RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	safinamide
Policy Number:	RxA.303
Drug(s) Applied:	Xadago®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Safinamide (Xadago®) is monoamine oxidase type B (MAO-B) inhibitor. Safinamide is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.

Limitation(s) of use: Xadago has not been shown to be effective as monotherapy for the treatment of PD.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Safinamide (Xadago®)	Adjunctive treatment tolevodopa/carbidopain patients with Parkinson's disease (PD) experiencing "off" episodes.	50 mg PO once daily; 100 mg PO once daily after 2 weeks if needed.	100 mg once daily.

Dosage Forms

- Tablets: 50 mg, 100 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. Parkinson's Disease (must meet all)**:**

1. Diagnosis of idiopathic Parkinson's disease (PD);
2. Member is experiencing " off " time (*see Appendix B*) on levodopa/carbidopa therapy;
3. Failure of two drugs, as specified below, unless contraindicated or clinically significant adverse effects are experienced (a and b):
    a. Rasagiline;
    b. One of the following drugs: entacapone (Comtan®/Stalevo®), ropinirole/ropinirole ER,pramipexole/pramipexole ER, Neupro®;

**Prior authorization may be required for the above agents*

4. Xadago is prescribed in combination with levodopa/carbidopa;
5. Dose does not exceed 100 mg per day.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Dose does not exceed 100 mg per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A*:* Abbreviation/Acronym Key
COMT: Catechol-O-methyl transferase
MAO B: Monoamine oxidase inhibitor
FDA: Food and Drug Administration
PD: Parkinson's disease
ER: Extended- release

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
COMT Inhibitors		
entacapone (Comtan)	Oral: 200 mg with each dose of levodopa/carbidopa.	1600 mg daily (divided doses)
carbadopa/levodopa/ entacapone (Stalevo)	Oral: 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.	1200 mg daily (divided doses)
MAO B Inhibitors		

rasagiline (Azilect)	Oral: Monotherapy or adjunctive therapy (not including levodopa): 1 mg once daily. Adjunctive therapy with levodopa: Initial: 0.5 mg once daily; may increase to 1 mg once daily based on response and tolerability.	1 mg once daily.
Dopamine agonists		
ropinirole (Requip)	Oral: 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 daily (divided doses).
ropinirole ER (Requip ER)	Oral: Initial dose: 2 mg once daily for 1 to 2 weeks, followed by increases of 2 mg/day at weekly or longer intervals based on therapeutic response and tolerability.	24 mg once daily.
pramipexole (Mirapex)	Oral: 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 daily (divided doses).
pramipexole ER (Mirapex ER)	Oral: Initial dose: 0.375 mg once daily; increase gradually not more frequently than every 5 to 7 days to 0.75 mg once daily and then, if necessary, by 0.75 mg per dose.	4.5 mg once daily.
Neupro (rotigotine)	Transdermal: Initial dose: 2 mg/24 hours for early-stage disease or 4 mg/24 hours for advanced-stage disease.	6 mg/24 hours for early-stage disease; 8 mg/24 hours for advanced-stage disease.

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 with MAOI class or other drugs that are potent inhibitors of monoamine oxidase (e.g., linezolid),

- Concomitant use of opioids (e.g., tramadol, meperidine and related derivatives)serotonin-norepinephrine reuptake inhibitors; tri-or tetra-cyclic or triazolopyridine antidepressants or triazolopyridine antidepressants, cyclobenzaprine, methylphenidate or amphetamine and its derivatives, St.John's wart
- Concomitant use with dextromethorphan
- Severe hepatic impairment (Child-Pugh C: 10-15)
- A history of a hypersensitivity to safinamide.

- Boxed warning(s):
  - None

APPENDIX D: General Information

- 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 levodopa (L-dopa) prevents conversion of L-dopa to dopamine in the systemic circulation and liver.
- Off time/episodes represent a return of PD symptoms (bradykinesia, rest tremor or rigidity) when the L-dopa treatment effect wears off after each dosing interval.

References

1. Xadago Prescribing Information. Louisville, KY: US WorldMeds, LLC; November 2019. Available at: http://xadago.com/. Accessed June 25, 2020.
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3. 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.
4. 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.
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7. 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.
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9. 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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	1/2020	02/07/2020

1) Policy title was updated. 2) Continued therapy therapy IIA1: approval was rephrased to ''currently receiving medication that has been authorized by RxAdvance..'' 3) Initial therapy and continued therapy: length of duration for commercial was updated 4) Appendix A updated 5) Contraindications were updated Reference were updated	06/25/2020	09/14/2020