# Clinical Policy: Deutetrabenazine (Austedo)

Reference Number: CP.PCH.42
Effective Date: 06.01.21
Last Review Date: 05.21
Line of Business: Commercial, HIM

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Deutetrabenazine (Austedo®) is a vesicular monoamine transporter 2 (VMAT2) inhibitor.

## FDA Approved Indication(s)

Austedo is indicated for the treatment of:

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

## Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that Austedo is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Chorea Associated with Huntington Disease** (must meet all)**:**

1. Diagnosis of chorea associated with Huntington disease;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Targeted mutation analysis demonstrates a cytosine-adenine-guanine (CAG) trinucleotide expansion of ≥ 36 repeats in the huntingtin (HTT) gene;
5. Evidence of chorea is supported by a Unified Huntington Disease Rating Scale (UHDRS) score ranging from 1 to 4 on any one of chorea items 1 through 7 (*see Appendix D*);
6. Austedo is not prescribed concurrently with tetrabenazine or Ingrezza®;
7. Dose does not exceed 48 mg per day.

**Approval duration:**
**HIM –** 6 months
**Commercial –** Length of Benefit

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

1. Diagnosis of TD secondary to treatment with a centrally acting dopamine receptor blocking agent (DRBA) (*see Appendix G*);
2. Prescribed by or in consultation with a psychiatrist or neurologist;
3. Age ≥ 18 years;

4. Evidence of moderate to severe TD is supported by an Abnormal Involuntary Movement Scale (AIMS) score of 3 or 4 on any one of items 1 through 9 (*see Appendix H*);
5. Austedo is not prescribed concurrently with tetrabenazine or Ingrezza;
6. Dose does not exceed 48 mg per day.

**Approval duration:**
**HIM –** 6 months
**Commercial –** Length of Benefit

**C. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

## II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. For Huntington disease: Member is responding positively to therapy as evidenced by a reduction since baseline in any one of UHDRS chorea items 1 through 7 (*see Appendix D*);
   b. For TD: Member is responding positively to therapy as evidenced by a reduction since baseline in any one of AIMS items 1 through 9 (*see Appendix H*);
3. Austedo is not prescribed concurrently with tetrabenazine or Ingrezza;
4. If request is for a dose increase, new dose does not exceed 48 mg per day.

**Approval duration:**
**HIM –** 12 months
**Commercial –** Length of Benefit

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

AAN: American Academy of Neurology
AIMS: Abnormal Involuntary Movement Scale
APA: American Psychiatry Association
DRBA: dopamine receptor blocking agent
DSM V: Diagnostic and Statistical Manual, Version 5
FDA: Food and Drug Administration
HTT: huntingtin
MAOI: monoamine oxidase inhibitor
TD: tardive dyskinesia
UHDRS: Unified Huntington Disease Rating Scale
VMAT: vesicular monoamine transporter

*Appendix B: Therapeutic Alternatives*

*Not applicable*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Suicidal or untreated/inadequately treated depression in patients with Huntington's disease
  - Hepatic impairment
  - Taking reserpine, MAOIs, tetrabenazine or valbenazine
- Boxed warning(s): depression and suicidality in patients with Huntington's disease

*Appendix D: Chorea: The Unified Huntington Disease Rating Scale (UHDRS)*

- The UHDRS encompasses motor, behavioral, cognitive, and functional components for use in evaluating patients with Huntington disease and is commonly used in both research and clinical practice.
- The American Academy of Neurology (AAN) guidelines evaluating pharmacologic therapies for chorea associated with Huntington disease describe the chorea subscore of the UHDRS motor component as a rating of 7 body regions (facial, bucco-oral-lingual, trunk, extremities) on a five-point scale from 0 to 4 with 0 representing no chorea.
- See Huntington Study Group 1996 and Mestre et al. 2018 for additional information about the UHDRS.

(AAN Guidelines 2012, Huntington Study Group 1996, Mestre 2018)

*Appendix E: Tardive Dyskinesia: 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.[5]
- Tardive dyskinesia is a type of movement disorder that occurs secondary to therapy with *centrally acting* DRBAs (*see Appendix F*). (DSM V)
- Typical therapeutic drug classes containing DRBAs include first- and second-generation antipsychotics, antiemetics, and tri-cyclic antidepressants (*see Appendix G*). (DSM V)
- Other therapeutic drug classes containing agents that have been variously associated with movement disorders are listed below: (Waln 2013, Meyer 2014, Lerner 2015)

- 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 F: Tardive Dyskinesia: DSM-V Definition*

| **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.<br>• 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. |

(DSM V)

*Appendix G: Tardive Dyskinesia: Centrally Acting Dopamine Receptor Blocking Agents (Neuroleptics)*

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

| Pharmacologic Class | Therapeutic Class | | |
|---|---|---|---|
| | First-generation (typical) antipsychotics | Antiemetic agents | Tri-cyclic antidepressants |
| Dibenzodiazephine | Clozapine, quetiapine | | |
| Benzisoxazole | Iloperidone | | |
| Benzisothiazole | Lurasidone, ziprasidone | | |
| Thienobenzodiazepine | Olanzapine | | |
| Pyrimidinone | Paliperidone, risperidone | | |

*(DSM V, Meyer 2014, Smith 2010, Clinical Pharmacology, Lexicomp)*
**First generation H1 antagonist*
***Off-label use*
*†A dibenzoxapine that shares properties with phenothiazines*

