Austedo (deutetrabenazine)
Policy Number: C12650-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
3/1/2018	09/11/2019	09/11/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J3490-(NOC) unclassified drugs	RxPA	Q4 2019 20191030C12650-a

PRODUCTS AFFECTED:
Austedo (deutetrabenazine)

DRUG CLASS:
Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Specialty Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

AVAILABLE DOSAGE FORMS:
Tablets: 6 mg, 9 mg, and 12 mg

FDA-APPROVED USES: indicated for the treatment of: Chorea associated with Huntington's disease and Tardive dyskinesia in adults

COMPENDIAL APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: Tardive Dyskinesia; Chorea associated with Huntington's Disease

REQUIRED MEDICAL INFORMATION:

A. TARDIVE DYSKINESIA (TD)

1. Diagnosis of TD according to the DSM V Criteria (i, ii, and iii) [DOCUMENTATION REQUIRED]: i) Involuntary athetoid or choreiform movements; AND ii) History of treatment with a neuroleptic agent (i.e. antipsychotic); AND iii) Symptoms lasting longer than 4-8 weeks AND
2. Member has had an inadequate response to at least ONE of the following alternative approaches to treat tardive dyskinesia:
   (a) Adjustments to possible offending medication(s) known to cause TD (dose reduction or discontinuation) were attempted but ineffective in resolving TD symptoms, OR (b) Switched from a first-generation to a second-generation antipsychotic, OR (c) Member is not a candidate for a trial of dose reduction, tapering, discontinuation of the offending medication

or switching to an alternative antipsychotic therapy [Appendix] [DOCUMENTATION REQUIRED]
AND

3. Documentation of a trial (4 weeks) and failure or labeled contraindication of ONE other guideline recommended treatment (clonazepam or amantadine,) AND Tetrabenazine (Xenazine) at up to 100 mg/day [3][DOCOMENTATION REQUIRED]- See Appendix 2 for guideline language.
   AND
4. Baseline evaluation of member's current AIMS score documented greater than or equal to 10. [DOCUMENTATION REQUIRED]
   Documentation of the member's current AIMS score from items 1-7 (results range from 0 to 28, with higher scores indicating more severe involuntary movements) required OR Extrapyramidal Symptom Rating Scale (ESRI)
   NOTE: Reauthorization requires positive response or demonstrated efficacy to therapy. Baseline score reviewed at Continuation of Therapy.

B. CHOREA ASSOCIATED WITH HUNTINGTON'S DISEASE

1. Diagnosis of Huntington's disease with chorea symptoms confirmed by documentation of: (a) Huntington Disease Mutation Analysis: indicating an expanded CAG repeat (≥ 36) in the huntington gene (HTT) (also known as HD gene), OR (b) A positive family history of HD, with autosomal dominant inheritance pattern [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attetsation of psych stuff prior to start
   AND
3. Documentation of trial, failure or contraindication to tetrabenazine up to 100mg/day
   AND
4. Baseline evaluation and documentation of Total Chorea Score ([using the Unified Huntington's Disease Rating Scale (UHDRS)]
   NOTE: Reauthorization requires positive response or demonstrated efficacy to therapy. Baseline score reviewed at Continuation of Therapy.

DURATION OF APPROVAL:
Initial authorization: 3 months, Continuation of Therapy: 12 months

QUANTITY:
Maximum dosage: 48 mg/day

PRESCRIBER REQUIREMENTS:
Tardive Dyskinesia: Prescribed by, or in consultation with, a board- certified psychiatrist or neurologist. Chorea associated with Huntington's Disease: Prescribed by, or in consultation with, a board-certified neurologist with expertise in HD.

NOTE: Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually. Submit consultation notes if applicable.

AGE RESTRICTIONS:
18 years of age and older

GENDER:
Male and female

CONTINUATION OF THERAPY:
A. FOR ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
   AND
2. Members continues to be monitored/followed-up by the prescriber/specialist. Chart notes or consultation notes (if applicable) must be submitted at least ONCE annually [DOCUMENTATION REQUIRED]
   AND
3. Member's condition has stabilized or improved based on Prescriber's assessment while on therapy:
   a. TD Disease stabilization or improvement in TD symptoms as documented by decrease from baseline in AIMS score of at least 2 points OR ESRI score of at least 4 points
   OR
   b. Chorea Associated with HD stabilization or improvement from baseline in Total Maximal Chorea Scores OR chorea symptoms

