Clinical Policy Title:	amantadine
Policy Number:	RxA.153
Drug(s) Applied:	(Gocovri®, Osmolex®ER)
Original Policy Date:	02/07/2020
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

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

Gocovri® is indicated for the treatment of dyskinesia in patients with Parkinson's disease receiving levodopa-based therapy, with or without concomitant dopaminergic medications and as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes.

Osmolex® ER is indicated for the treatment of Parkinson's disease and for the treatment of drug-induced extrapyramidal reactions in adult patients.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
amantadine ER (Gocovri®)	Dyskinesia in Parkinson's disease	137 mg orally every bedtime for 1 week. After 1 week, increase to 274 mg (two 137 mg capsules) orally every bedtime. For Renal Impairment: CrCl 30 to 59 mL/minute: 68.5 mg orally once daily at bedtime. Increase if needed after 1 week to a maximum of 137 mg once daily at bedtime. CrCl 15 to 29 mL/minute: 68.5 mg orally once daily at bedtime. CrCl less than 15 mL/minute: Use is contraindicated.	274 mg/day
amantadine ER (Osmolex® ER)	Dyskinesia in Parkinson's disease; drug induced extrapyramidal reaction	129 mg orally once daily in the morning, increase dose in weekly intervals to a maximum daily dose of 322 mg once daily in the morning. For Renal Impairment: CrCl 30 to 59 mL/minute: 129 mg orally once every 48 hours initially. May increase every 3 weeks up to a maximum of 322 mg once every 48 hours. CrCl 15 to 29 mL/minute: 129 mg orally once every 96 hours initially. May increase every 4 weeks up to a maximum of 322 mg once every 96 hours. CrCl less than 15 mL/minute: Use is contraindicated.	322 mg/day

Dosage Forms

- Amantadine ER (Gocovri®): Extended-release capsules: 68.5 mg and 137 mg
- Amantadine ER (Osmolex® ER): Extended-release tablets: 129 mg, 193 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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Parkinson's disease (must meet all):

1. Diagnosis of dyskinesia in patients with Parkinson's disease;
2. Diagnosis of experiencing off episodes for Gocovri® (e.g. muscle stiffness, slow movements, or difficulty starting movements);
3. If the request is for Gocovri®, member is currently receiving levodopa-based therapy;
4. Meets one of the following (a or b):
   a. Failure of a 2-week trial of immediate-release amantadine unless contraindicated or clinically significant adverse effects are experienced;
   b. Medical justification supports inability to continue use of immediate-release amantadine (e.g., contraindications to excipients);
5. Dose does not exceed 274 mg per day for Gocovri® or 322 mg per day for Osmolex® ER.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Drug Induced Extrapyramidal Reactions (must meet all)**:**

1. Diagnosis of a drug induced extrapyramidal reaction;
2. Request is for Osmolex® ER;
3. Meets one of the following (a or b):
   a. Failure of a 2-week trial of immediate-release amantadine unless contraindicated or clinically significant adverse effects are experienced;
   b. Medical justification supports inability to continue use of immediate-release amantadine (e.g., contraindications to excipients);
4. Dose does not exceed 322 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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 per day for Gocovri® or 322 mg per day for Osmolex® ER.

Approval Duration

Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
NMDA: N-methyl-D-aspartate

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug	Indication	Dosing Regimen	Maximum Dose
amantadine immediate-release	Parkinson's Disease/Syndrome; Drug-Induced Extrapyramidal Reactions	100 mg orally twice daily	300 mg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

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

*Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information
None

References

1. Gocovri® Prescribing Information. Emeryville, CA: Adamas Pharma, LLC; January 2021. Available at: https://www.gocovri.com/pi . Accessed January 05, 2022.
2. Osmolex ER® Prescribing Information. Bridgewater, NJ: Vertical Pharmaceuticals, LLC; March 2021. Available at: https://www.osmolex.com/wp-content/uploads/2021/01/Prescribing_Information.pdf . Accessed January 05, 2022.
3. Oertel W, Eggert Karla, Pahwa R, et al. Randomized, placebo-controlled trial of ADS-5102 (amantadine) extended-release capsules for levodopa-induced dyskinesia in Parkinson's disease (EASE LID 3). Mov Disord. 2017 August 21; Available at Doi: 10.1002/mds.27131. Accessed January 05, 2022.
4. Pahwa R, Tanner CM, Hauser RA, et al. ADS-5102 (amantadine) extended-release capsules for levodopa-induced dyskinesia in Parkinson disease (EASE LID Study). JAMA Neurol. 2017;74(8):941-949. Doi:10.100/jamaneurol.2017.0943. Available at: https://pubmed.ncbi.nlm.nih.gov/28604926/ . Accessed January 05, 2022.
5. Amantadine. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, OH. Available at: https://online.lexi.com. Accessed January 05, 2022.

Review/Revision History	Review/Revised Date	P&T Approval

		Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Continued Therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 3. Updated Commercial Approval Duration from length of benefit to 12 months. 4. References were updated.	06/26/2020	09/14/2020
Policy was reviewed: 1. Background was updated to the indication of “as adjunctive treatment to levodopa/carbidopa in patients with Parkinson’s disease experiencing “off” episodes” for Gocovri® 2. Statement about provider sample, ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 3. Appendix B: Statement under Therapeutic Alternatives was changed to “Below are suggested therapeutic alternatives based on...” 4. References were reviewed and updated.	03/02/2021	06/10/2021
Policy was reviewed: 1. Dosing Information, Dosing Regimen, Updated: 2. Gocovri: to include renal impairment dosing information for indication Dyskinesia in Parkinson’s disease. 3. Osmolex® ER: Updated to include renal impairment dosing information for indication Dyskinesia in Parkinson’s disease; drug induced extrapyramidal reaction. 4. Dosage Forms: Updated dosage form from Amantadine ER (Osmolex® ER): Extended-release tablets: 129 mg, 193 mg, 258 mg to Amantadine ER (Osmolex® ER): Extended-release tablets: 129 mg, 193 mg. 5. Initial Approval Criteria I.A.3 was added to include, diagnosis of experiencing off episodes for Gocovri® (e.g. muscle stiffness, slow movements, or difficulty starting movements). 6. Initial Approval Criteria 1.A.4 was updated from ,Member is currently receiving levodopa based therapy to if the request is for Gocovri®, member is currently receiving levodopa based therapy. 7. Disclaimer about contraindications "Contraindications listed reflect statements	01/05/2022	04/18/2022

made in the manufacturer's package insert..." was added to Appendix C. 8. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 9. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 10. Appendix A: Updated to remove abbreviations PO, QHS, QAM, FDA. 11. Appendix A: Updated to include abbreviation for NMDA. 12. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 13. Appendix B, Maximum Dose, amantadine immediate-release: Updated maximum dose information from 400 mg to 300 mg for indication Parkinson's Disease/Syndrome; Drug-Induced Extrapyramidal Reactions. 14. Appendix B, Dosing Regimen, amantadine immediate-release : Updated dosing information from Titrated up to 100 mg orally QID to 100 mg PO twice daily for indication Parkinson's Disease/Syndrome; Drug-Induced Extrapyramidal Reactions. 15. References were reviewed and updated.		