Clinical Policy: Valbenazine (Ingrezza)

Reference Number: CP.PHAR.340
Effective Date: 07.01.17
Last Review Date: 05.19
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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 capsule) per day.

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;

3. Tetrabenazine or deutetrabenazine is not prescribed concurrently;
4. If request is for a dose increase, new dose does not exceed 80 mg (1 capsule) per day.

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. 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		

Pharmacologic Class	Therapeutic Class		
	First-generation (typical) antipsychotics	Antiemetic agents	Tri-cyclic antidepressants
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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Tardive dyskinesia	40 mg PO once daily; after a week, increase to 80 mg if needed	80 mg/day

VI. Product Availability

Capsules: 40 mg, 80 mg

VII. References

1. Ingrezza Prescribing Information. San Diego, CA: Neurocrine Biosciences, Inc.; December 2018. Available at: http://www.ingrezza.com. Accessed February 26, 2019.
2. Reglan Prescribing Information. Baudette, MN: ANI Pharmaceuticals, Inc.; August 2011. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/017854s058lbl.pdf. Accessed June 1, 2017.
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4. Hauser RA, Factor SA, Marder SR. KINECT 3: A phase 3 randomized, double-blind, placebo-controlled trial of valbenazine for tardive dyskinesia. Am J Psychiatry. May 1, 2017; 174(5): 476-484. doi: 10.1176/appi.ajp.2017.16091037. Epub 2017 Mar 21.
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6. Bhidayasiri R, Fahn S, Weiner WJ, et al. Evidence-based guideline: Treatment of tardive syndromes. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013; 31: 463-469.
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12. Smith HS, Cox LR, Smith BR. Dopamine receptor antagonists. Annals of Palliative Medicine. July 2012; 1(2). DOI: 10.3978/j.issn.2224-5820.2012.07.09.
13. O'Brian CF, Jimenez R, Hauser RA, et al. NBI-98854, a selective monoamine transport inhibitor for the treatment of tardive dyskinesia: A randomized, double-blind, placebo-controlled study. Movement Disorders. 2015; 30(12): 1681-1687.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.17	08.17
Added new capsule strength: 80 mg. Added statement about duplicate VMAT2 inhibitor therapy in general information appendix.	11.07.17	02.18
2Q 2018 annual review: no significant changes; policies combined for Medicaid and Commercial lines of business; added caution to prevent duplicate therapy with similar agents; references reviewed and updated.	01.31.18	05.18
2Q 2019 annual review: no significant changes; revised requirement for non-concomitant use from valbenazine to deutetrabenazine; references reviewed and updated.	02.26.19	05.19
Removed repeat header for table in Appendix F	05.23.20	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.