



5.60.29

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Subsection:	Central Nervous System Drugs	Original Policy Date:	May 5, 2017
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Last Review Date: June 16, 2022

Ingrezza

Description

Ingrezza (valbenazine)

Background

Ingrezza is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia. The mechanism of action of valbenazine in the treatment of tardive dyskinesia is unknown but is thought to be mediated through the reversible inhibition of vesicular monoamine transporter 2 (VMAT2), a transporter that regulates monoamine uptake from the cytoplasm to the synaptic vesicle for storage and release (1).

Regulatory Status

FDA-approved indication: Ingrezza is a vesicular monoamine transporter 2 (VMAT2) inhibitor indicated for the treatment of adults with tardive dyskinesia (1).

Ingrezza should be avoided in patients taking MAOIs and within 20 days of discontinuing MAOI therapy. Concomitant use may increase the concentration of monoamine neurotransmitters in the synapses, potentially leading to increased risk of serotonin syndrome, or attenuated treatment effect of Ingrezza (1).

Ingrezza was conducted in patients with moderate to severe tardive dyskinesia as determined by clinical observation. Patients had underlying schizophrenia, schizoaffective disorder, or a mood disorder (1). Two commonly used scales, the Abnormal Involuntary Movement Scale (AIMS) and Extrapyrimal Symptom Rating Scale (ESRS) are used to evaluate the severity of the tardive dyskinesia (2-3).

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When clinically appropriate, pharmacologic interventions may be considered for patients who are developing signs of TD. The two main strategies are discontinuation of the offending drug and switching from first to second generation antipsychotic drugs. For patients with a diagnosis of TD, additional pharmacologic interventions include the following: use of benzodiazepines, botulinum toxin injections, tetrabenazine, or anticholinergic drugs to control symptoms of TD, or paradoxically, resuming treatment with antipsychotic drugs in order to suppress TD (4).

Ingrezza may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. In patients taking a strong CYP2D6 or CYP3A4 inhibitor, or who are CYP2D6 poor metabolizers, Ingrezza concentrations may be higher and QT prolongation clinically significant. For patients who are CYP2D6 poor metabolizers or are taking a strong CYP2D6 inhibitor, dose reduction may be necessary. Ingrezza should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval (1).

Safety and efficacy of Ingrezza have not been established in pediatric patients (1).

Related policies

Austedo, Xenazine

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ingrezza may be considered **medically necessary** in patients 18 years of age and older with tardive dyskinesia and if the conditions indicated below are met.

Ingrezza may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age: 18 years of age or older

Diagnosis

Patient must have the following:

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Moderate to severe tardive dyskinesia

AND ALL of the following:

1. Inadequate treatment response, intolerance or contraindication to **ONE** of the following:
 - a. Benzodiazepine
 - b. Second generation antipsychotic (e.g., Seroquel, clozapine)
 - c. Xenazine
2. Documented baseline evaluation of the condition using **ONE** of the following scoring tools:
 - a. Abnormal Involuntary Movement Scale (AIMS)
 - b. Extrapyramidal Symptom Rating Scale (ESRS)
3. **NO** dual therapy with other vesicular monoamine transporter 2 (VMAT2) inhibitors
4. **NO** concomitant use of a MAOI (monoamine oxidase inhibitor) or reserpine (must be >20 days post discontinuing therapy)
5. Prescriber has reduced the dosage or cessation of all offending medications including antipsychotic medication and metoclopramide (Reglan)
6. Patient has a functional impairment that justifies treatment with Ingrezza

Prior – Approval *Renewal* Requirements

Age: 18 years of age or older

Diagnosis

Patient must have the following:

Tardive dyskinesia

AND ALL of the following:

1. Documented improvement using **ONE** of the following scores:
 - a. Abnormal Involuntary Movement Scale (AIMS)
 - b. Extrapyramidal Symptom Rating Scale (ESRS)
2. **NO** dual therapy with other vesicular monoamine transporter 2 (VMAT2) inhibitors
3. **NO** concomitant use of a MAOI (monoamine oxidase inhibitor) or reserpine (must be >20 days post discontinuing therapy)

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Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 90 capsules per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Ingrezza is approved for the treatment of adults with tardive dyskinesia. Velbenazine and its active metabolite reversibly inhibit VMAT2, which decreases the uptake of monoamines into synaptic vesicles and depletes monoamine stores. Ingrezza should not be used in combination with MAOIs due to increased risk of adverse effects. Safety and efficacy of Ingrezza have not been established in pediatric patients (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Ingrezza while maintaining optimal therapeutic outcomes.

References

1. Ingrezza [package insert]. San Diego, CA: Neurocrine Biosciences, Inc.; April 2021.
2. G Gharabawi, C Bossie, et al. Abnormal Involuntary Movement Scale (AIMS) and Extrapyrimal Symptom Rating Scale (ESRS): Cross-scale comparison in assessing tardive dyskinesia. *Schizophrenia Research* 77 (2005) 119–128.
3. G Chouinard, H Margolese. Manual for the Extrapyrimal Symptom Rating Scale (ESRS). *Schizophrenia Research* 76 (2005) 247–265.
4. UpToDate: Tardive dyskinesia: Prevention and treatment. Accessed on April 18, 2022.

Policy History

Date	Action
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May 2017	Addition to PA
June 2017	Annual review
September 2017	Annual review Addition of prescriber has reduced the dosage or cessation of all offending medications including antipsychotic medication and metoclopramide (Reglan); and patient has a functional impairment that justifies treatment with Ingrezza per SME
October 2017	Revision of quantity limits
December 2017	Annual review
November 2018	Annual review and reference update
December 2019	Annual review and reference update
May 2020	Removed specific AIMS and ESRS score requirements per FEP
June 2020	Annual review
June 2021	Annual review and reference update
June 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.