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## VALBENZAZINE (Ingrezza) Fact Sheet

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### Bottom Line:

Valbenazine was the first 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 (once daily) 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.

### Off-Label Uses:

Tourette's and other tic disorders; Huntington's chorea.

### Dosage Forms:

**Capsules:** 40 mg, 60 mg, 80 mg.

### Dosage Guidance:

Start 40 mg once daily. After one week, ↑ to usual dose of 80 mg once daily.

**Monitoring:** ECG if cardiac disease.

**Cost:** \$\$\$\$

### Side Effects:

- Most common: Sedation, somnolence, akathisia, restlessness.
- Serious but rare: QT interval prolongation; caution in those with increased risk (congenital long QT syndrome, electrolyte disturbances, poor 2D6 metabolizers, concomitant 2D6 or 3A4 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 by CYP2D6 and 3A4 (primary); t<sub>1/2</sub>: 15–22 hours.
- Avoid MAOIs. Decrease valbenazine dose in presence of 2D6 or 3A4 inhibitors.

### Clinical Pearls:

- Clinical trials of valbenazine for TD found an impressive 40% response rate (meaning a 50% improvement in TD symptoms) vs a 9% response rate for patients taking placebo.
- Increased depression and suicidality have been reported with use of a similar VMAT2 inhibitor, tetrabenazine (Xenazine, used for Huntington's chorea). Paucity of long-term data with valbenazine makes it difficult to determine whether this will be of concern with valbenazine as well.
- A one-year course costs over \$80,000.

### Fun Fact:

Reserpine, an antihypertensive and antipsychotic used in the 1950s, was a VMAT1/VMAT2 inhibitor. Cases of depression reported with its use led to the monoamine hypothesis of depression.