Movement Disorder Agents: Valbenazine (Ingrezza)

WA.PHAR.139 Effective Date: 10/1/2024

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: *https://www.coordinatedcarehealth.com/content/dam/centene/centene-pharmacy/pdl/FORMULARY-CoordinatedCare_Washington.pdf*

Medical necessity

Drug	Medical Necessity
Valbenazine (Ingrezza)	**Valbenazine** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Chorea associated with Huntington's disease Valbenazine (Ingrezza)	Valbenazine (Ingrezza) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Prescribed by, or in consultation with a neurologist or psychiatrist; **AND** 3. Diagnosis of Huntington's Disease; **AND** 4. Baseline assessment has been completed using any of the following sections of the Unified Huntington's Disease Rating Scale (UHDRS): a. Motor; OR b. Cognitive; OR c. Behavioral; OR d. Functional Assessment; OR e. Independence Scale; OR f. Total Functional Capacity; AND 5. Medication will not be used in combination with another VMAT2 inhibitor (e.g. tetrabenazine), or monoamine oxidase inhibitors

	(MAOI) (e.g. isocarboxazid, phenelzine, tranylcypromine, reserpine); **AND** 6. Treatment with deutetrabenazine or deutetrabenazine ER is contraindicated, or has been ineffective or not tolerated [minimum trial of 12 weeks] If ALL criteria are met, the request will be authorized for **12 months.** **Criteria (Reauthorization)** Valbenazine (Ingrezza) may be approved when all the following documented criteria are met: 1. Criteria #5 from the initial authorization criteria continues to be met**; AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g, reduction in involuntary movements, decrease in total maximal chorea score). If ALL criteria are met, the request will be authorized for **12 months.**
Tardive dyskinesia (TD) Valbenazine (Ingrezza)	Valbenazine (Ingrezza) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with a neurologist or psychiatrist; **AND** 3. Diagnosis of tardive dyskinesia (TD); **AND** 4. Baseline assessments using one of the following tests has been completed: a. Abnormal Involuntary Movement Scale (AIMS) b. Clinical Global Impression of Change- Tardive Dyskinesia (CGI-TD) 5. Not used in combination with another VMAT2 inhibitor (e.g. tetrabenazine) or monoamine oxidase inhibitors (MAOI) (e.g. isocarboxazid, phenelzine, tranylcypromine, reserpine); **AND** 6. Patient continues to experience persistent TD after trying **ONE** of the following treatment approaches, unless contraindicated, not tolerated or put psychiatric stability at risk : a. Switching from a 1st generation to a 2nd generation antipsychotic; **OR** b. Trial of two 2nd generation antipsychotics; **OR** c. Has a history of discontinuation or dose modification of the offending medication with continued symptoms; **AND** 7. Treatment with deutetrabenazine or deutetrabenazine ER is contraindicated, or has been ineffective or not tolerated [minimum trial of 12 weeks]

	If ALL criteria are met, the request will be authorized for **12 months.**
	Criteria (Reauthorization) Valbenazine (Ingrezza) may be approved when all the following documented criteria are met: 1. Criteria #5 from initial authorization criteria continues to be met; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g, reduction in involuntary movements, improvement in AIMS score, improvement in CGI-TD score). If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
valbenazine (Ingrezza)	Tardive Dyskinesia Chorea associated with Huntington's disease	Tardive Dyskinesia 40 mg once daily. After one week, increase the dose to 80 mg once daily Chorea associated with Huntington's Disease 40 mg once daily. Increase the dose in 20 mg increments every two weeks to 80 mg once daily	• 40 mg capsules: #30 capsules/30 days • 40 mg capsule sprinkles: #30 capsules/30 days • 60 mg capsules: #30 capsules/30 days • 60 mg capsule sprinkles: #30 capsules/30 days • 80 mg capsules: #30 capsules/30 days • 80 mg capsule sprinkles: #30 capsules/30 days

Background:

