
TETRABENAZINE (Xenazine) Fact Sheet [G]

Bottom Line:

Tetrabenazine was the original VMAT inhibitor brought to market and approved for the treatment of Huntington's disease. It's an off-label alternative to deutetrabenazine and valbenazine for treating tardive dyskinesia (TD). Although it's much less expensive, it requires more frequent dosing and may have a higher likelihood of causing depression.

FDA Indications:

Huntington's chorea.

Off-Label Uses:

TD; Tourette's and other tic disorders.

Dosage Forms:

Tablets (G): 12.5 mg, 25 mg.

Dosage Guidance:

Start 12.5 mg QAM for one week. Titrate at weekly intervals by 12.5 mg/day increments; increase to maximum dose of 100 mg/day. Should be given in divided doses of BID to QID with no more than 25 mg/dose.

Monitoring: ECG if cardiac disease.

Cost: \$\$\$\$

Side Effects:

- Most common: Sedation, somnolence, fatigue, diarrhea.
- Serious but rare: Risk of depression and suicidality; QT interval prolongation; caution in those with increased risk (congenital long QT syndrome, electrolyte disturbances, poor 2D6 metabolizers, concomitant 2D6 inhibitors).

Mechanism, Pharmacokinetics, and Drug Interactions:

- Reversible inhibitor of vesicular monoamine transporter 2 (VMAT2). This prevents VMAT2 from transporting monoamines including dopamine back into presynaptic vesicles, resulting in metabolism of monoamines, ultimately leading to depletion of monoamine stores and less dopamine being around. This treats TD symptoms, which are likely caused by hypersensitivity to dopamine.
- Metabolized primarily by CYP2D6; $t_{1/2}$: 5–7 hours.
- Avoid MAOIs. Decrease tetrabenazine dose in presence of 2D6 inhibitors or poor metabolizers.

Clinical Pearls:

- One double-blind study and seven open-label studies support the efficacy of tetrabenazine for TD.
- Increased depression and suicidality have been reported with tetrabenazine; use caution in patients with a history of depression and monitor all patients for symptoms.
- Genotyping for 2D6 metabolism is recommended for doses >50 mg/day.

Fun Fact:

Tetrabenazine was initially developed in the 1950s as an antipsychotic to replace reserpine because it had less severe depressive and hypotensive effects.