

Clinical Policy: Safinamide (Xadago)  
Reference Number: CP.PMN.113  
Effective Date: 07.01.17  
Last Review Date: 05.18  
Line of Business: Commercial, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Safinamide (Xadago<sup>®</sup>) is monoamine oxidase type B (MAO-B) inhibitor.

### **FDA approved indication**

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

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

### **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<sup>®</sup> 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 Parkinson's disease (PD);
2. Member is experiencing "off" time (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 (Azilect<sup>®</sup>);
  - b. One of the following drugs: entacapone (Comtan/Stalevo), ropinirole/ropinirole ER (Requip<sup>®</sup>/Requip ER<sup>®</sup>), pramipexole/promipexole ER (Mirapex<sup>®</sup>/Mirapex ER<sup>®</sup>), Neupro (ritigotine);  
*\*Prior authorization is (or may be) required*
4. Xadago is prescribed in combination with levodopa/carbidopa;
5. Dose does not exceed 100 mg once daily.

**Approval duration: 6 months**

### **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. Parkinson’s Disease** (must meet all):

2. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Documentation of positive response to therapy;
4. Dose does not exceed 100 mg once daily.

**Approval duration:**

**Medicaid** - 12 months

**Commercial** - Length of Benefit

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

1. Currently receiving medication via health plan 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*

COMP: catechol-O-methyl transferase

FDA: Food and Drug Administration

MAO B: monoamine oxidase inhibitor

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

<b>Drug</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
entacapone (Comtan) <i>COMP inhibitor</i>	Oral: 200 mg with each dose of levodopa/carbidopa.	1600 mg daily (divided doses).
carbidopa/levodopa/ entacapone (Stalevo) <i>COMP inhibitor</i>	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).
rasagiline (Azilect) <i>MAO B inhibitor</i>	Oral: Monotherapy or adjunctive therapy (not including levodopa): 1 mg once daily. Adjunctive therapy with levodopa: Initial: 0.5	1 mg once daily.

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
	mg once daily; may increase to 1 mg once daily based on response and tolerability.	
ropinirole (Requip) <i>Dopamine agonist</i>	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) <i>Dopamine agonist</i>	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) <i>Dopamine agonist</i>	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) <i>Dopamine agonist</i>	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) <i>Dopamine agonist</i>	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<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

**Appendix C: Definition of Wearing Off Time**

- 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.

**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.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Adjunctive treatment to levodopa/carbidopa in patients with Parkinson’s disease (PD) experiencing “off” episodes.	50 mg once daily; 100 mg once daily after 2 weeks if needed.	100 mg once daily.

**VI. Product Availability**

Tablets: 50 mg, 100 mg

**VII. References**

1. Xadago Prescribing Information. Louisville, KY: US WorldMeds, LLC; May 2017. Available at: <http://xadago.com/>. Accessed February 2018.
2. Pahwa MD, Factor SA, Lyons KE, et al. Practice Parameter: Treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. April 2006; 66: 983-995.
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. doi:10.1001/jamaneurol.2016.4467.
5. 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.
6. Parkinson Study Group. Entacapone improves motor fluctuations in levodopa-treated parkinson’s disease patients. *Ann Neurol*. 1997; 42: 747-755.
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.
8. 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*. 2005; 62: 241-248.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.17	06.17
2Q 2018 annual review: policies combined for Medicaid and Commercial lines of business; Medicaid: added the trial of preferred agent; Commercial: removed the mandated trial of Comtan and added requirement for trial of any of the following agent: entacapone, ropinirole/ropinirole ER; pramipexole/promipexole ER, ritigotine, in line with previously approved clinical guidance; references reviewed and updated.	03.12.18	05.18

**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.

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**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.

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