Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors Prior Authorization with Quantity Limit Program Summary

Program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date
03-01-2024

Date of Origin
10-01-2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Austedo® (deutetrabenazine) Tablet	Treatment of adults with chorea associated with Huntington's disease Treatment of adults with tardive dyskinesia		1
Austedo XR® (deutetrabenazine er) Tablet	Treatment of adults with chorea associated with Huntington's disease Treatment of adults with tardive dyskinesia		8
Ingrezza® (valbenazine) Capsule	Treatment of adults with tardive dyskinesia Treatment of adults with chorea associated with Huntington's disease		2
Xenazine® (tetrabenazine) Tablet	Treatment of chorea associated with Huntington's disease	*generic available	3

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Huntington's Disease	Huntington's Disease (HD) is a hereditary neurodegenerative disorder caused by an expansion of a repeating cytosine-adenine-guanine (CAG) triplet series in the HTT (huntingtin) gene on chromosome 4. It is inherited in an autosomal dominant pattern with each child of an affected parent having a 50% chance of developing the disease. There is currently no cure or treatment which can halt, slow, or reverse the progression of the disease. The average length of survival after clinical diagnosis is typically 10-20 years.(6) Huntington's Disease manifests as a triad of motor, cognitive, and psychiatric

	disorders that begin gradually and progress over many years. These disorders of HD cannot be considered in isolation with disabilities in one area leading to problems in another area. The cognitive disorder is characterized by a reduction of speed and flexibility of mental processing. The psychiatric disorder is less predictable. People may suffer from depression, mania, obsessive compulsive disorder and various forms of psychosis. Almost all people with HD will experience disease-specific personality and behavioral changes that result in severe consequences to their marital, social, and economic well-being. The movement disorder includes emergence of involuntary movements (chorea) and the impairment of voluntary movements which results in reduced manual dexterity, slurred speech, swallowing difficulties, problems with balance, and falls. The most recognized motor symptom is chorea, and the clinical diagnosis of Huntington's Disease traditionally is based on the observation of this symptom. More than 90% of people affected by HD have chorea, which is characterized by involuntary movements that are often sudden, irregular, and purposeless. The movements are often more prominent in the extremities early in the disease, but may eventually include facial grimacing, eyelid elevation, neck, shoulder, trunk, and leg movements as the disease progresses. Chorea typically increases in frequency and amplitude over time and may peak about 10 years after disease onset.(6) Treating chorea is an important part of HD management and should be considered if chorea causes the patient distress or discomfort. Vesicular monoamine transporter 2 (VMAT 2) inhibitors are FDA labeled agents for treatment and are considered first-line treatment unless the patient suffers from not well-managed depression or suicidal thoughts.(4) The precise mechanism of action is unknown, but VMAT2 inhibitors are believed to exert their anti-chorea effects as a reversible depletor of monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals. They reversibly inhibit VMAT2, a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle resulting in decreased uptake of monoamines and depletion of monoamine stores. (1-3,8)
Tardive dyskinesia	Tardive syndromes are persistent abnormal involuntary movement disorders caused by sustained exposure to antipsychotic medication, the most common of which are tardive dyskinesia, tardive dystonia, and tardive akathisia. They begin later in treatment than acute dystonia, akathisia, or medication-induced parkinsonism and they persist and may even increase, despite reduction in dose or discontinuation of the antipsychotic medication. Tardive dyskinesia has been reported after exposure to any of the available antipsychotic medications. It occurs at a rate of approximately 4-8% per year in adult patients treated with first generation antipsychotics. Evaluation of the risk of tardive dyskinesia is complicated by the fact that dyskinetic movements may be observed with a reduction in antipsychotic medication dose. Fluctuations in symptoms are also common and may be influenced by factors such as psychosocial stressors. Regular assessment of patients for tardive syndromes through clinical examination or through the use of a structured evaluative tool, such as the Abnormal Involuntary Movement Scale (AIMS), can aid in identification, clarifying the likely etiology, monitoring, and determining the effects of medication changes or treatments for tardive dyskinesia. It should be noted that there is no specific score threshold that suggests a need for intervention, although ranges of scores are noted to correspond with mild, moderate, and severe symptoms. If no other contributing etiology is identified and moderate to severe or disabling tardive dyskinesia persists, treatment with a VMAT2 inhibitor is recommended. A change in antipsychotic therapy to a lower potency medication and particularly to clozapine may be associated with a reduction in tardive dyskinesia. The potential benefits of changing medication should be considered in light of the possibility of symptom recurrence.(7)
Safety	VMAT2 inhibitors (including Austedo/Austedo XR, Ingrezza, and Xenazine) have a boxed warning due to an increased risk of depression and suicidal thoughts and behavior in patients with Huntington’s disease. Anyone considering the use of VMAT2 inhibitors (including Austedo/Austedo XR, Ingrezza, and Xenazine) must balance the risks of depression and suicidal ideation and behavior with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidal ideation, or unusual changes in behavior. Inform patients, their caregivers, and families of the risk of depression and suicidal ideation and behavior and instruct them to report behaviors of concern promptly to the treating physician.

