RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Austedo is FDA approved for the treatment of chorea (involuntary jerky movements) associated with Huntington's disease (HD). 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 anti-chorea effects through reversible depletion of monoamines from nerve terminals. Major circulating metabolites of Austedo (α-dihydrotetrabenazine [HTBZ] and β-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 indication: Austedo is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of chorea associated with Huntington’s disease (1).

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 (1).

Austedo is 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.
AUSTEDO
(deutetrabenazine)

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).

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

Summary
Austedo is approved for the treatment of chorea associated with Huntington’s disease (HD). Major circulating metabolites of Austedo (α-dihydrotetrabenazine [HTBZ] and β-HTBZ) reversibly inhibit VMAT2, which decreases the uptake 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