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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	April 14, 2017
Subject:	Austedo	**Page:**	1 of 6

Last Review Date: March 12, 2021

Austedo

Description

Austedo (deutetrabenazine)

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 (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: (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 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, and the maximum single dose of Austedo should not exceed 18 mg 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).

Related policies
Ingrezza, Xenazine

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Austedo may be considered **medically necessary** in patients 18 years of age or older with Huntington's chorea or moderate to severe tardive dyskinesia, and if the conditions indicated below are met.

Austedo may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age: 18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Moderate to severe tardive dyskinesia

   AND ALL of the following:
   a. Inadequate treatment response, intolerance or contraindication to **ONE** of the following:
      i. Benzodiazepine
      ii. Second generation antipsychotic (i.e. Seroquel, clozapine)
      iii. Xenazine
   b. Documented baseline evaluation of the condition using **ONE** of the following scoring tools:
      i. Abnormal Involuntary Movement Scale (AIMS)
      ii. Extrapyramidal Symptom Rating Scale (ESRS)
   c. Prescriber has reduced the dosage or discontinued all causative medications including antipsychotic medication and metoclopramide (Reglan)
   d. Patient has a functional impairment that justifies treatment with Austedo

2. Chorea associated with Huntington's disease

AND NONE of the following for **ALL Diagnoses**:

1. Actively suicidal
2. Untreated or inadequately treated depression
3. Concomitant use of a MAOI (monoamine oxidase inhibitor) (must be >14 days post discontinuing therapy)
4. Concomitant use of reserpine (must be >20 days post discontinuing therapy)
5. Hepatic impairment
6. Dual therapy with other vesicular monoamine transporter 2 (VMAT2) inhibitors

Prior – Approval *Renewal* Requirements

Age: 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Tardive dyskinesia

   AND ALL of the following:
   a. Documented improvement using **ONE** of the following scores:
      i. Abnormal Involuntary Movement Scale (AIMS)
      ii. Extrapyramidal Symptom Rating Scale (ESRS)

2. Chorea associated with Huntington's disease

AND NONE of the following for **ALL Diagnoses**:

1. Actively suicidal
2. Untreated or inadequately treated depression
3. Concomitant use of a MAOI (monoamine oxidase inhibitor) (must be >14 days post discontinuing therapy)
4. Concomitant use of reserpine (must be >20 days post discontinuing therapy)
5. Hepatic impairment
6. Dual therapy with other vesicular monoamine transporter 2 (VMAT2) inhibitors

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 360 tablets per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

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 (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

1. Austedo [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; December 2020.
2. G Gharabawi, C Bossie, et al. Abnormal Involuntary Movement Scale (AIMS) and Extrapyramidal Symptom Rating Scale (ESRS): Cross-scale comparison in assessing tardive dyskinesia. Schizophrenia Research 77 (2005) 119–128. Accessed February 2021.
3. G Chouinard, H Margolese. Manual for the Extrapyramidal Symptom Rating Scale (ESRS). Schizophrenia Research 76 (2005) 247–265. Accessed February 2021.

4. UpToDate: Tardive dyskinesia: Prevention, prognosis and treatment. January 2021. Accessed February 2021.

Policy History

Date	Action
April 2017	Addition to PA
June 2017	Annual editorial review Change of Severe hepatic impairment requirement to Hepatic impairment per SME
September 2017	Annual Review Addition of indication of tardive dyskinesia and no dual therapy with other vesicular monoamine transporter 2 (VMAT2) inhibitors and change in quantity limits of the 6mg from 720 to 450 tabs Addition of prescriber has reduced the dosage or cessation of all offending medications including antipsychotic medication and metoclopramide (Reglan); and patient has a functional impairment that justifies treatment with Austedo per SME
December 2017	Annual review
March 2019	Revised quantity limits to 4 per day of all strengths
June 2019	Annual review
May 2020	Removed specific AIMS and ESRS score requirements per FEP
June 2020	Annual review
March 2021	Annual editorial review and reference update

Keywords

This policy was approved by the FEP® Pharmacy Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.