	Particular caution should be exercised in treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in patients with Huntington's disease.(1-3,8) Austedo/Austedo XR are contraindicated in patients:(1,8) • with Huntington's disease who are suicidal, or have untreated or inadequately treated depression • with hepatic impairment • taking reserpine. At least 20 days should elapse after stopping reserpine before starting Austedo/Austedo XR. • taking monoamine oxidase inhibitors (MAOIs). Austedo/Austedo XR should not be used in combination with an MAOI, or within 14 days of discontinuing therapy with an MAOI. • taking tetrabenazine or valbenazine Ingrezza is contraindicated in patients with a history of hypersensitivity to valbenazine or any components of Ingrezza. Rash, urticaria, and reactions consistent with angioedema (e.g., swelling of the face, lips, and mouth) have been reported.(2) Xenazine is contraindicated in patients:(3) • who are actively suicidal, or in patients with untreated or inadequately treated depression • with hepatic impairment • taking monoamine oxidase inhibitors (MAOIs). Tetrabenazine should not be used in combination with an MAOI, or within a minimum of 14 days of discontinuing therapy with an MAOI. • taking reserpine. At least 20 days should elapse after stopping reserpine before starting Xenazine. • taking deutetrabenazine or valbenazine

REFERENCES

Number	Reference
1	Austedo prescribing information. Teva Neuroscience, Inc. February 2023.
2	Ingrezza prescribing information. Neurocrine Biosciences, Inc. August 2023.
3	Xenazine Prescribing Information. Bausch Health Companies, Inc. November 2019.
4	Bachoud-Lévi, A.-C., Ferreira, J., Massart, R., Youssov, K., Rosser, A., Busse, M., Craufurd, D., Reilmann, R., De Michele, G., Rae, D., Squitieri, F., Seppi, K., Perrine, C., Scherer-Gagou, C., Audrey, O., Verny, C., & Burgunder, J.-M. (2019). International Guidelines for the Treatment of Huntington's Disease. Frontiers in Neurology, 10(710). https://doi.org/10.3389/fneur.2019.00710
5	Reference no longer used
6	Nance, M., Paulsen, J., Rosenblatt, A., & Wheelock, V. (2011). A Physician's Guide to the Management of Huntington's Disease (3rd edition). Huntington's Disease Society of America. https://hdsa.org/wp-content/uploads/2015/03/PhysiciansGuide_3rd-Edition.pdf
7	Keepers, G. A., Fochtmann, L. J., Anzia, J. M., Benjamin, S., Lyness, J. M., Mojtabai, R., Servis, M., Walaszek, A., Buckley, P., Lenzenweger, M. F., Young, A. S., Degenhardt, A., & Hong, S.-H. (2020). The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. American Journal of Psychiatry, 177(9), 868–872. https://doi.org/10.1176/appi.ajp.2020.177901
8	Austedo XR prescribing information. Teva Neuroscience, Inc. February 2023.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Austedo	deutetrabenazine tab	12 MG ; 6 MG ; 9 MG	M ; N ; O ; Y	N		
Austedo xr	deutetrabenazine tab er	12 MG ; 24 MG ; 6 MG	M ; N ; O ; Y	N		
Austedo xr patient titrat	deutetrabenazine tab er titration pack	6 & 12 & 24 MG	M ; N ; O ; Y	N		
Xenazine	tetrabenazine tab	12.5 MG ; 25 MG	M ; N ; O ; Y	O ; Y		
Ingrezza	valbenazine tosylate cap	40 MG ; 60 MG ; 80 MG	M ; N ; O ; Y	N		
