Clinical Policy Title:	carbidopa and levodopa extended-release capsules
Policy Number:	RxA.464
Drug(s) Applied:	Rytary®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Carbidopa and levodopa extended-release capsules (Rytary®) is a combination of carbidopa (an aromatic amino acid decarboxylation inhibitor) and levodopa (an aromatic amino acid). It is indicated for the treatment of Parkinson's disease (PD), post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
carbidopa and levodopa extended-release capsules (Rytary®)	PD; Parkinsonism	Levodopa-naive patients: Starting dose is 23.75 mg/95 mg orally three times daily; may increase to 36.25 mg/145 mg orally three times daily on the fourth day of treatment; may increase dose up to carbidopa 97.5 mg/levodopa 390 mg orally three times daily; frequency of dosing may be increased to a maximum of 5 times daily if needed and tolerated. Patients converting from IR carbidopa-levodopa to ER carbidopa-levodopa: Please refer PI	carbidopa 612.5 mg /levodopa 2450 mg per day

Dosage Forms

- ER capsule: carbidopa/levodopa 23.75 mg/95 mg, 36.25 mg/145 mg, 48.75 mg/195 mg, 61.25 mg/245 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 or Parkinsonism (must meet all)**:**

1. Diagnosis of PD or parkinsonism;
2. Age ≥ 18 years;
3. Documented intolerance or contraindication* to carbidopa-levodopa sustained release tablets (Sinemet® CR) that would not apply to Rytary®;
4. Dose does not exceed carbidopa 612.5 mg/levodopa 2,450 mg per day.

*Examples of acceptable intolerance or contraindications include inability to swallow pills or intolerance or contraindications to excipients in carbidopa-levodopa sustained released tablets. Note: Failure of carbidopa-levodopa sustained released tablets is NOT an acceptable rationale for use of Rytary® over Sinemet CR.

Approval duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Parkinson's Disease or Parkinsonism (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed carbidopa 612.5 mg/levodopa 2,450 mg per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MAO: Monoamine oxidase
PD: Parkinson's disease
IR: immediate-release
ER: extended release

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 Name	Dosing Regimen	Dose Limit/ Maximum Dose
carbidopa and levodopa sustained released tablets (Sinemet CR)	Patients not currently receiving levodopa: Initial: carbidopa 50 mg/levodopa 200 mg orally twice daily. Patients currently receiving levodopa: *Note: Levodopa must be discontinued at least 12 hours before starting carbidopa/levodopa therapy.* Initial: Sinemet CR should be substituted at a dosage that will provide approximately 25% of the previous levodopa dosage; usual initial dose in mild to moderate disease is carbidopa 50 mg/levodopa 200 mg twice daily.	Most patients are adequately controlled on doses that provide up to 1,600 mg/day of levodopa.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Patients converting from immediate-release (IR) formulation to controlled release: Initial: Dosage should be substituted at an amount that provides ~10% more of levodopa/day; total calculated dosage is administered in divided doses 2 to 3 times/day (or ≥ 3 times/day for patients maintained on levodopa ≥ 700 mg). Depending on clinical response, dosage may need to be increased to provide up to 30% more levodopa/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):
  - Concomitant use of nonselective monoamine oxidase (MAO) inhibitor (e.g., phenelzine, tranylcypromine) or have recently (within 2 weeks) taken a nonselective MAO inhibitor. Hypertension can occur if these drugs are used concurrently.

- Boxed warning(s):
  - None reported.

APPENDIX D: General Information

- May cause falling asleep during activities of daily living.
- Avoid sudden discontinuation or rapid dose reduction to reduce the risk of withdrawal-emergent hyperpyrexia and confusion.
- Cardiovascular Events: Monitor patients with a history of cardiovascular disease.
- Hallucinations/Psychosis may occur.
- Impulse Control Disorders: Consider dose reduction or stopping Rytary® if occurs.
- May cause or exacerbate dyskinesia: Consider dose reduction.

References

1. Rytary® Prescribing Information. Bridgewater, NJ: Amneal Specialty, a division of Amneal Pharmaceuticals LLC; December 2019. Available at: https: //rytary.com. Accessed June 24, 2021.
2. Sinemet CR Prescribing Information. Whitehouse Station, NJ: Merck and Co., Inc.; March 2020. Available at https://dailymed.nlm.nih.gov. Accessed June 24, 2021.
3. Rytary®. Dosage. Lexicomp. Wolters Kluwer. Hudson, Oh. Available at https://online.lexi.com . Accessed June 30, 2021.
4. Sinemet CR. Indications/Dosage. Clinical Pharmacoly. Elsevier Inc. RELX Group™ Available at: https://www.clinicalkey.com/pharmacology/ . Accessed July 02, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	03/06/2020

Policy was reviewed: 1. Policy description table updated. 2. Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy”. 3. Initial therapy and continued therapy approval duration updated. 4. References were updated.	07/31/2020	09/14/2020
Policy was reviewed: 1. Dosing Information drug name was updated to include generic drug carbidopa and levodopa extended release capsules. 2. Dosing Information dosing regimen was updated to remove "Initial dose based off of total current daily dose of levodopa in IR carbidopa/levodopa (frequency of dosing may be increased to a maximum of 5 times daily if needed and tolerated)”. 3. Dosing Information was updated to include "Please refer PI”. 4. Statement about provider sample "The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 5. Appendix A was updated include abbreviations IR and ER. 6. Appendix B: Therapeutic Alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance..". 7. Statement about drug listing format in Appendix B is updated 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." was updated. 8. Appendix C contraindications was updated to include “Hypertension can occur if these drugs are used concurrently.” 9. Appendix D was updated to include “May cause falling asleep during…”, “Avoid sudden discontinuation or rapid dose reduction…”, “Cardiovascular Events…”, “Hallucinations/Psychosis…”, “Impulse Control Disorders…”, and “May cause or exacerbate dyskinesia…”. 10. References were reviewed and updated.	06/24/2021	09/14/2021