea (4%)

Miscellaneous: Laceration (6%, head)

Contraindications

Hepatic impairment; patients who are actively suicidal or who have untreated or inadequately treated depression; coadministration of MAOIs or use of tetrabenazine within 2 weeks of discontinuation of MAOI therapy; coadministration with reserpine, ≥20 days should pass after discontinuing reserpine before initiating tetrabenazine therapy; coadministration with deutetrabenazine or valbenazine

Canadian labeling: Additional contraindications (not in US labeling): Hypersensitivity to tetrabenazine or any component of the formulation; history or current episode of clinical depression unless under the care of a psychiatrist who is familiar with the patient's disorder and tetrabenazine’s pharmacology

Warnings/Precautions

Concerns related to adverse effects:

- Akathisia: Use has been associated with akathisia; monitor for signs and symptoms of restlessness and agitation. Dosage reduction or discontinuation may be necessary.

- CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery or driving).

- Depression/suicidal ideation: **[US Boxed Warning]: Use can increase risk for depression and suicidal thoughts and behavior in patients with Huntington disease; closely monitor for emergence or worsening of depression, suicidality, or unusual behavioral changes. Use with caution in patients with a history of depression or prior suicide attempts or ideation; monitor patients closely for new or worsening signs or symptoms of depression. Use is contraindicated in patients who are actively suicidal, and in patients with untreated or inadequately treated depression.** Consider discontinuing use if depression/suicidal ideation does not resolve.

- Esophageal dysmotility/aspiration: Use has been associated with esophageal dysmotility, dysphagia, and aspiration; use with caution in patients at risk of aspiration pneumonia.

- Neuroleptic malignant syndrome (NMS): Use may be associated with NMS; monitor for mental status changes, fever, muscle rigidity and/or autonomic instability. Discontinue with confirmed NMS; may recur with reintroduction of treatment; monitor carefully.

- Ophthalmic effects: Binds to melanin-containing tissues in animal studies; may result in accumulation and toxicity with extended use and long-term ophthalmic effects. Clinical relevance and monitoring recommendations are unknown.

- Orthostatic hypotension: May cause orthostatic hypotension; monitor patients at risk closely.

- Parkinsonism: May cause parkinsonism symptoms (ie, bradykinesia, hypertonia, rigidity). Dose reduction or discontinuation of therapy may be necessary.

- QT prolongation: Has been shown to prolong the QT interval alone (minimal) and with other drugs with comparable effects on the QT interval (additive). Avoid use in patients with congenital QT prolongation, a history of cardiac arrhythmias, or concomitant drugs known to cause QT prolongation.

- Tardive dyskinesia: May cause dyskinetic movements; discontinue use if signs and symptoms of tardive dyskinesia occur.

Special populations:

- CYP2D6 poor metabolizers: CYP2D6 poor metabolizers have increased levels of primary drug metabolites. Patients should be tested for the CYP2D6 gene prior to initiating doses >50 mg/day; maximum dosage should not exceed 50 mg/day in poor metabolizers.

- Huntington disease: May worsen mood, cognition, rigidity, and functional capacity in patients with Huntington disease, which can be difficult to differentiate from progression of the underlying disease. Underlying chorea may improve over time in some patients, thereby decreasing the need for therapy. Re-evaluate patients need for treatment by periodically assessing the effect on chorea and possible adverse effects. Dose reduction or discontinuation of therapy may be necessary.

Other warnings/precautions:

- Appropriate use: Should not be used to treat levodopa-induced dyskinesia.

Mechanism of Action

Acts as a reversible inhibitor of the human vesicular monamine transporter type 2 (VMAT-2) and thereby decreases the uptake of monoamines (including dopamine, serotonin, norepinephrine, and histamine) into synaptic vesicles and depletes the monoamine stores; hydroxytetrabenazine (HTBZ) also inhibits VMAT-2; weak binding affinity for dopamine D_2 receptors.

Brand Names: International

- Choreazine (JP);

- Dystardis (AT);

- Feinardon (AR);

- Motetis (HU);

- Nitoman (DE, DK, ES, IE, PT, TW);

- Revocon (IN, MT);

- Tetmodis (AT, CZ, ES, HR, IE, LT, LV, MT, RO);
- Tetrazin (BD);
- Trenazin (AR);
- Xenazina (IT);
- Xenazine (BB, FR, GB, HU, IL, KR, LB, LT, MT, NL, NZ, PL, SI, SK)