Ingrezza	valbenazine tosylate cap therapy pack	40 & 80 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Austedo	Deutetrabenazine Tab 12 MG	12 MG	120	Tablets	30	DAYS			
Austedo	Deutetrabenazine Tab 6 MG	6 MG	60	Tablets	30	DAYS			
Austedo	Deutetrabenazine Tab 9 MG	9 MG	120	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	6 MG	30	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	12 MG	30	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	24 MG	60	Tablets	30	DAYS			
Austedo xr patient titrat	deutetrabenazine tab er titration pack	6 & 12 & 24 MG	42	Tablets	180	DAYS			
Ingrezza	Valbenazine Tosylate Cap	60 MG	30	Capsules	30	DAYS			
Ingrezza	Valbenazine Tosylate Cap 40 MG (Base Equiv)	40 MG	30	Capsules	30	DAYS			
Ingrezza	Valbenazine Tosylate Cap 80 MG (Base Equiv)	80 MG	30	Capsules	30	DAYS			
Ingrezza	Valbenazine Tosylate Cap Therapy Pack 40 MG (7) & 80 MG (21)	40 & 80 MG	28	Capsules	180	DAYS			
Xenazine	Tetrabenazine Tab 12.5 MG	12.5 MG	240	Tablets	30	DAYS			
Xenazine	Tetrabenazine Tab 25 MG	25 MG	120	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Austedo	deutetrabenazine tab	12 MG ; 6 MG ; 9 MG	Medicaid
Austedo xr	deutetrabenazine tab er	12 MG ; 24 MG ; 6 MG	Medicaid
Austedo xr patient titrat	deutetrabenazine tab er titration pack	6 & 12 & 24 MG	Medicaid
Ingrezza	valbenazine tosylate cap	40 MG ; 60 MG ; 80 MG	Medicaid
Ingrezza	valbenazine tosylate cap therapy pack	40 & 80 MG	Medicaid
Xenazine	tetrabenazine tab	12.5 MG ; 25 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Austedo	Deutetrabenazine Tab 12 MG	12 MG	Medicaid
Austedo	Deutetrabenazine Tab 6 MG	6 MG	Medicaid
Austedo	Deutetrabenazine Tab 9 MG	9 MG	Medicaid
Austedo xr	deutetrabenazine tab er	12 MG	Medicaid
Austedo xr	deutetrabenazine tab er	6 MG	Medicaid
Austedo xr	deutetrabenazine tab er	24 MG	Medicaid
Austedo xr patient titrat	deutetrabenazine tab er titration pack	6 & 12 & 24 MG	Medicaid
Ingrezza	Valbenazine Tosylate Cap	60 MG	Medicaid
Ingrezza	Valbenazine Tosylate Cap 40 MG (Base Equiv)	40 MG	Medicaid
Ingrezza	Valbenazine Tosylate Cap 80 MG (Base Equiv)	80 MG	Medicaid
Ingrezza	Valbenazine Tosylate Cap Therapy Pack 40 MG (7) & 80 MG (21)	40 & 80 MG	Medicaid
Xenazine	Tetrabenazine Tab 12.5 MG	12.5 MG	Medicaid
Xenazine	Tetrabenazine Tab 25 MG	25 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is Austedo/deutetrabenazine, Austedo XR/deutetrabenazine ER, or Ingrezza/valbenazine AND ONE of the following: 1. The patient has a diagnosis of tardive dyskinesia AND BOTH of the following: A. ONE of the following: 1. The prescriber has reduced the dose or discontinued any medications known to cause tardive dyskinesia (i.e., dopamine receptor blocking agents) **OR** 2. The prescriber has provided clinical rationale indicating that a reduced dose or discontinuation of any medications known to cause tardive dyskinesia is not appropriate **AND** B. The prescriber has documented the patient's baseline Abnormal Involuntary Movement Scale (AIMS) score **OR** 2. The patient has a diagnosis of chorea associated with Huntington's disease **OR** 3. The patient has another FDA approved indication for the requested agent **OR** 4. The patient has another indication that is supported in compendia for the requested agent **OR** B. The requested agent is Xenazine/tetrabenazine and ONE of the following:

