VMAT2 Inhibitors Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
04-01-2025

FDA LABELED 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 Sprinkle	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.(7) Regular assessment of patients for tardive syndromes through clinical examination or through the use of a structured evaluative tool can aid in identifying tardive syndromes, clarifying their likely etiology, monitoring their longitudinal course, and determining the effects of medication changes or treatments for tardive dyskinesia. The Abnormal Involuntary Movement Scale (AIMS) and the Dyskinesia Identification System: Condensed User Scale (DISCUS) are examples of such tools. 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. In addition, the same total score can be associated with significantly different clinical manifestations and varying impacts on the patient. Assessment with a structured instrument (e.g., AIMS, DISCUS) should be performed at a minimum of every 6 months in patients at high risk of tardive dyskinesia and at least every 12 months in other patients as well as if a new onset or exacerbation of preexisting movements is detected at any visit.(7) If no other contributing etiology is identified and moderate to severe or disabling tardive dyskinesia persists, treatment with a VMAT2 inhibitor is recommended. Treatment with a VMAT2 inhibitor can also be considered for patients with mild tardive dyskinesia on the basis of such factors as patient preference, associated impairment, or effect on psychosocial functioning. 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 for depression and suicidality in patients with Huntington's disease. • VMAT2 inhibitors can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease. Anyone considering the use of VMAT2 inhibitors must balance the risks of depression and suicidality with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidality, or unusual changes in behavior. Patients, their caregivers, and families should be informed of the risk of depression and suicidality and should be instructed 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. VMAT2 inhibitors are contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression.(1-3,5,8) 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/Ingrezza Sprinkle are 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 with use of Ingrezza.(2,5) 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). Xenazine 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. July 2024.
2	Ingrezza prescribing information. Neurocrine Biosciences, Inc. April 2024.
3	Xenazine Prescribing Information. Lundbeck Pharmaceuticals LLC. November 2019.

Number	Reference
4	Bachoud-Lévi AC, Ferreira JJ, Massart R, et al. International Guidelines for the treatment of Huntington's Disease. *Frontiers in Neurology*. 2019;10. doi:10.3389/fneur.2019.00710
5	Ingrezza Sprinkle prescribing information. Neurocrine Biosciences, Inc. April 2024.
6	Nance MA, Paulsen JS, Rosenblatt A, Wheelock V. A Physician's Guide to the Management of Huntington's Disease (3rd edition). Huntington's Disease Society of America. 2011. https://hdsa.org/wp-content/uploads/2015/03/PhysiciansGuide_3rd-Edition.pdf
7	Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. *American Journal of Psychiatry*. 2020;177(9):868-872. doi:10.1176/appi.ajp.2020.177901
8	Austedo XR prescribing information. Teva Neuroscience, Inc. July 2024.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Austedo ; Austedo patient titration ; Austedo xr ; Austedo xr patient titration	deutetrabenazine tab ; deutetrabenazine tab er ; deutetrabenazine tab er titration pack ; deutetrabenazine tab titration pack	12 & 18 & 24 & 30 MG ; 12 MG ; 18 MG ; 24 MG ; 30 MG ; 36 MG ; 42 MG ; 48 MG ; 6 & 12 & 24 MG ; 6 & 9 & 12 MG ; 6 MG ; 9 MG	M ; N ; O ; Y	N		
Xenazine	tetrabenazine tab	12.5 MG ; 25 MG	M ; N ; O ; Y	O ; Y		
Ingrezza	valbenazine tosylate cap ; valbenazine tosylate cap therapy pack ; valbenazine tosylate capsule sprinkle	40 & 80 MG ; 40 MG ; 60 MG ; 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	18 MG	30	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	24 MG	30	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	30 MG	30	Tablets	30	DAYS			

