SmartPA Criteria Proposal

Drug/Drug Class:	Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors PDL Edit
First Implementation Date:	April 1, 2021
Revised Date:	May 13, 2021
Prepared For:	MO HealthNet
Prepared By:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☒Revision of Existing Criteria ☐New Criteria

Executive Summary

Purpose: The MO HealthNet Pharmacy Program will implement a state-specific preferred drug list.

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). AIMS 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.

Total program savings for the PDL classes will be regularly reviewed.

Program-Specific Information:	Preferred Agents	Non-Preferred Agents
	• Austedo® • Tetrabenazine	• Ingrezza® • Xenazine®

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

- **For Austedo and Ingrezza only:** Participant is aged 18 years or older **AND**
- For chorea associated with Huntington's Disease:
  - Claim is for generic Xenazine **OR**
  - Claim is for Austedo: Documented diagnosis of Huntington's Disease **OR**
  - Failure to achieve desired therapeutic outcomes with trial on 2 or more preferred agents:
    - Documented trial period for preferred agents (90 out of 120 days) **OR**
    - Documented ADE/ADR to preferred agents
- For moderate to severe or disabling Tardive Dyskinesia:
  - Documented diagnosis of Tardive Dyskinesia **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 **AND**
  - Claim is for Ingrezza:
    - Documentation of baseline Abnormal Involuntary Movement Scale (AIMS) score ≥ 8 **AND**
    - Failure to achieve desired therapeutic outcomes with trial on Austedo:
      - Documented trial period of Austedo (90 out of 120 days) **OR**
      - Documented ADE/ADR to Austedo
    - 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**
      - 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:

Drug Description	Generic Equivalent	Max Dosing Limitation
AUSTEDO	DEUTETRABENAZINE	4 tablets per day
INGREZZA	VALBENAZINE	1 capsule per day
XENAZINE	TETRABENAZINE	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:	

Disposition of Edit

Denial: Exception Code "0160" (Preferred Drug List)
Rule Type: PDL

Default Approval Period

1 year

References

1. Xenazine® [package insert]. Deerfield, IL: Lundbeck; 11/2019.
2. Austedo® [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; 2/2020.
3. Ingrezza® [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.; 4/2020.
4. 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.
5. 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]
6. 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. J Neurol Sci. 2018 Jun 15;389:67-75. doi: 10.1016/j.jns.2018.02.010. Epub 2018 Feb 5.
7. Owens, D. (2019). Tardive dyskinesia update: Treatment and management. BJPsych Advances, 25(2), 78-89. doi:10.1192/bja.2018.46
8. Solmi M, Pigato G, Kane JM, Correll CU. Treatment of tardive dyskinesia with VMAT-2 inhibitors: a systematic review and meta-analysis of randomized controlled trials. *Drug Des Devel Ther*. 2018 May 14;12:1215-1238. doi: 10.2147/DDDT.S133205. PubMed PMID: 29795977; PubMed Central PMCID: PMC5958944.
9. Institute for Clinical and Economic Review (ICER). Vesicular Monoamine Transporter 2 Inhibitors for Tardive Dyskinesia: Effectiveness and Value. Final Evidence Report. December 22, 2017.
10. IPD Analytics. Rx Insights: Central Nervous System. Movement Disorders: Drug Management Strategy. May 31, 2017.
11. 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
12. Stacy M, Sajatovic M, Kane JM, et al. Abnormal involuntary movement scale in tardive dyskinesia: Minimal clinically important difference [published correction appears in Mov Disord. 2019 Nov;34(11):1753-1754]. Mov Disord. 2019;34(8):1203-1209. doi:10.1002/mds.27769
13. Evidence-Based Medicine and Fiscal Analysis: "Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors – Therapeutic Class Review", Conduent Business Services, L.L.C., Richmond, VA; October 2020.
14. Evidence-Based Medicine Analysis: "Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors", UMKC-DIC; October 2020.