# Clinical Policy: Amantadine ER (Gocovri, Osmolex ER)

Reference Number: ERX.NPA.58
Effective Date: 03.01.18
Last Review Date: 02.22
Line of Business: Commercial, 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.*

*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 Gocovri and Osmolex 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 –** 12 months
**Commercial –** Length of Benefit

**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 –** Length of Benefit

**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 –** 12 months
**Commercial –** Length of Benefit

**D. 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. All Indications in Section I** (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 (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 –** 12 months
**Commercial –** Length of Benefit

## 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*
FDA: Food and Drug Administration
PD: Parkinson's disease

*Appendix B: Therapeutic Alternatives*

| Drug Name | Dosing Regimen | Dose Limit / Maximum Dose |
|---|---|---|
| amantadine immediate-release | Titrated up to 100 mg PO QID | 400 mg/day |

| Drug Name | Dosing Regimen | Dose Limit / Maximum Dose |
|---|---|---|
| **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 |
| **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 | 02.18 |
| 1Q 2019 annual review: new drug added (Osmolex); 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 |
| 1Q 2020 annual review: no significant changes; added Medicaid line of business with 12 month approval durations; references reviewed and updated. | 10.30.19 | 02.20 |
| 1Q 2021 annual review: 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; added quantity limits corresponding to FDA max doses; references reviewed and updated. | 02.13.21 | 02.21 |
| 1Q 2022 annual review: no significant changes; 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.

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.

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