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 xr	deutetrabenazine tab er	36 MG	30	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	42 MG	30	Tablets	30	DAYS			
Austedo xr	deutetrabenazine tab er	48 MG	30	Tablets	30	DAYS			
Austedo xr patient titrat	deutetrabenazine tab er titration pack	12 & 18 & 24 & 30 MG	28	Tablets	180	DAYS			
Austedo xr patient titration pack	deutetrabenazine tab er titration pack	6 & 12 & 24 MG	1	Kit	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			
Ingrezza	valbenazine tosylate capsule sprinkle	40 MG	30	Capsules	30	DAYS			
Ingrezza	valbenazine tosylate capsule sprinkle	60 MG	30	Capsules	30	DAYS			
Ingrezza	valbenazine tosylate capsule sprinkle	80 MG	30	Capsules	30	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 ; Austedo patient titration ; Austedo xr ; Austedo xr patient titration	deutetrabenazine tab ; deutetrabenazine tab er ; deutetrabenazine tab er titration pack ; deutetrabenazine tab titration pack	12 & 18 & 24 & 30 MG ; 12 MG ; 18 MG ; 24 MG ; 30 MG ; 36 MG ; 42 MG ; 48 MG ; 6 & 12 & 24 MG ; 6 & 9 & 12 MG ; 6 MG ; 9 MG	Commercial ; HIM ; ResultsRx
Ingrezza	valbenazine tosylate cap ; valbenazine tosylate cap therapy pack ; valbenazine tosylate capsule sprinkle	40 & 80 MG ; 40 MG ; 60 MG ; 80 MG	Commercial ; HIM ; ResultsRx
Xenazine	tetrabenazine tab	12.5 MG ; 25 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Austedo	Deutetrabenazine Tab 12 MG	12 MG	Commercial ; HIM ; ResultsRx
Austedo	Deutetrabenazine Tab 6 MG	6 MG	Commercial ; HIM ; ResultsRx
Austedo	Deutetrabenazine Tab 9 MG	9 MG	Commercial ; HIM ; ResultsRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Austedo xr	deutetrabenazine tab er	36 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	30 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	24 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	6 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	48 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	12 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	42 MG	Commercial ; HIM ; ResultsRx
Austedo xr	deutetrabenazine tab er	18 MG	Commercial ; HIM ; ResultsRx
Austedo xr patient titrat	deutetrabenazine tab er titration pack	12 & 18 & 24 & 30 MG	Commercial ; HIM ; ResultsRx
Austedo xr patient titration pack	deutetrabenazine tab er titration pack	6 & 12 & 24 MG	Commercial ; HIM ; ResultsRx
Ingrezza	Valbenazine Tosylate Cap	60 MG	Commercial ; HIM ; ResultsRx
Ingrezza	Valbenazine Tosylate Cap 40 MG (Base Equiv)	40 MG	Commercial ; HIM ; ResultsRx
Ingrezza	Valbenazine Tosylate Cap 80 MG (Base Equiv)	80 MG	Commercial ; HIM ; ResultsRx
Ingrezza	Valbenazine Tosylate Cap Therapy Pack 40 MG (7) & 80 MG (21)	40 & 80 MG	Commercial ; HIM ; ResultsRx
Ingrezza	valbenazine tosylate capsule sprinkle	40 MG	Commercial ; HIM ; ResultsRx
Ingrezza	valbenazine tosylate capsule sprinkle	60 MG	Commercial ; HIM ; ResultsRx
Ingrezza	valbenazine tosylate capsule sprinkle	80 MG	Commercial ; HIM ; ResultsRx
Xenazine	Tetrabenazine Tab 12.5 MG	12.5 MG	Commercial ; HIM ; ResultsRx
Xenazine	Tetrabenazine Tab 25 MG	25 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**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 patient is not taking any medications known to cause tardive dyskinesia (i.e., dopamine receptor blocking agents) **OR** 2. The prescriber has reduced the dose or discontinued any medications known to cause tardive dyskinesia **OR** 3. A reduced dose or discontinuation of any medications known to cause tardive dyskinesia is not appropriate **AND** B. The prescriber has evaluated the patient's tardive dyskinesia through clinical examination or through a structured evaluative

Module	Clinical Criteria for Approval

tool (e.g., Abnormal Involuntary Movement Scale [AIMS], Dyskinesia Identification System: Condensed User Scale [DISCUS]) **OR**

2. The patient has a diagnosis of chorea associated with Huntington's disease **OR**
3. The patient has another FDA labeled indication for the requested agent and route of administration **OR**
4. The patient has another indication that is supported in compendia for the requested agent and route of administration **OR**

B. The requested agent is Xenazine/tetrabenazine and ONE of the following:

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

Brand	Generic Equivalent
Xenazine	tetrabenazine

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. There is support for the use of the requested brand agent over the generic equivalent **AND**

3. If the patient has an FDA labeled indication, then ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. There is support for 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 VMAT2 Inhibitor agent for the requested indication **AND**
6. The patient does NOT have any FDA labeled contraindications to the requested agent

Compendia Allowed: AHFS or DrugDex 1 or 2a level of evidence

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

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

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 [Note: patients not previously approved for the requested agent will require initial evaluation review] **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. The patient has had clinical benefit with the requested agent **AND**

Module	Clinical Criteria for Approval
	4. If the request is for one of the following brand agents with an available generic equivalent (listed below), then ONE of the following: **Brand** / **Generic Equivalent** Xenazine / tetrabenazine 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. There is support for the use of the requested brand agent over the generic equivalent **AND** 5. The patient will NOT be using the requested agent in combination with another VMAT2 Inhibitor agent for the requested indication **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS or DrugDex 1 or 2a level of evidence **Length of Approval**: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**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. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval:** up to 12 months