SmartPA Criteria Proposal

Drug/Drug Class:	Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors Clinical Edit
First Implementation Date:	TBD
Proposed Date:	September 17, 2020
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☐Revision of Existing Criteria ☒New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors

Why Issue Selected: Huntington's Disease (HD) is an inherited autosomal dominant progressive neurodegenerative disorder characterized by psychiatric and behavioral symptoms, involuntary movements (chorea), and progressive dementia. The estimated prevalence of HD in Europe and North America is 5-8 per 100,000 persons. Symptomatic improvement of chorea in HD is evaluated using the Total Maximal Chorea Score in the United Huntington's Disease Rating Scale (UHDRS).

Tardive Dyskinesia (TD) is a neurological disorder characterized by repetitive involuntary movements; it is usually linked with use of dopamine receptor blockers such as antipsychotics or metoclopramide. Symptomatic improvement in TD is often evaluated using the Abnormal Involuntary Movement Scale (AIMS), which assesses the severity of involuntary movements across body regions ranging from 0 (no dyskinesia) to 28 (maximal amplitude dyskinesia), with a decrease in score indicating improvement. The two main strategies for prevention of TD are discontinuation of the offending drug and switching from first to second generation antipsychotic drugs. If drug treatment with antipsychotics is required, patients should use the lowest effective dose and consider decrease or discontinuation within 6-12 months of therapy.

Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors block a brain protein (VMAT2) which controls the storage of dopamine and other neurotransmitters for release in the nerve synapse; by blocking VMAT2 the number of neurotransmitters available for release is decreased. Xenazine® (tetrabenazine) was the first VMAT2 inhibitor approved in the US in 2008 for the treatment of chorea associated with HD; it has also been used off label for TD. In 2017, the FDA approved two new VMAT2 inhibitors, Austedo® (deutetrabenazine) and Ingrezza® (valbenazine). In Austedo, the replacement of hydrogen with deuterium at sites of primary metabolism gave a slower metabolic clearance compared to Xenazine, thus allowing less frequent dosing. Austedo is FDA approved for the treatment of chorea associated with HD and the treatment of TD. Ingrezza is FDA approved for the treatment of TD only. Ingrezza has more specificity for VMAT2 than the other agents, thus it may be less likely to cause adverse events such as akathisia, agitation, and restlessness.

Program-Specific Information:

Date Range FFS 7-1-2019 to 6-30-2020			
Drug	**Claims**	**Spend**	**Avg spend per claim**
AUSTEDO 6 MG TABLET	184	$596,503.98	$3,241.86
AUSTEDO 9 MG TABLET	119	$521,780.89	$4,384.71
AUSTEDO 12 MG TABLET	178	$1,107,131.10	$6,219.83
INGREZZA 40 MG CAPSULE	383	$2,352,788.75	$6,143.05
INGREZZA 80 MG CAPSULE	607	$3,924,294.36	$6,465.06
INGREZZA INITIATION PACK	6	$39,281.12	$6,546.85
XENAZINE 12.5 MG TABLET	80	$42,353.92	$536.12
XENAZINE 25 MG TABLET	140	$137,035.96	$978.82

Type of Criteria: ☐ **Increased risk of ADE** ☐ **Preferred Drug List** ☒ **Appropriate Indications** ☒ **Clinical Edit**

Data Sources: ☐ **Only Administrative Databases** ☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors
- Age range: All appropriate MO HealthNet participants aged 18 years or older

Approval Criteria

Initial Therapy:

- Participant is aged 18 years or older **AND**
- Claim is for Xenazine **OR**
- For chorea associated with Huntington's Disease:
  - Claim is for Austedo **AND**
  - Documented diagnosis of Huntington's Disease **AND**
  - Documentation of baseline Total Maximal Chorea Score from the United Huntington's Disease Rating Scale (UHDRS) **OR**
- For moderate to severe or disabling Tardive Dyskinesia:
  - Claim is for Austedo or Ingrezza **AND**
  - Documented diagnosis of Tardive Dyskinesia **AND**
  - Documentation of baseline Abnormal Involuntary Movement Scale (AIMS) score ≥ 10 **AND**
  - Documentation that the prescriber has conducted a comprehensive review of all of the participant's current medications and TD risk mitigation strategies, which include the following, have been tried and failed (unless contraindicated or inappropriate in order to maintain stable psychiatric function):
    - Switching to a 2nd generation (or atypical) antipsychotic **OR**
    - Discontinuation or dose modification of the offending medication

Continuation of Therapy:

- Initial approval of prior authorization is for 6 months; renewal of prior authorization may be given for an additional 6 months following documentation of the following:
  - Documentation of benefit of therapy (i.e. improved quality of life) **AND**
  - For chorea associated with Huntington's Disease: documentation of current Total Maximal Chorea Score indicating a reduction in the Total Maximal Chorea Score since baseline **OR**
  - For Tardive Dyskinesia: documentation of current Abnormal Involuntary Movement Scale (AIMS) score indicating a reduction in AIMS score of at least 2 from baseline

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Documented history of MAOI therapy in the past 45 days
- Concurrent therapy with any other VMAT2 agent in the past 45 days
- For Xenazine or Austedo: Documented history of hepatic impairment
- For Ingrezza: Claim for 80 mg strength and documented history of hepatic impairment
- Claim exceeds quantity limitations:
  - Ingrezza: 1 capsule per day
  - Austedo: 4 tablets per day
  - Xenazine:
    - 12.5 mg tablets: 4 tablets per day
    - 25 mg tablets: 2 tablets per day

Required Documentation

Laboratory Results:		Progress Notes:	X
MedWatch Form:		Other:	X

Disposition of Edit

Denial: Exception code "0682" (Clinical Edit)
Rule Type: CE

Default Approval Period

6 months

References

- Xenazine® [package insert]. Deerfield, IL: Lundbeck; 11/2019.
- Austedo® [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; 10/2019.
- Ingrezza® [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.; 7/2019.
- The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia – DRAFT. https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines. Accessed April 8, 2020.
- Bhidayasiri R, Fahn S, Weiner WJ, Gronseth GS, Sullivan KL, Zesiewicz TA; American Academy of Neurology. Evidence-based guideline: treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of Neurology [published correction appears in *Neurology*. 2013;81(22):1968]. *Neurology*. 2013;81(5):463-469.[PubMed 23897874]
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- Institute for Clinical and Economic Review (ICER). Vesicular Monoamine Transporter 2 Inhibitors for Tardive Dyskinesia: Effectiveness and Value. Final Evidence Report. December 22, 2017.
- IPD Analytics. Rx Insights: Central Nervous System. Movement Disorders: Drug Management Strategy. May 31, 2017.
- Bachoud-Lévi AC, Ferreira J, Massart R, et al. International Guidelines for the Treatment of Huntington's Disease. Front Neurol. 2019;10:710. Published 2019 Jul 3. doi:10.3389/fneur.2019.00710
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