Clinical Policy Title:	deutetrabenazine
Policy Number:	RxA.349
Drug(s) Applied:	Austedo®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Deutetrabenazine (Austedo®) is a vesicular monoamine transporter 2 (VMAT2) inhibitor. Deutetrabenazine is indicated for the treatment of:

- Chorea associated with Huntington's disease
- Tardive dyskinesia in adults

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
deutetrabenazine (Austedo®)	Huntington's chorea	6 mg/day (6 mg once daily) orally; may be increased weekly by increments of 6 mg/day to a maximum of 48 mg/day	48 mg/day (18 mg/dose and 36 mg/day in poor CYP2D6 metabolizers and strong CYP2D6 inhibitors
	Tardive dyskinesia	12 mg/day (6 mg twice daily) orally; may be increased weekly by increments of 6 mg/day to a maximum of 48 mg/day	48 mg/day (18 mg/dose and 36 mg/day in poor CYP2D6 metabolizers and strong CYP2D6 inhibitors

Dosage Forms

- Tablets: 6 mg, 9 mg, 12 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Huntington's Disease (must meet all)**:**

1. Diagnosis of chorea associated with Huntington's disease;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;

4. Failure of tetrabenazine at up to 100 mg/day, unless contraindicated or clinically significant adverse effects are experienced;
5. At the time of request, reserpine, MAOIs, tetrabenazine, or valbenazine is not prescribed concurrently;
6. Dose does not exceed 48 mg/day.

Approval duration
Commercial: 6 months
Medicaid: 6 months

B. Tardive Dyskinesia (must meet all)**:**

1. Diagnosis of tardive dyskinesia secondary to a centrally acting dopamine receptor blocking agent (DRBA);
   **See Appendix F; if the offending agent is not included in Appendix F, the status of the agent as a centrally acting DRBA as well as its association with tardive dyskinesia should be confirmed.*
2. Prescribed by or in consultation with a psychiatrist or neurologist;
3. Age ≥ 18 years;
4. At the time of request, reserpine, MAOIs, tetrabenazine, or valbenazine is not prescribed concurrently;
5. Dose does not exceed 48 mg/day.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Reserpine, MAOIs, tetrabenazine or valbenazine is not prescribed concomitantly;
4. If request is for a dose increase, new dose does not exceed 48 mg/day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
DRBA: dopamine receptor blocking agent
FDA: Food and Drug Administration
MAOI: monoamine oxidase inhibitor
VMAT: vesicular monoamine transporter

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
tetrabenazine (Xenazine®)	**Huntington's Chorea** 12.5 mg orally once daily for 1 week, then 12.5 mg twice daily, then titrated by 12.5 mg weekly to a	25 mg/dose and 50 mg/day (37.5 mg/dose and 100 mg/day for CYP2D6 intermediate or extensive metabolizers)

	tolerated dose up to maximum of 50 mg/day (100 mg/day for CYP2D6 intermediate or extensive metabolizers)	

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Suicidal, or untreated/inadequately treated depression in patients with Huntington's disease.
  - Hepatic impairment.
  - Taking reserpine. At least 20 days should elapse after stopping reserpine before starting Austedo®.
  - Taking monoamine oxidase inhibitors (MAOIs). Austedo® should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with an MAOI.
  - Taking tetrabenazine (Xenazine®) or valbenazine.

- Boxed warning(s):
  - Depression and suicidality in patients with Huntington's Disease.

APPENDIX D: General Information

- Medication-induced movement disorders, including tardive dyskinesia, are organized in the DSM V as follows: neuroleptic-induced parkinsonism/other medication-induced parkinsonism, neuroleptic malignant syndrome, medication-induced acute dystonia, medication-induced acute akathisia, tardive dyskinesia, tardive dystonia/tardive akathisia, medication-induced postural tremor, other medication-induced movement disorder, antidepressant discontinuation syndrome, and other adverse effects of medication.
- Tardive dyskinesia is a type of movement disorder that occurs secondary to therapy with centrally acting DRBAs (see Appendix E).
- Typical therapeutic drug classes containing DRBAs include first- and second-generation antipsychotics, antiemetics, and tri-cyclic antidepressants (see Appendix F).
- Other therapeutic drug classes containing agents that have been variously associated with movement disorders are listed below:
  - Antiarrhythmics
  - Antibiotics
  - Anticholinergics
  - Antidepressants
  - Antiepileptics
  - Antihistamines
  - Antimanics
  - Bronchodilators
  - Calcium channel blockers
  - Central nervous system stimulants
  - Dopamine agonists
  - Dopamine depleting agents

- Dopaminergics
- Glucocorticoids
- Immunosuppressants
- Mood stabilizers
- Muscle relaxants
- Oral contraceptives

APPENDIX E: DSM-V Definition of Tardive Dyskinesia

- **Tardive Dyskinesia *(ICD-9 333.85/ICD-10 G24.01)***
  - Involuntary athetoid or choreiform movements (lasting at least a few weeks) generally of the tongue, lower face and jaw, and extremities (but sometimes involving the pharyngeal, diaphragmatic, or trunk muscles) developing in association with the use of a neuroleptic medication for at least a few months.
  - Symptoms may develop after a shorter period of medication use in older persons. In some patients, movements of this type may appear after discontinuation, or after change or reduction in dosage, of neuroleptic medications, in which case the condition is called neuroleptic withdrawal emergent dyskinesia. Because withdrawal emergent dyskinesia is usually time limited, lasting less than 4-8 weeks, dyskinesia that persists beyond this window is considered to be tardive dyskinesia.

APPENDIX F: Centrally Acting Dopamine Receptor Blocking Agents (Neuroleptics)

Pharmacologic Class	Therapeutic Class		
	First-generation (typical) antipsychotics	Antiemetic agents	Tri-cyclic antidepressants
Phenothiazine	Chlorpromazine Fluphenazine Perphenazine Thioridazine Thiothixene Trifluoperazine	Chlorpromazine Perphenazine Prochlorperazine Promethazine* Thiethylperazine	Amoxapine†
Butryophenone	Haloperidol	Droperidol Haloperidol**	
Substituted benzamide		Metoclopromide Trimethobenzamide	
Dibenzazepine	Loxapine		
Diphenylbutylpiperidine	Pimozide		
Second-generation (atypical) antipsychotics			
Quinolone	Aripiprazole, brexpiprazole		
Dibenzazepine	Asenapine		
Piperazine	Cariprazine		
Dibenzodiazephine	Clozapine, quetiapine		
Benzisoxazole	Iloperidone		

Benzisothiazole	Lurasidone, ziprasidone
Thienobenzodiazepine	Olanzapine
Pyrimidinone	Paliperidone, risperidone

**First generation H1 antagonist*
***Off-label use*
†A dibenzoxapine that shares properties with phenothiazines

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 3. Age symbols and approval duration was updated in initial and continued therapy	08/26/2020	09/14/2020

approval. 4. Appendix C contraindications and boxed warnings were updated to be more specific. 5. Updating initial and continued therapy approval criteria to include avoidance of concurrent reserpine and MAOI therapy. 6. QD was updated to "once daily" in document. 7. References were updated.		
Policy was reviewed. 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Dosing Information was updated to include ”strong CYP2D6 inhibitors” to maximum dose. 3. Initial Therapy Criteria and Continued Therapy Criteria have been updated to remove approval duration for HIM. 4. Appendix B verbiage was rephrased to “Below are suggested therapeutic alternatives…….”. 5. Appendix B footnote was updated to, ”Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only”. 6. Appendix C: Contraindication verbiage was rephrased as per PI. 7. References were reviewed and updated.	06/01/2021	09/14/2021