Clinical Policy: Amantadine ER (Gocovri, Osmolex ER)

Reference Number: CP.PMN.89
Effective Date: 10.10.17
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid Revision Log

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

Description
Amantadine extended-release (Gocovri®, Osmolex ER®) is a weak uncompetitive antagonist of the N-methyl-D-aspartate (NMDA) receptor.

FDA Approved Indication(s)
Gocovri is indicated:

- For the treatment of dyskinesia in patients with Parkinson's disease (PD) receiving levodopa-based therapy, with or without concomitant dopaminergic medications;
- As adjunctive treatment to levodopa/carbidopa in patients with PD experiencing "off" episodes.

Osmolex ER is indicated for the treatment of PD and for the treatment of drug-induced extrapyramidal reactions in adult patients.

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 Gocovri and Osmolex ER are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Dyskinesia in Patients with Parkinson's Disease (must meet all)**:**

1. Diagnosis of dyskinesia in patients with PD;
2. Age ≥ 18 years;
3. Member is receiving levodopa-based therapy;
4. Member must use immediate-release amantadine, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 274 mg (2 capsules) per day for Gocovri or 322 mg (2 tablets) per day for Osmolex ER.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Parkinson's Disease With "Off" Episodes (must meet all)**:**

1. Diagnosis of PD;
2. Request is for Gocovri;

3. Age ≥ 18 years;
4. Member is experiencing "off" time (*see Appendix D*) on levodopa/carbidopa therapy;
5. 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: rasagiline;
   b. COMT inhibitor: entacapone (Comtan®/Stalevo®), tolcapone;
   c. Dopamine agonist: ropinirole/ropinirole ER, pramipexole/pramipexole ER;

   **Prior authorization may be required for the above agents*
6. Member must use immediate-release amantadine, unless contraindicated or clinically significant adverse effects are experienced;
7. Prescribed in combination with levodopa/carbidopa;
8. Dose does not exceed 274 mg (2 capsules) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Drug Induced Extrapyramidal Reactions (must meet all)**:**
1. Diagnosis of a drug induced extrapyramidal reaction;
2. Request is for Osmolex ER;
3. Age ≥ 18 years;
4. Member must use immediate-release amantadine, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 322 mg (2 tablets) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

D. 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. All Indications in Section I (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 (e.g., reductions in OFF time, improvement in dyskinesia symptoms);
3. If request is for a dose increase, new dose does not exceed 274 mg (2 capsules) per day for Gocovri or 322 mg (2 tablets) per day for Osmolex ER.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 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 policy – 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
FDA: Food and Drug Administration
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.

Drugs	Dosing Regimen	Dose Limit/ Maximum Dos
amantadine immediate-release	Titrated up to 100 mg PO QID	400 mg/day
COMT Inhibitors		
carbadopa/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 levodopa/day (divided doses)
entacapone (Comtan)	PO: 200 mg with each dose of levodopa/carbidopa	1,600 mg/day (divided doses)
tolcapone (Tasmar®)	PO: 100 mg 3 times daily, as adjunct to levodopa/carbidopa	300 mg/day

Drugs	Dosing Regimen	Dose Limit/ Maximum Dos
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 XL)	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: Contraindications/Boxed Warnings

- Contraindication(s): end-stage renal disease
- 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.

- Parkinson's disease symptoms, resulting from too little levodopa (L-dopa), are in contrast with dyskinesia which typically results from too much L-dopa. The alterations between "on" time (the time when Parkinson's disease 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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Amantadine ER (Gocovri)	Dyskinesia or "off" episodes in PD	137 mg PO QHS for 1 week. After 1 week, increase to 274 mg (two 137 mg capsules) PO QHS	274 mg/day
Amantadine ER (Osmolex ER)	Dyskinesia in PD; drug induced extrapyramidal reaction	129 mg PO QAM, increase dose in weekly intervals	322 mg/day

VI. Product Availability

Drug Name	Availability
Amantadine ER (Gocovri)	Extended-release capsules: 68.5 mg, 137 mg
Amantadine ER (Osmolex ER)	Extended-release tablets: 129 mg, 193 mg, 258 mg

VII. References

1. Gocovri Prescribing Information. Emeryville, CA: Adamas Pharma, LLC; January 2021. Available at: https://www.gocovrihcp.com. Accessed October 18, 2021.
2. Osmolex ER Prescribing Information. Bridgewater, NJ: Vertical Pharmaceuticals, LLC; January 2020. Available at: www.osmolex.com. Accessed October 18, 2021.
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;33(8):1248-1266.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.10.17	01.18
Per SDC, added requirement for medical justification that supports inability to use immediate-release amantadine	04.12.18	
Added Osmolex ER per SDC based on approved clinical guidance; added criteria set for drug induced extrapyramidal reaction.	09.18.18	
1Q 2019 annual review; no significant changes; immediate-release amantadine two-week trial and medical justification requirements are edited to reflect either/or; references reviewed and updated.	11.13.18	02.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; references reviewed and updated.	10.30.19	02.20
1Q 2021 annual review: added HIM line of business; no significant changes; RT4: added criteria for Gocovri for newly FDA-approved indication of PD "off" episodes, to align with previously P&T-approved approach for this diagnosis for other similarly FDA-approved agents; added age requirement for all existing indications per Gocovri and Osmolex labeling; simplified language re: past trial of immediate-release amantadine to reflect recent template changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	02.13.21	02.21
1Q 2022 annual review: no significant changes; changed commercial approval duration from length of benefit to 12 months or duration of request, whichever is less; revised Appendix D General Information; references reviewed and updated.	10.18.21	02.22

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.