09-J2000-81

Original Effective Date: 07/15/17

Reviewed: 09/13/23

Revised: 10/15/23

Subject: Valbenazine (Ingrezza)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Tardive dyskinesia is a drug-induced hyperkinetic movement disorder that is most commonly associated with the use of central dopamine receptor-blocking agents such as antipsychotics. Symptoms include involuntary movements of the face, trunk, and extremities and may persist after dose reduction or discontinuation. Approximately 20 to 30% of patients with chronic exposure to antipsychotics may develop tardive dyskinesia.

The Food and Drug Administration (FDA) approved valbenazine in April 2017 for the treatment of adults with tardive dyskinesia. Valbenazine is a reversible inhibitor of vesicular monamine transporter 2 (VMAT2) which regulates monamine uptake to the synaptic vesicle for storage and release resulting in the inhibition of dopamine release. The modulation of dopamine by VMAT2 inhibition is thought to improve movement-related disorders such as tardive dyskinesia. Valbenazine was also granted FDA approval for the treatment of chorea in people with Huntington's disease.

In a randomized, double-blind, placebo-controlled trial, valbenazine 40 to 80 mg per day was evaluated in patients with moderate to severe tardive dyskinesia. Patients with schizophrenia, schizoaffective disorder or a mood disorder were included and permitted to continue medications for the management of psychiatric conditions if on a stable treatment regimen for at least 30 days. Patients with a risk of suicide or violent behavior or unstable psychiatric symptoms were excluded. The mean change from baseline in the Abnormal Involuntary Movement Scale (AIMS) dyskinesia total score (items 1 through 7) at week 6 was the primary efficacy endpoint. Valbenazine 80 mg significantly decreased dopamine receptor blocker-induced tardive dyskinesia severity compared with placebo at week 6, as measured by least-square mean difference from baseline on AIMS Dyskinesia Total score (-3.2 vs -0.1); however valbenazine 40 mg was not significantly different from placebo (-1.9 vs -0.1). Valbenazine 40 mg and 80 mg provided a significantly greater proportion of patients with at least a 50% reduction in AIMS score at

week 6 as compared to placebo (23.8% and 40% vs 8.7%). The most common adverse reactions were somnolence, akathisia, and dry mouth.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

I. Initiation of valbenazine (Ingrezza) **meets the definition of medical necessity** when **ALL** of the following criteria are met:
    1. Chorea associated with Huntington's Disease
        a. Member is not receiving therapy an additional VMAT2 inhibitor (e.g., deutetrabenazine, xenazine)
        b. Member is not actively suicidal or diagnosed with depression that is untreated or inadequately treated
    2. Tardive dyskinesia
        a. Member is diagnosed with tardive dyskinesia that has persisted for 3 months or more – documentation must be provided
        b. Baseline assessment of the member's Abnormal Involuntary Movement Scale (AIMS) score – documentation must be provided
        c. **ONE** of the following:
            i. Member had an inadequate response to alternative approaches to alleviate symptoms of tardive dyskinesia (e.g., dose adjustment of the offending agent, discontinuation of the offending agent, switching to an alternative therapy) – documentation must be provided
            ii. Antipsychotic therapy is unable to be adjusted to alleviate symptoms of tardive dyskinesia due to risk of destabilizing the member's psychiatric condition– documentation must be provided
        d. Member is diagnosed with schizophrenia, schizo-affective disorder, or a mood disorder
        e. Member's psychiatric status is stable
        f. Member does not have a history of suicide or violent behavior
        g. Member does not have congenital long QT syndrome or a history of arrhythmias associated with a prolonged QT interval
        h. Member is not receiving concomitant monoamine oxidase inhibitor (MAOI) therapy (e.g., selegiline [Carbex], rasagiline [Azilect]), a strong CYP3A4 inducer (e.g.,

carbamazepine, phenytoin, rifampin), reserpine (Serpalan) or an additional VMAT2 inhibitor (e.g., deutetrabenazine, tetrabenazine).

i. Dose does not exceed 80 mg/day – dosage will be achieved using the fewest number of tablets per day

Approval duration: 3 months

II. Continuation of valbenazine (Ingrezza) **meets the definition of medical necessity** for the treatment of tardive dyskinesia or chorea associated with Huntington's Disease in members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years, **OR** the member has previously met all indication-specific initiation criteria
2. Member has demonstrated a beneficial response to valbenazine (i.e., For tardive dyskinesia indication, improvement in the member's AIMS score from baseline) – documentation must be provided
3. Dose does not exceed 80 mg/day – dosage will be achieved using the fewest number of tablets per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Valbenazine is indicated for the treatment of adults with tardive dyskinesia and the initial dose is 40 mg once daily. After one week, increase the dose to the recommended dose of 80 mg once daily.