*Appendix H: Tardive Dyskinesia: The Abnormal Involuntary Movement Scale (AIMS)*

- The AIMS is a clinician-rated 12-item assessment tool developed by the National Institute of Mental Health to evaluate severity of involuntary movements in multiple movement disorders including TD. The AIMS is commonly used in both research and clinical practice.
- AIMS items 1-10 are rated on a 5-point scale (0 - none; 1 - minimal; 2 - mild; 3 - moderate; 4 - severe). Items 1-7 assess dyskinesia severity by body region (items 1-4 orofacial; items 5-7 extremity and trunk). Items 8-10 assess overall severity, incapacitation, and patient awareness respectively - item 8 uses the highest score of any one of items 1-7. Items 11 (dental) and 12 (dentures) are yes/no questions which help characterize lip, jaw, and tongue movements.
- The American Psychiatric Association (APA) guidelines recommend that patients who have moderate to severe or disabling TD be treated with a reversible VMAT2 inhibitor; the guidelines note that the AIMS tool can be instrumental in such decision-making.
- See Munetz 1988 for additional information about the AIMS.

(APA Guidelines 2020, Munetz 1988)

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Huntington's chorea | 6 mg/day (6 mg once daily) PO; 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) |
| TD | 12 mg/day (6 mg twice daily) PO; 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) |

## VI. Product Availability

Tablets: 6 mg, 9 mg, 12 mg

## VII. References

1. Austedo Prescribing Information. North Wales, PA. Teva Pharmaceuticals USA, Inc; December 2020. Available at: www.austedo.com. Accessed January 24, 2021.

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at www.clinicalpharmacology.com.

*Huntington Disease*

3. Frank S, et al. Effect of deutetrabenazine on chorea among patients with Huntington disease. JAMA. July 2016; 316(1):40-50.
4. O Classen D, et al. Indirect tolerability comparison of deutetrabenazine and tetrabenazine for Huntington disease. J Clin Mov Disord. 2107;4(3):1-11.
5. Potter NT, Spector EB, Prior TW. Technical standards and guidelines for Huntington disease testing. Genet Med. 2004:6(1):61-65.
6. ACMG/ASHG STATEMENT. Laboratory guidelines for Huntington disease genetic testing. The American College of Medical Genetics/American Society of Human Genetics Huntington Disease Genetic Testing Working Group. Am. J. Hum. Genet. 1998; 62:000–000.
7. Kremer B, Goldberg P, Andrew SE. A worldwide study of the Huntington's disease mutation: the sensitivity and specificity of measure CAG repeats. NEJM. May 19, 1994; 330(20):1401-1406.
8. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. August 7, 2012;79:598-603.
9. Unified Huntington's disease rating scale: reliability and consistency. Movement Disorder Society. Movement Disorders. 1996;11(2):136-143.
10. Mestre TA, Forjaz MJ, Mahlknecht P, et al. Rating scales for motor symptoms and signs in Huntington's disease: Critque and recommendation. International Parkinson and Movement Disorders Society. Movement Disorders Clinical Practice. 2018;5(2):111-117. DOI:10.1002/mdc3.1257.

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11. Medication-induced movement disorders and other adverse effects of medication. Diagnostic and statistical manual of mental disorders, 5th Ed. American Psychiatric Association.
12. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. 2020. Third Ed. Available at https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines. Accessed January 24, 2021.
13. Munetz MR, Sheldon B. How to examine patients using the abnormal involuntary movement scale. Hospital and Community Psychiatry. November 1988;39(11):1172-77.
14. Bhidayasiri R, Jitkritsadakul O, Friedman JH, Fahn S. Updating the recommendations for treatment of tardive syndromes: a systematic review of new evidence and practical treatment algorithm. Journal of the Neurological Sciences. 2018;389:67-75.
15. Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: treatment of tardive syndromes. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013;31:463-469.
16. Waln O, Jankovic J. An update on tardive dyskinesia: from phenomenology to treatment. Tremor Other Hyperkinet Mov (N Y). July 12, 2013;3:tre-03-161-4138-1. DOI:10.7916/D88P5Z71. Print 2013.
17. Witter DP, Holbert RC, Suryadevara U. Pharmacotherapy for the treatment of tardive dyskinesia in schizophrenia patients. Expert Opin Pharmacother. April 26, 2017. DOI:10.1080/14656566.2017.1323874. [Epub ahead of print.]

18. Meyer TA, Belson TE, McAllister R. Tardive dyskinesia: a distressing drug-induced movement disorder. US Pharm. 2014;39(1):HS13-HS16.
19. Lerner PP, Miodownik C, Lerner V. Tardive dyskinesia (syndrome): current concept and modern approaches to its management. Psychiatry Clin Neurosci. June 2015;69(6):321-34.
20. Rao AS, Camilleri M. Review article: metoclopramide and tardive dyskinesia. Alimentary Pharmacology and Therapeutics. January 2010;31(1):11-19.
21. Smith HS, Cox LR, Smith BR. Dopamine receptor antagonists. Annals of Palliative Medicine. July 2012;1(2). DOI: 10.3978/j.issn.2224-5820.2012.07.09.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created; split from CP.PHAR.341; removed redirection to tetrabenazine for chorea per Trade. | 03.04.21 | 05.21 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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