Chorea associated with Huntington's disease

Huntington disease (HD) is an inherited progressive neurodegenerative disorder characterized by choreiform movements, psychiatric problems, and dementia. It is caused by a cytosine-adenine-guanine (CAG) trinucleotide repeat expansion in the huntingtin (HTT) gene on chromosome 4p and inherited in an autosomal dominant pattern. The pathophysiology of HD is not fully understood, although it is thought to be related to toxicity of the mutant huntingtin protein. As there is no known cure, treatment is symptomatic and remains supportive. The American Academy of Neurology (AAN) recommends the use of tetrabenazine (Xenazine), amantadine, or riluzole when medication therapy for chorea is warranted. Per the Physician's Guide to the Management of Huntington's Disease 3rd edition, providers often treat chorea with neuroleptics (e.g. aripiprazole, haloperidol, fluphenazine, risperidone, olanzapine) based on clinical experience and due to safety concerns associated with VMAT2-inhibitors, namely: decreased cognition and mood, increased suicidality and depression. Studies of the anti-choreic effects of neuroleptics were excluded from the AAN guideline review due to criteria set forth; however, the AAN acknowledges neuroleptics are commonly used in clinical practice to treat chorea and recommends additional study in recognition of this use. In consideration of the Boxed Warnings and adverse effects associated with this class, a trial of therapy often considered in standards-of-care is reasonable.

Movement Disorder Agents

The efficacy of valbenazine for the use in chorea associated with Huntington's disease was assessed using results from the KINECT-HD study. KINECT-HD was a randomized, double-blind, placebo-controlled study. Participants had a genetically confirmed diagnosis of Huntington's disease and chorea. They were randomized 1:1 to oral placebo or valbenazine ≤ 80 mg as tolerated for 12 weeks of double-blinded treatment. The primary endpoint was a least-squares mean change in the UHDRS total maximal chorea score from screening and baseline to the maintenance period. Of 128 randomly assigned participants, 125 were included in the full analysis set (64 to valbenazine and 61 to placebo) and 127 were included in the safety-analysis set (64 to valbenazine and 63 to placebo). Least-square mean changes from the screen and baseline period to the maintenance period in the UHDRS total maximal chorea score were -4.6 for valbenazine and -1.4 for placebo (least-square mean different -3.2, 95% CI -4.4 to -2.0; p <0.0001).

Tardive Dyskinesia

Tardive dyskinesia (TD) is a medication-induced hyperkinetic movement disorder caused by exposure to dopamine receptor-blocking agents, most often antipsychotic drugs, that persists for at least a month after discontinuation of the offending agent. When clinically appropriate, the two main strategies of pharmacotherapy in patients who are showing signs of tardive dyskinesia include discontinuation of the offending drug and switching from a first- to a second-generation antipsychotic drug because second generation neuroleptics have a lower risk of TD. Additional pharmacologic options [e.g. benzodiazepines, anticholinergic drugs (trihexyphenidyl, benztropine)] have been used in clinical practice for many years. The American Academy of Neurology (AAN) recommends treatment with dopamine-depleting agents with level C evidence but treatment with these agents has been established as standard of care.

The efficacy of valbenazine was assessed using results from the KINECT-3 study which was a randomized, double-blind, placebo-controlled, parallel-group, fixed dose trial. A total of 234 participants were enrolled and participants had underlying schizophrenia, schizoaffective disorder, or a mood disorder and moderate-to-severe tardive dyskinesia. Subjects at significant risk for suicidal or violent behaviors and individuals with unstable psychiatric symptoms were excluded. Participants were randomized to treatment with valbenazine 80 mg once daily, valbenazine 40 mg once daily or placebo in a 1:1:1 ratio for six weeks. All participants were put on once daily 40 mg or 80 mg of valbenazine through week 48 upon completion of the six week placebo-controlled dosing. The primary efficacy endpoing was the mean change from baseline in the AIMS dyskinesia total score at the end of week six. Results showed that participants treated with 80 mg once daily met the primary endpoint of change from baseline in AIMS at six weeks compared to placebo. Valbenazine 40 mg reduced the AIMS score by 1.9 points, 80 mg reduced the AIMS score by 3.2 and a 0.1 point decrease was show with placebo. Statistically significant differences were shown between the 40 mg and 80 mg strengths at weeks 2, 4, and 6 in the intent-to-treat population. Of the 79 participants, 43 taking the 80 mg completed a 48-week extension. Efficacy was sustained in this group however when valbenazine was discontinued at week 48, the AIMS scores returned to baseline after four weeks.

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History

Approved Date	Effective Date	Version	Action and Summary of Changes
04/17/2024	10/01/2024	62.38.00-1	New policy created Approved by DUR Board