CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
3Q17- July – August

BRAND NAME
Austedo™

GENERIC NAME
deutetrabenazine

MANUFACTURER
Teva Pharmaceuticals, USA.

DATE OF APPROVAL
April 3, 2017

PRODUCT LAUNCH DATE
April 3, 2017

REVIEW TYPE

☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Reviews for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
Austedo (deutetrabenazine) is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of chorea associated with Huntington's disease.

OFF-LABEL USES (possible)
Tardive Dyskinesia, Tourette's syndrome

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CLINICAL EFFICACY[1]

The efficacy of Austedo in the treatment of chorea associated with Huntington's disease was established in a 12-week Phase 3, randomized, double-blind, placebo-controlled, multi-center trial (N=90) that evenly randomized patients to receive either placebo or Austedo 6 mg per day, titrated to a maximum dose of 48 mg per day.

The primary outcome of the study was change from baseline to maintenance phase in the Total Maximal Chorea Score (TMCS), which is one item within the Unified Huntington's Disease Rating Scale (UHDRS). The maintenance phase is defined as the average of the score from Week 9 and Week 12. The TMCS is rated on a scale from 0 to 4 (with 0 representing no chorea) for 7 different parts of the body. The total score ranges from 0 to 28. Secondary outcomes included the proportion of patients who achieved treatment success on the Patient Global Impression of Change (PGIC) scale or the Clinical Global Impression of Change (CGIC) scale, change in the SF-36 physical functioning subscale and the change in the Berg Balance Test.

Study patients taking Austedo experienced an improvement from baseline to maintenance in the TCMS of –4.4 (95% CI, –5.3 to –3.6) vs. the placebo group improvement of –1.9 (95% CI, –2.8 to –1.1), with a treatment difference (TD) of –2.5 (95% CI, –3.7 to –1.3; P < .001). On the PGIC scale, 23 patients (51%) in the Austedo group reported treatment success vs. 9 patients (20%) in the placebo group, with a TD of 31.1% (95% CI, 12.4-49.8; P = .002). On the CGIC scale: 19 patients (42%) in the Austedo group reported treatment success vs. 6 patients (13%) in the placebo group, with a TD of 28.9% (95% CI, 11.4 to 46.4; P = .002). On the SF-36 physical functioning subscale, Austedo-treated patients improved by 0.7 (95% CI, –2.0 to 3.4) for Austedo and worsened by –3.6 (95% CI,–6.4 to –0.8) for the placebo group, with a TD of 4.34 (95% CI, 0.4 to 8.3; P = .03). On the Berg Balance Test, Austedo-treated patients improved by 2.2 (95% CI, 1.3-3.1) for Austedo vs. 1.3 (95% CI, 0.4-2.2) for placebo, with a TD of 1.0 (95% CI, –0.3 to 2.3; P =0.14 [not statistically significant]).

Zero Austedo-treated patients and one placebo patient withdrew from the study due to lack of efficacy. Meanwhile, one patient each from the Austedo group and the placebo group withdrew from the study due to adverse effects.

CONTRAINDICATIONS

- Suicidal patients with untreated or inadequately treated depression;
- Hepatic impairment
- Monoamine oxidase inhibitors (MAOIs). Austedo should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with an MAOI;
- Concomitant use with reserpine. At least 20 days should elapse after stopping reserpine before starting Austedo;

- Taking tetrabenazine (Xenazine®).

BLACK BOX WARNINGS

- Increased risk of depression and suicidal thoughts and behavior (suicidality);
- Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in Huntington's disease.

DRUG INTERACTIONS

- Strong CYP2D6 Inhibitors (e.g., paroxetine, fluoxetine, quinidine, bupropion)
- Reserpine
- MAOIs
- Neuroleptic Drugs
- Alcohol or Other Sedating Drugs
- Drugs that Cause QTc Prolongation
- Tetrabenazine

ADVERSE REACTIONS

Adverse reactions occurring in 4% or more of patients treated with Austedo, and with a greater incidence than in patients on placebo, were somnolence, diarrhea, dry mouth, fatigue, urinary tract infection, insomnia, anxiety, constipation and contusion.

The most common adverse reaction resulting in dose reduction in patients receiving Austedo was dizziness (4%).

DOSAGE AND ADMINISTRATION

Initially 6 mg PO once daily. Increase the dosage at weekly intervals by increments of 6 mg/day to a maximum total daily dose of 48 mg. Do not exceed 18 mg/dose or 36 mg/day in patients who are poor CYP2D6 metabolizers. Administer total daily dosages of 12 mg or more in two divided doses.

PRODUCT AVAILABILITY

Tablets: 6 mg, 9 mg, 12 mg

THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
Xenazine® (tetrabenazine)	Initially, 12.5 mg PO each morning. After one week, increase to 12.5 mg PO twice daily up to 100 mg/day PO in	Austedo is the deuterated form of Xenazine.

	patients who express CYP2D6; 50 mg/day PO in patients who do not express CYP2D6.	

Utilization Management Recommendation
• There is significant potential for inappropriate use and utilization management should be considered for the following reason(s): ☒ To ensure appropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcomes. i. Potential exists for off-label usage for Tourette's syndrome, for which supportive data is lacking. • Recommended utilization management tool: ☒ Prior authorization
Product Comparison
• CPAC score: 58 vs. Xenazine - Equal therapeutic outcomes are anticipated • Equal therapeutic outcomes are anticipated; therefore, it would be clinically appropriate to provide equal access to both Austedo and Xenazine, or to require a trial of one before the other.

[1] Huntington Study Group. Effect of deutetrabenazine on chorea among patients with Huntington Disease. JAMA July 5, 2016;316(1):40-50.