Valbenazine is indicated for the treatment of chorea associated with Huntington's disease. The initial dose is 40 mg once daily. Increase the dose in 20 mg increments every two weeks to the recommended dosage of 80 mg once daily.

A dosage of 40 mg or 60 mg once daily may be considered depending on response and tolerability. Can be taken with or without food.

Dose Adjustments

- The recommended dose for patients with moderate or severe hepatic impairment is 40 mg once daily.
- Reduce dose to 40 mg once daily in known CYP2D6 poor metabolizers.
- Avoid use with monoamine oxidase inhibitors and strong CYP3A4 inducers.
- Reduce dose to 40 mg once daily for use with strong CYP3A4 inhibitors and strong CYP2D6 inhibitors.

Drug Availability

- 40 mg, 60 mg, and 80 mg capsule

PRECAUTIONS:

Contraindications

- Known hypersensitivity to valbenazine or any components of Ingrezza.

Precautions/Warnings

- Depression and suicidal ideation and behavior in patients with Huntington's disease.
- Hypersensitivity, including angioedema may occur. Discontinue if this occurs.
- Somnolence: May impair patient's ability to drive or operate hazardous machinery.
- QT Prolongation: May cause an increase in QT interval. Avoid use in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval.
- Neuroleptic Malignant Syndrome. Discontinue if this occurs.
- Parkinsonism: Cases of Parkinson-like symptoms, some severe, have been reported in the postmarketing period. Reduce the dose or discontinue treatment in patients who develop clinically significant Parkinson-like signs or symptoms.
- May cause fetal harm.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

G10	Huntington's chorea
G24.01	Drug-induced subacute dyskinesia

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

DEFINITIONS:

None.

RELATED GUIDELINES:

Tetrabenazine (Xenazine) and Deutetrabenazine (Austedo), 09-J1000-07

OTHER:

Abnormal Involuntary Movement Scale (AIMS)	**Movement Rating** **0 = none** **1 = minimal** **2 = mild** **3 = moderate** **4 = severe**
I. Facial and Oral Movements	
1. Muscles of Facial Expression (e.g., movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing)	**0 1 2 3 4**
2. Lips and Perioral Area (e.g., puckering, pouting, smacking)	**0 1 2 3 4**
3. Jaw (e.g., biting, clenching, chewing, mouth opening, lateral movement)	**0 1 2 3 4**
4. Tongue Rate only increases in movement both in and out of mouth, not inability to sustain movement	**0 1 2 3 4**
II. Extremity Movements	
5. Upper (arms, wrists, hands, fingers) Include choreic movements (ie, rapid, objectively purposeless,irregular, spontaneous); athetoid movements (i.e., slow, irregular, complex, serpentine). Do not include tremor (ie, repetitive, regular, rhythmic).	**0 1 2 3 4**
6. Lower (legs, knees, ankles, toes) (e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot)	**0 1 2 3 4**
III. Trunk Movements	
7. Neck, shoulders, hips (e.g., rocking, twisting, squirming, pelvic gyrations)	**0 1 2 3 4**
IV. Global Judgement	
8. Severity of abnormal movements overall	**0 1 2 3 4**
9. Incapacitation due to abnormal movements	**0 1 2 3 4**
10. Patient's awareness of abnormal movements (rate only patient's report)	**0 1 2 3 4**
V. Dental Status	
11. Current problems with teeth and/or dentures?	**Yes or No**
12. Does patient usually wear dentures?	**Yes or No**
13. Endentia?	**Yes or No**
14. Do movements disappear with sleep?	**Yes or No**

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 09/13/23.

GUIDELINE UPDATE INFORMATION:

07/15/17	New Medical Coverage Guideline.
07/15/18	Review and revision to guideline; consisting of updating drug availability and references.
07/15/19	Review and revision to guideline; consisting of updating references
07/15/20	Review and revision to guideline; consisting of updating dosing and references.
04/15/21	Revision to guideline; consisting of updating the position statement.
01/15/22	Review and revision to guideline; consisting of updating the position statement and references.
03/15/22	Revision to guideline; consisting of updating the position statement.
06/15/23	Review and revision to guideline; consisting of updating the references.
10/15/23	Review and revision to guideline; consisting of updating the position statement to include the use for chorea associated with Huntington's disease.