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Austedo (deutetrabenazine) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. History of hypersensitivity to deutetrabenazine or any of its components, Hepatic impairment. For members with Huntington disease: who are suicidal or have untreated or inadequately treated depression; or history of untreated or inadequately treated depression or suicidal ideation. Concomitant therapy with ANY of the following: Other VMAT2 inhibitors: Ingrezza (valbenazine) or tetrabenazine (Xenazine), MAOIs [e.g., selegiline (Emsam), isocarboxazid (Marplan), phenelzine(Nardil), tranylcypromine (Parnate)]-- coadministration with or within 14 days of discontinuing MAOIs, Reserpine-- coadministration with or within 20 days of discontinuing reserpine, QTc-prolonging agents [e.g., antipsychotic agents (e.g., chlorpromazine, haloperidol), antibiotics (e.g., moxifloxacin), class IA and III antiarrhythmic agents]

OTHER SPECIAL CONSIDERATIONS:
Black Box Warnings: Deutetrabenazine product labeling includes a boxed warning regarding an increased risk for depression and suicidality. Patients with Huntington disease are at increased risk for depression and suicidal ideation; deutetrabenazine and tetrabenazine may increase the risk. In clinical trials, depression was reported in 4% and suicidal ideation was reported in 2% of patients treated with deutetrabenazine; patients with uncontrolled depression were excluded from the trials.
Recommended Dose:
ChoreaassociatedwithHuntington'sdisease
Initial Dose: 6 mg/day
Recommended Dose: 6 mg – 48 mg/day
Maximum Dose: 48 mg/day
Tardivedyskinesiainadults
Initial Dose: 12 mg/day
Recommended Dose: 12 mg – 48 mg/day
Maximum Dose: 48 mg/day

BACKGROUND:

APPENDIX:
Appendix 1: Centrally-Acting Dopamine Receptor Blocking Agents (Neuroleptics)

Drugs that most commonly cause TD are older antipsychotic agents such as haloperidol, chlorpromazine, and thioridazine; other drugs that may be associated with TD include antidepressants (amitriptyline, fluoxetine, phenelzine, sertraline, and trazodone), anti-Parkinson's drugs (levodopa), epilepsy drugs (phenobarbital and phenytoin), and metoclopramide

Appendix 2:
Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Jul 30;81(5):463-9. doi: 10.1212/WNL.0b013e31829d86b6.

Clonazepam probably improves TDD and ginkgo biloba probably improves TDS (both Level B); both should be considered as treatment. Risperidone may improve TDS but cannot be recommended as treatment because neuroleptics may cause TDS despite masking symptoms. **Amantadine and tetrabenazine** might be considered as TDS treatment (Level C). Diltiazem should not be considered as TDD treatment (Level B); galantamine and eicosapentaenoic acid may not be considered as treatment (Level C). Data are insufficient to support or refute use of acetazolamide, bromocriptine, thiamine, baclofen, vitamin E, vitamin B6, selegiline, clozapine, olanzapine, melatonin, nifedipine, fluperlapine, sulpiride, flupenthixol, thiopropazate, haloperidol, levetiracetam, quetiapine, ziprasidone, sertindole, aripiprazole, buspirone, yi-gan san, biperiden discontinuation, botulinum toxin type A, electroconvulsive therapy, α-methyldopa, reserpine, and pallidal deep brain stimulation as TDS treatments (Level U). Data are insufficient to support or refute TDS treatment by withdrawing causative agents or switching from typical to atypical DRBA (Level U).
Updating the recommendations for treatment of tardive syndromes: A systematic review of new evidence and practical treatment algorithm. J Neurol Sci. 2018 Jun 15;389:67-75. doi: 10.1016/j.jns.2018.02.010. Epub 2018 Feb 5.

RESULTS AND RECOMMENDATIONS:
New evidence was combined with the existing guideline evidence to inform our recommendations. Deutetrabenazine and valbenazine are established as effective treatments of TD (Level A) and must be recommended as treatment. **Clonazepam** and Ginkgo biloba probably improve TD (Level B) and should be considered as treatment. **Amantadine** and tetrabenazine might be considered as TD treatment (Level C). Pallidal deep brain stimulation possibly improves TD and might be considered as a treatment for intractable TD (Level C). There is insufficient evidence to support or refute TS treatment by withdrawing causative agents or switching from typical to atypical DRBA (Level U).

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Documentation Requirements: *Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.*

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