Clinical Policy: Valbenazine (Ingrezza)

Reference Number: PA.CP.PHAR.340
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

Description
Valbenazine (Ingrezza™) is a vesicular monoamine transporter 2 (VMAT2) inhibitor.

FDA approved indication
Ingrezza is indicated for the treatment of adults with tardive dyskinesia.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of PA Health and Wellness® that Ingrezza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Tardive Dyskinesia (must meet all)**:**

1. Diagnosis of tardive dyskinesia secondary to a centrally acting dopamine receptor blocking agent (DRBA);
   **See Appendix F; if the offending agent is not included in Appendix F, the status of the agent as a centrally acting DRBA as well as its association with tardive dyskinesia should be confirmed*
2. Prescribed by or in consultation with a psychiatrist or neurologist;
3. Age ≥ 18 years;
4. At the time of request, tetrabenazine or deutetrabenazine is not prescribed concurrently;
5. Dose does not exceed 80 mg (1 capsules) per day.

Approval duration: 6 months

B. Other diagnoses/indications:

1. Refer to PA.CP.PMN.53.

II. Continued Therapy

A. Tardive Dyskinesia (must meet all)**:**

1. Currently receiving medication via PA Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care Policy, PA.LTSS.PHAR.01, applies;
2. Member is responding positively to therapy;
3. Tetrabenazine or deutetrabenazine is not prescribed concurrently;
4. Dose does not exceed 80 mg (1 capsules) per day.

Approval duration: 6 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy or the Continuity of Care Policy, PA.LTSS.PHAR.01, applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
DRBA: dopamine receptor blocking agent
FDA: Food and Drug Administration
VMAT2: vesicular monoamine transporter 2

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to valbenazine or any components of Ingrezza
- Boxed warning(s): none reported

Appendix D: General Information

- Ingrezza should not be used concurrently with other VMAT2 inhibitors such as tetrabenazine or deutetrabenazine as this is considered duplicate therapy.
- Medication-induced movement disorders, including tardive dyskinesia, are organized in the DSM V as follows: neuroleptic-induced parkinsonism/other medication-induced parkinsonism, neuroleptic malignant syndrome, medication-induced acute dystonia, medication-induced acute akathisia, tardive dyskinesia, tardive dystonia/tardive akathisia, medication-induced postural tremor, other medication-induced movement disorder, antidepressant discontinuation syndrome, and other adverse effects of medication.[5]
- Tardive dyskinesia is a type of movement disorder that occurs secondary to therapy with *centrally acting* DRBAs (Appendix E).[5]
- Typical therapeutic drug classes containing DRBAs include first- and second-generation antipsychotics, antiemetics, and tri-cyclic antidepressants (Appendix F).[5]
- Other therapeutic drug classes containing agents that have been variously associated with movement disorders are listed below:[6-8]
  - Antiarrhythmics
  - Antibiotics
  - Anticholinergics
  - Antidepressants
  - Antiepileptics
  - Antihistamines
  - Antimanics
  - Bronchodilators
  - Calcium channel blockers
  - Central nervous system stimulants
  - Dopamine agonists
  - Dopamine depleting agents
  - Dopaminergics
  - Glucocorticoids
  - Immunosuppressants
  - Mood stabilizers
  - Muscle relaxants
  - Oral contraceptives

Appendix E: DSM-V Definition of Tardive Dyskinesia[5]

Tardive Dyskinesia *(ICD-9 333.85/ICD-10 G24.01)*
• Involuntary athetoid or choreiform movements (lasting at least a few weeks) generally of the tongue, lower face and jaw, and extremities (but sometimes involving the pharyngeal, diaphragmatic, or trunk muscles) developing in association with the use of a neuroleptic medication for at least a few months. • Symptoms may develop after a shorter period of medication use in older persons. In some patients, movements of this type may appear after discontinuation, or after change or reduction in dosage, of neuroleptic medications, in which case the condition is called neuroleptic withdrawal emergent dyskinesia. Because withdrawal emergent dyskinesia is usually time limited, lasting less than 4-8 weeks, dyskinesia that persists beyond this window is considered to be tardive dyskinesia.

Appendix F: Centrally Acting Dopamine Receptor Blocking Agents (Neuroleptics)[5,6,9,10]

Pharmacologic Class	**Therapeutic Class**		
	First-generation (typical) antipsychotics	**Antiemetic agents**	**Tri-cyclic antidepressants**
Phenothiazine	Chlorpromazine Fluphenazine Perphenazine Thioridazine Thiothixene Trifluoperazine	Chlorpromazine Perphenazine Prochlorperazine Promethazine* Thiethylperazine	Amoxapine†
Butryophenone	Haloperidol	Droperidol Haloperidol**	
Substituted benzamide		Metoclopromide Trimethobenzamide	
Dibenzazepine	Loxapine		
Diphenylbutylpiperidine	Pimozide		
	Second-generation (atypical) antipsychotics		
Quinolone	Aripiprazole, brexpiprazole		
Dibenzazepine	Asenapine		
Piperazine	Cariprazine		
Dibenzodiazephine	Clozapine, quetiapine		
Benzisoxazole	Iloperidone		
Benzisothiazole	Lurasidone, ziprasidone		
Thienobenzodiazepine	Olanzapine		
Pyrimidinone	Paliperidone, risperidone		

**First generation H1 antagonist*
***Off-label use*
†A dibenzoxapine that shares properties with phenothiazines

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

Tardive dyskinesia.	40 mg once daily; after a week, increase to 80 mg if needed.	80 mg/day

V. Product Availability

Ingrezza oral capsules: 40 mg, 80 mg

VI. References

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Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review:; added caution to prevent duplicate therapy with similar agents; references reviewed and updated	01.37.18	
2Q 2019 annual review: revised requirement for non-concomitant use from valbenazine to deutetrabenazine; references reviewed and updated.	04.17.19	