

Clinical Policy: Sildenafil (Xadago)

Reference Number: CP.PMN.113

Effective Date: 07.01.17

Last Review Date: 02.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

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

Description

Sildenafil (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.

It is the policy of health plans affiliated with Centene Corporation® 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 B*) on levodopa/carbidopa therapy;
4. Failure of two of the following adjunct drugs prescribed in combination with levodopa/carbidopa, each from different classes, unless contraindicated or clinically significant adverse effects are experienced: *
 - a. MAO-B inhibitor: rasagiline;
 - b. COMT inhibitor: entacapone (Comtan®/Stalevo®), tolcapone;
 - c. Dopamine agonist: ropinirole/ropinirole ER, pramipexole/pramipexole ER;
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 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy**A. Parkinson's Disease** (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. If request is for a dose increase, new dose does not exceed 100 mg (1 tablet) per day.

Approval duration:

HIM/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, HIM.PA.154 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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 for all relevant lines of business 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.	1200 mg/day (divided doses)
entacapone (Comtan)	PO: 200 mg with each dose of levodopa/carbidopa	1600 mg/day (divided doses)
tolcapone (Tasmar [®])	PO: 100 mg 3 times daily, as adjunct to levodopa/carbidopa	300 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
MAO-B Inhibitors		
rasagiline (Azilect)	PO: 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/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)
pramipexole ER (Mirapex ER)	PO: 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/day
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)
ropinirole ER (Requip ER)	PO: 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/day

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 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 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 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*. 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.

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, rotigotine, in line with previously approved clinical guidance; references reviewed and updated.	03.12.18	05.18
2Q 2019 annual review: no significant changes; added contraindications; no significant changes; references reviewed and updated.	02.25.19	05.19
1Q 2020 annual review: added HIM line of business; added age ≥ 18 years; revised criteria to add "failure of two of the following adjunct drugs prescribed in combination with levodopa/carbidopa, each from different classes" and indicated drug class names; added tolcapone as an additional agent for trial of COMT inhibitor; per SDC, removed Neupro from criteria; references reviewed and updated.	10.30.19	02.20
1Q 2021 annual review: monotherapy limitation of use removed per FDA label update - indication for adjunctive use remains unchanged; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.20.20	02.21

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. 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.

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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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