

Movement Disorder Agents: Valbenazine (Ingrezza)

Medical policy no. 62.38.00.AA-1
Year

Effective Date: Month, 1,

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 Apple Health Preferred Drug List (AHPDL), please visit: <https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx>

Medical necessity

Drug	Medical Necessity
Valbenazine (Ingrezza)	<p>Valbenazine may be considered medically necessary in patients who meet the criteria described in the clinical policy below.</p> <p>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.</p>

Clinical policy:

Clinical Criteria	
<p>Chorea associated with Huntington’s disease Valbenazine (Ingrezza)</p>	<p>Valbenazine (Ingrezza) may be approved when all the following criteria are met:</p> <ol style="list-style-type: none"> 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): <ol style="list-style-type: none"> a. Motor; OR b. Cognitive; OR c. Behavioral; OR d. Functional Assessment; OR e. Independence Scale; OR

	<p>f. Total Functional Capacity; AND</p> <p>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</p> <p>6. Treatment with deutetrabenazine or deutetrabenazine ER is contraindicated, or has been ineffective or not tolerated for a minimum of 12 weeks</p> <p>If ALL criteria are met, the request will be authorized for 12 months.</p> <p>Criteria (Reauthorization)</p> <p>Valbenazine (Ingrezza) may be approved when all the following criteria are met:</p> <ol style="list-style-type: none"> 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]. <p>If ALL criteria are met, the request will be authorized for 12 months.</p>
<p>Tardive dyskinesia Valbenazine (Ingrezza)</p>	<p>Valbenazine (Ingrezza) may be approved when all the following criteria are met:</p> <ol style="list-style-type: none"> 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; AND 4. Baseline assessments using <u>one</u> of the following tests has been completed: <ol style="list-style-type: none"> 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. At least one of the following treatment approaches was ineffective, unless all are contraindicated, not tolerated, or put psychiatric stability at risk: <ol style="list-style-type: none"> a. Switching from a 1st generation to a 2nd generation antipsychotic; OR b. Patient has a history of discontinuation or dose modification of the offending medication

	<p>7. Treatment with deutetrabenazine or deutetrabenazine ER is contraindicated, or has been ineffective or not tolerated for a minimum of 12 weeks</p> <p>If ALL criteria are met, the request will be authorized for 12 months.</p>
	Criteria (Reauthorization)
	<p>Valbenazine (Ingrezza) may be approved when all the following criteria are met:</p> <ol style="list-style-type: none"> 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]. <p>If ALL criteria are met, the request will be authorized for 12 months.</p>

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
valbenazine (Ingrezza)	Tardive Dyskinesia Chorea associated with Huntington's disease	<p><u>Tardive Dyskinesia</u> 40 mg once daily. After one week, increase the dose to 80 mg once daily</p> <p><u>Chorea associated with Huntington's Disease</u> 40 mg once daily. Increase the dose in 20 mg increments every two weeks to 80 mg once daily</p>	<ul style="list-style-type: none"> 40 mg capsules: #30 capsules/30 days 60 mg capsules: #30 capsules/30 days 80 mg capsules: #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.

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, bztropine)] 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 endpoint 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 shown 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.

References

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History

Approved Date	Effective Date	Version	Action and Summary of Changes
MM/DD/YYYY	MM/DD/YYYY	XX.XX.XX-X	Pending Approval (draft/unpublished version) -New policy created

DRAFT

Movement Disorder Agents (Ingrezza)

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible. **Without this information, we may deny the request in seven (7) working days.**

Apple Health Preferred Drug list: <https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx>

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength		Directions for use	Qty/Days supply

- Is this request for a continuation of therapy? Yes No
If yes, does patient have clinical documentation demonstrating disease stability or a positive clinical response (e.g, reduction in involuntary movements, decrease in total maximal chorea score, or improvement in AIMS or CGI-TD score)?
 Yes No
- Indicate patient's diagnosis:
 Chorea associated with Huntington's disease
 Tardive dyskinesia
 Other. Specify: _____
- Is this being prescribed by or in consultation with a psychiatrist or neurologist? Yes No
- Has a baseline assessment been completed using any of the following? Check all that apply:
 The Unified Huntington's Disease Rating Scale (UHDRS). Specify section completed:
 Motor
 Cognitive
 Behavioral
 Functional Assessment
 Independence Scale
 Total Functional Capacity
 Abnormal Involuntary Movement Scale (AIMS)
 Clinical Global Impression of Change – Tardive Dyskinesia (CGI-TD)
- Will this be used in combination with a monoamine oxidase inhibitor (MAOI) [e.g. isocarboxazid, phenelzine, tranylcypromine, reserpine] or another vesicular monoamine transporter 2 (VMAT2) inhibitor [e.g. tetrabenazine]? Yes No
- Has patient had treatment (minimum of 12 weeks) with deutetrabenazine or deutetrabenazine ER that has been ineffective, not tolerated, or is treatment contraindicated? Yes No

For diagnosis of tardive dyskinesia

7. Has at least one of the following treatment approaches been ineffective, contraindicated, not tolerated, or put the patient's psychiatric stability at risk?

Switching from a 1st generation to a 2nd generation antipsychotic

Patient has a history of discontinuation or dose modification of the offending medication

CHART NOTES ARE REQUIRED WITH THIS REQUEST

Prescriber signature

Prescriber specialty

Date