



**AUSTEDO  
(deutetrabenazine)**

**RATIONALE FOR INCLUSION IN PA PROGRAM**

**Background**

Austedo (deutetrabenazine) is FDA approved for the treatment of chorea (involuntary jerky movements) associated with Huntington's disease (HD). Austedo is also indicated for the treatment of tardive dyskinesia (TD). HD is a progressive neurological disorder which may cause changes in mood, cognition, chorea, rigidity, and functional capacity over time. Although the exact mechanism is unknown, Austedo is believed to exert its effects through reversible depletion of monoamines from nerve terminals. Major circulating metabolites of Austedo ( $\alpha$ -dihydrotetrabenazine [HTBZ] and  $\beta$ -HTBZ) reversibly inhibit VMAT2, which decreases the uptake of monoamines into synaptic vesicles and depletes monoamine stores (such as dopamine, serotonin, norepinephrine, and histamine) (1).

**Regulatory Status**

FDA-approved indications: Austedo is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for: (1)

- The treatment of chorea associated with Huntington's disease
- The treatment of tardive dyskinesia in adults

Austedo carries a boxed warning regarding the increased risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease. The risks of depression and suicidality should be balanced with the clinical need of Austedo therapy for the control of chorea. Austedo is contraindicated in patients who are actively suicidal, and in patients with untreated or inadequately treated depression (1).

Prescribers should periodically re-evaluate the need for Austedo in their patients by assessing the effect on chorea and possible adverse effects, including sedation/somnolence, depression and suicidality, parkinsonism, akathisia, restlessness, and cognitive decline. It may be difficult to distinguish between adverse reactions and progression of the underlying disease; decreasing the dose or stopping the drug may help the clinician to distinguish between the two possibilities. In some patients, the underlying chorea itself may improve over time, decreasing the need for Austedo (1).

Austedo is contraindicated in patients with impaired hepatic function. Austedo is also

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contraindicated in patients taking MAOIs, reserpine or tetrabenazine. Austedo should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with an MAOI. Reserpine binds irreversibly to VMAT2 and the duration of its effect is several days. Prescribers should wait for chorea to reemerge before administering Austedo to help reduce the risk of overdose and major depletion of serotonin and norepinephrine in the central nervous system. At least 20 days should elapse after stopping reserpine before starting Austedo. Austedo may be initiated the day following discontinuation of tetrabenazine (1).

Austedo should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. Also, concomitant use of strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion) has been shown to increase the systemic exposure to the active dihydro-metabolites of deutetrabenazine by approximately 3-fold. The daily dose of Austedo should not exceed 36 mg per day in patients taking strong CYP2D6 inhibitors. Austedo should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval (1).

When clinically appropriate, pharmacologic interventions may be considered for patients who are developing signs of TD. The two main strategies are discontinuation of the offending drug and switching from first to second generation antipsychotic drugs. For patients with a diagnosis of TD, additional pharmacologic interventions include the following: use of benzodiazepines, botulinum toxin injections, tetrabenazine, or anticholinergic drugs to control symptoms of TD, or paradoxically, resuming treatment with antipsychotic drugs in order to suppress TD (2).

Two commonly used scales, the Abnormal Involuntary Movement Scale (AIMS) and Extrapyramidal Symptom Rating Scale (ESRS) are used to evaluate the severity of the tardive dyskinesia (3-4).

Safety and efficacy of Austedo have not been established in pediatric patients (1).

**Summary**

Austedo (deutetrabenazine) is approved for the treatment of chorea associated with Huntington's disease (HD) or tardive dyskinesia (TD). Major circulating metabolites of Austedo ( $\alpha$ -dihyrotetrabenazine [HTBZ] and  $\beta$ -HTBZ) reversibly inhibit VMAT2, which decreases the uptake



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of monoamines into synaptic vesicles and depletes monoamine stores. Austedo carries a boxed warning regarding the increased risk of depression and suicidal thoughts and behavior (suicidality) in patients. Austedo is contraindicated in patients with impaired hepatic function. Austedo is also contraindicated if used in combination with MAOIs, reserpine, or tetrabenazine. Safety and efficacy of Austedo have not been established in pediatric patients (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Austedo while maintaining optimal therapeutic outcomes.

### **References**

1. Austedo [package insert]. Parsippany, NJ: Teva Neuroscience, Inc; July 2024.
2. G Gharabawi, C Bossie, et al. Abnormal Involuntary Movement Scale (AIMS) and Extrapyrimal Symptom Rating Scale (ESRS): Cross-scale comparison in assessing tardive dyskinesia. Schizophrenia Research 77 (2005) 119–128.
3. G Chouinard, H Margolese. Manual for the Extrapyrimal Symptom Rating Scale (ESRS). Schizophrenia Research 76 (2005) 247–265.
4. UpToDate: Tardive dyskinesia: Prevention, prognosis and treatment. January 2021.