Module	Clinical Criteria for Approval

1. The patient has a diagnosis of chorea associated with Huntington's disease **OR**
2. The patient has another FDA approved indication for the requested agent **OR**
3. The patient has another indication that is supported in compendia for the requested agent **AND**

2. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following:
   A. The patient has an intolerance or hypersensitivity to the generic equivalent that is not expected to occur with the brand agent **OR**
   B. The patient has an FDA labeled contraindication to the generic equivalent that is not expected to occur with the brand agent **OR**
   C. The prescriber has provided information to support the use of the requested brand agent over the generic equivalent **OR**

Brand	Generic Equivalent
Xenazine	tetrabenazine

   D. BOTH of the following:
      1. The prescriber has stated that the patient has tried the generic equivalent **AND**
      2. ONE of the following:
         A. The generic equivalent was discontinued due to lack of effectiveness or an adverse event **OR**
         B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the generic equivalent **OR**
   E. The patient is currently being treated with the requested agent as indicated by ALL of the following:
      1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
      2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
      3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**
   F. The prescriber has provided documentation that the generic equivalent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND**
3. If the patient has an FDA labeled indication ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**
4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., psychiatrist, neurologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
5. The patient will NOT be using the requested agent in combination with another agent included in this Prior Authorization program **AND**
6. The patient does NOT have any FDA labeled contraindications to the requested agent

Compendia Allowed: CMS Approved Compendia

Length of Approval: Tardive dyskinesia - 3 months, all other indications - 12 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Module	Clinical Criteria for Approval
	Renewal Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., psychiatrist, neurologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. ONE of the following: A. The patient has a diagnosis of tardive dyskinesia AND has had improvements or stabilization from baseline in their Abnormal Involuntary Movement Scale (AIMS) score **OR** B. The patient has a diagnosis is other than tardive dyskinesia AND the patient has had clinical benefit with the requested agent **AND** 4. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following: A. The patient has an intolerance or hypersensitivity to the generic equivalent that is not expected to occur with the brand agent **OR** B. The patient has an FDA labeled contraindication to the generic equivalent that is not expected to occur with the brand agent **OR** C. The prescriber has provided information to support the use of the requested brand agent over the generic equivalent **OR** | Brand | Generic Equivalent | | --- | --- | | Xenazine | tetrabenazine | D. BOTH of the following: 1. The prescriber has stated that the patient has tried the generic equivalent **AND** 2. ONE of the following: A. The generic equivalent was discontinued due to lack of effectiveness or an adverse event **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the generic equivalent **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that the generic equivalent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 5. The patient will NOT be using the requested agent in combination with another agent included in this Prior Authorization program **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval**: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: Initial: tardive dyskinesia - 3 months, all other indications - 12 months Renewal: 12 months