

Clinical Policy Title:	valbenazine
Policy Number:	RxA.172
Drug(s) Applied:	Ingrezza®
Original Policy Date:	02/07/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Valbenazine (Ingrezza®) is a vesicular monoamine transporter 2 (VMAT2) inhibitor. Valbenazine is indicated for the treatment of adults with tardive dyskinesia.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
valbenazine (Ingrezza®)	Tardive dyskinesia	40 mg PO once daily; after one week, increase to 80 mg PO once daily if needed. For patients with moderate to severe hepatic impairment (Child-Pugh score 7 to 15): 40 mg PO daily For patients who are known CYP2D6 poor metabolizers: 40 mg PO daily	80 mg/day

Dosage Forms

- Capsules: 40 mg, 80 mg

Clinical Policy

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

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;

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

3. Age 18 years of age or greater;
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

Commercial: 12 months

Medicaid: 6 months

II. Continued Therapy Approval

A. Tardive Dyskinesia (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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

Commercial: 12 months

Medicaid: 6 months

III. Appendices

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 valbenazine
- Boxed Warning(s):
 - None reported

APPENDIX D: General Information

- Valbenazine 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-5 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 effect 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 depleting agents
 - Dopaminergic agents
 - Glucocorticoids
 - Immunosuppressants
 - Mood stabilizers
 - Muscle relaxants
 - Oral contraceptives

APPENDIX E: DSM-5 Definition of Tardive Dyskinesia⁵

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 [†]
Butyrophenone	haloperidol	droperidol	

		haloperidol**	
Substituted benzamide		metoclopramide trimethobenzamide	
Dibenzazepine	loxapine		
Pharmacologic Class	Therapeutic Class		
	First-generation (typical) antipsychotics	Antiemetic agents	Tri-cyclic antidepressants
Diphenylbutylpiperidine	Pimozide		
Second-generation (atypical) antipsychotics			
Quinolone	aripiprazole, brexpiprazole		
Dibenzazepine	asenapine		
Piperazine	cariprazine		
Dibenzodiazepine	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

APPENDIX G: Dose adjustments due to drug interactions:

Factors	Dose Adjustments for valbenazine
Use of MAOIs with valbenazine	Avoid concomitant use with MAOIs.
Use of strong CYP3A4 inducers with valbenazine	Concomitant use is not recommended.
Use of strong CYP3A4 inhibitors with valbenazine	Recommended dosage is 40 mg once daily.
Use of strong CYP2D6 inhibitors with valbenazine	Recommended dosage is 40 mg once daily.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: <ol style="list-style-type: none"> 1. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 2. Reference reviewed and updated. 3. Added Appendix G Dose adjustments due to drug interactions (based on package insert) 4. Approval duration for commercial was updated to 12 months from length of benefit. 	06/18/2020	12/07/2020