
DEUTETRABENAZINE (Austedo) Fact Sheet

Bottom Line:

Deutetrabenazine was the second of the VMAT inhibitors to be approved for the treatment of tardive dyskinesia (TD) in 2017. Its advantage over off-label tetrabenazine is less frequent dosing and less likelihood of causing depression. However, it is extremely expensive—about \$7,000/month as opposed to \$700/month for tetrabenazine.

FDA Indications:

TD; Huntington's chorea.

Off-Label Uses:

Tourette's and other tic disorders.

Dosage Forms:

- **Tablets:** 6 mg, 9 mg, 12 mg.
- **ER tablets:** 6 mg, 12 mg, 24 mg.

Dosage Guidance:

- **IR:** Start 6 mg BID with food. Titrate at weekly intervals by 6 mg/day increments; increase to maximum dose of 48 mg/day with food (doses \geq 12 mg/day should be divided BID).
- **ER:** Start 12 mg QD with food. Titrate at weekly intervals by 6 mg/day increments; increase to maximum dose of 48 mg QD with food.
- Decrease deutetrabenazine dose in presence of 2D6 inhibitors or poor metabolizers (max 36 mg/day).

Monitoring: ECG if cardiac disease.

Cost: \$\$\$\$

Side Effects:

- Most common: Sedation, somnolence, fatigue, diarrhea.
- Serious but rare: 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; $t_{1/2}$: 9–10 hours.
- Avoid MAOIs.

Clinical Pearls:

- Deutetrabenazine is a deuterated form of tetrabenazine (Xenazine), a similar VMAT2 inhibitor, which is approved for treatment of Huntington's chorea.
- Increased depression and suicidality have been reported with tetrabenazine. Paucity of long-term data with deutetrabenazine makes it difficult to determine whether it will pose these concerns as well.
- A one-year course costs over \$80,000.

Fun Fact:

Chemistry course refresher! Deuterated drugs are created by replacing one or more of the hydrogen atoms of the drug molecule with deuterium. This may significantly slow drug metabolism, resulting in a longer half-life of the drug.