Austedo

(deutetrabenazine)

New Product Slideshow

MPR

Introduction

- **Brand name:** Austedo
- **Generic name:** Deutetrabenazine
- **Pharmacological class:** Vesicular monoamine transporter 2 (VMAT2) inhibitor
- **Strength and Formulation:** 6mg, 9mg, 12mg; tablets
- **Manufacturer:** Teva Pharmaceuticals
- **How supplied:** Bottle—60
- **Legal Classification:** Rx

Indications

- Huntington’s chorea

Dosage & Administration

- Swallow whole
- Take with food
- Individualize
- Initially 6mg once daily
- May titrate at weekly intervals by 6mg/day increments; max 48mg/day

Dosage & Administration

- Total daily dose ≥12mg: give in 2 divided doses
- Switching from tetrabenazine: see full labeling
- **Concomitant strong CYP2D6 inhibitors** or **poor CYP2D6 metabolizers:** max 36mg/day (max 18mg/dose)

Considerations for Special Populations

- **Pregnancy:** Inadequate data on the developmental risk associated with Austedo in pregnant women
- **Nursing mothers:** Consider benefits and adverse effects on the breastfed infant
- **Pediatric:** Not established
- **Elderly:** Insufficient number of subjects included in studies

Contraindications

- Depression
- Suicidal ideation
- Hepatic impairment
- During or within 14 days of discontinuing an MAOI
- During or within 20 days of discontinuing reserpine
- Concomitant tetrabenazine

Warnings/Precautions

- **Increased risk** of depression and suicidality; monitor for emergence or worsening of depression, suicidality, or unusual changes in behavior
- **Avoid** in congenital long QT syndrome or history of cardiac arrhythmias
- Bradycardia
- Hypokalemia
- Hypomagnesemia
- **Monitor** for neuroleptic malignant syndrome (NMS); discontinue and treat if develops

Warnings/Precautions

- **Reduce dose** or **discontinue** if akathisia or parkinsonism develops
- History of breast cancer
- **Consider discontinuing** if symptomatic hyperprolactinemia develops
- Reevaluate periodically
- Poor CYP2D6 metabolizers

Interactions

- See **Contraindications**
- **Avoid** concomitant other drugs that can cause QT prolongation (eg, chlorpromazine, haloperidol, thioridazine, ziprasidone, moxifloxacin, quinidine, procainamide, amiodarone, sotalol)

Interactions

- **Potentiated** by strong CYP2D6 inhibitors (eg, quinidine, paroxetine, fluoxetine, bupropion)
- **Increased risk** of parkinsonism, NMS, akathisia with dopamine antagonists or antipsychotics
- Additive CNS effects with alcohol or other sedatives

Adverse Reactions

- Somnolence
- Diarrhea
- Dry mouth
- Fatigue
- UTI
- Insomnia
- Anxiety
- Constipation
- Contusion
- NMS
- QTc prolongation
- Akathisia
- Agitation
- Restlessness
- Parkinsonism
- Possible ophthalmic effects

Mechanism of Action

- Deutetrabenazine exerts its action after getting metabolized to α-dihydrotetrabenazine (HTBZ) and β-HTBZ, its major metabolites that reversibly inhibit VMAT2, which results in decreased uptake of monoamines (eg, dopamine, serotonin, norepinephrine, histamine) into synaptic vesicles and depletion of monoamine stores
- The exact mechanism of deutetrabenazine's anti-chorea effects is unknown, but it is believed to be related to the reversible monoamine depletion

Clinical Trials

- The efficacy of Austedo was evaluated in a randomized, double-blind, placebo-controlled, multicenter trial (**Study 1**) in 90 patients with Huntington's chorea
- Patients were randomized to receive either Austedo or placebo for 12 weeks, followed by a 1-week washout period

Clinical Trials

- In the Austedo group, patients initially received a dose of 6mg once daily and titrated upward in 6mg increments at weekly intervals until a satisfactory dose was achieved, intolerable side effects occurred, or until a maximum dose of 48mg/day was reached

Clinical Trials

- The **primary efficacy endpoint** was the Total Maximal Chorea (TMC) Score, an item of the Unified Huntington's Disease Rating Scale, which rates chorea from 0–4 (0 represents no chorea) for 7 different parts of the body (total score range: 0–28)

Clinical Trials

- At **endpoint**, treatment with Austedo showed improvement in the TMC Score as compared to placebo
- A change in total score from baseline to maintenance period (average of Week 9 and Week 12) was approximately 4.4 units in Austedo-treated patients vs. 1.9 units in the placebo group
- The **treatment effect** of –2.5 units was statistically significant ($P<0.0001$)

Clinical Trials

- Furthermore, **51%** of patients treated with Austedo rated their overall Huntington's disease symptoms as "Much Improved" or "Very Much Improved" in a patient-rated global impression of change assessment, vs. **20%** in the placebo group
- In a physician-rated clinical global impression of change assessment, 42% vs. 13%, respectively, rated their symptoms as "Much Improved" or "Very Much Improved" at the end of treatment
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/austedo/drug/34665/