Clinical Policy: Safinamide (Xadago)

Reference Number: IL.ERX.NPA.45
Effective Date: 06.01.21
Last Review Date: 05.21
Line of Business: Illinois Medicaid

Revision Log

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

Description
Safinamide (Xadago®) is monoamine oxidase type B (MAO-B) inhibitor.

FDA Approved Indication(s)
Xadago is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Xadago is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Parkinson's Disease (must meet all)**:**

1. Diagnosis of idiopathic PD;
2. Age ≥ 18 years;
3. Member is experiencing "off" time (*see Appendix C*) on levodopa/carbidopa therapy;
4. Failure of two of the following adjunct drugs prescribed in combination with levodopa/carbidopa, each from different classes, unless clinically significant adverse effects are experienced or all are contraindicated:*
   a. MAO-B inhibitor: selegiline;
   b. COMT inhibitor: entacapone;
   c. Dopamine agonist: ropinirole, pramipexole;
   **Prior authorization may be required for the above agents*
5. Prescribed in combination with levodopa/carbidopa;
6. Dose does not exceed 100 mg (1 tablet) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Parkinson's Disease (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 100 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COMT: catechol-O-methyl transferase
FDA: Food and Drug Administration
MAO-B: monoamine oxidase type B
PD: Parkinson's disease

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
COMT Inhibitors		
carbidopa/levodopa/ entacapone (Stalevo®)	PO: Dose should be individualized based on therapeutic response; doses may be adjusted by changing strength or adjusting interval. Fractionated doses are not recommended and only 1 tablet should be given at each dosing interval.	1,200 mg/day (divided doses)
entacapone (Comtan®)	PO: 200 mg with each dose of levodopa/carbidopa	1,600 mg/day (divided doses)
MAO-B Inhibitors		
selegiline (Eldepryl®)	PO: adjunctive therapy (in combination with levodopa or levodopa/carbidopa): 5 mg PO BID.	10 mg/day
Dopamine Agonists		
pramipexole (Mirapex®)	PO: Initial dose: 0.125 mg 3 times daily, increase gradually every 5 to 7 days; maintenance (usual): 0.5 to 1.5 mg 3 times daily	4.5 mg/day (divided doses)
ropinirole (Requip®)	PO: Recommended starting dose: 0.25 mg 3 times/day. Based on individual patient response, the dosage should be titrated with weekly increments: Week 1: 0.25 mg 3 times/day; total daily dose: 0.75 mg; week 2: 0.5 mg 3 times/day; total daily dose: 1.5 mg; week 3: 0.75 mg 3 times/day; total daily dose: 2.25 mg; week 4: 1 mg 3 times/day; total daily dose: 3 mg. After week 4, if necessary, daily dosage may be increased by 1.5 mg/day on a weekly basis up to a dose of 9 mg/day, and then by up to 3 mg/day weekly to a total of 24 mg/day.	24 mg/day (divided doses)

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindication/Boxed Warnings

- Contraindication(s):
  - Concomitant use of the following drugs:
    - Other monoamine oxidase inhibitors or other drugs that are potent inhibitors of monoamine oxidase (e.g., linezolid)
    - Opioid drugs (e.g., tramadol, meperidine and related derivatives); serotonin-norepinephrine reuptake inhibitors; tri-or tetra-cyclic or triazolopyridine antidepressants; cyclobenzaprine; methylphenidate, amphetamine, and their derivatives; St. John's wort
    - Dextromethorphan
  - A history of a hypersensitivity to safinamide
  - Severe hepatic impairment (Child-Pugh C: 10-15)
- Boxed warning(s): none reported

Appendix D: General Information

- Off time/episodes represent a return of PD symptoms (bradykinesia, rest tremor or rigidity) when the levodopa (L-dopa) treatment effect wears off after each dosing interval.
- PD symptoms, resulting from too little L-dopa, are in contrast with dyskinesia which typically results from too much L-dopa. The alterations between "on" time (the time when PD symptoms are successfully suppressed by L-dopa) and "off" time is known as "motor fluctuations".
- The addition of carbidopa to L-dopa prevents conversion of L-dopa to dopamine in the systemic circulation and liver.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Adjunctive treatment to levodopa/ carbidopa in patients with PD experiencing "off" episodes	50 mg PO QD; 100 mg PO QD after 2 weeks if needed	100 mg/day

VI. Product Availability

Tablets: 50 mg, 100 mg

VII. References

1. Xadago Prescribing Information. Louisville, KY: US WorldMeds, LLC; November 2020. Available at: http://xadago.com/. Accessed October 20, 2020.
2. Pahwa MD, Factor SA, Lyons KE, et al. Practice Parameter: Treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review): [RETIRED] Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. April 2006; 66: 983-995.
3. Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and Movement Disorder Society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord*. 2018 Aug;33(8):1248-1266.
4. Borgohain R, Szasz J, Stanzione P, et al. Randomized trial of safinamide add-on to levodopa in Parkinson's disease with motor fluctuations. *Movement Disorders*. 2014; 29(2): 229-237.
5. Schapira AHV, Fox SH, Hauser RA, et al. Assessment of safety and efficacy of safinamide as a levodopa adjunct in patients with Parkinson disease and motor fluctuations: A randomized clinical trial. *JAMA Neurol*. December 12, 2016.
6. Rinne UK, Larsen JP, Siden A, et al. Nomecomt Study Group. Entacapone enhances the response to levodopa in parkinsonian patients with motor fluctuations. *Neurology*. November 1998; 51(5): 1309-14.
7. Parkinson Study Group. Entacapone improves motor fluctuations in levodopa-treated parkinson's disease patients. *Ann Neurol*. 1997; 42: 747-755.
8. Rascol O, Brooks DJ, Melamed E, et al. Rasagiline as an adjunct to levodopa in patients with Parkinson's disease and motor fluctuations (LARGO, Lasting effect in Adjunct therapy with Rasagiline Given Once daily, study): a randomised, double-blind, parallel-group trial. *Lancet*. 2005; 365: 947-54.

9. Parkinson Study Group. A randomized placebo-controlled trial of rasagiline in levodopa-treated patients with Parkinson disease and motor fluctuations: The PRESTO study. *Arch Neurol*. 2205; 62: 241-248.
10. Poewe WH, Rascol O, Quinn N, et al. Efficacy of pramipexole and transdermal rotigotine in advanced Parkinson's disease: A double-blind, double-dummy, randomized controlled trial. *Lancet Neurol*. June 2007; 6(6): 513-20.
11. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc. Available at: http://www.clinicalpharmacology-ip.com/. Accessed April 22, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.22.21	05.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.