Carbidopa/ Levodopa Extended Release Capsules (Rytary)
Criteria for Use
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VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive Carbidopa/ Levodopa Extended Release Capsules.*

- ☐ Treatment of any indication other than parkinsonism
- ☐ Currently taking a nonselective monoamine oxidase (MAO) inhibitor (e.g., phenelzine and tranylcypromine) or have recently (within 14 days) taken a nonselective MAO inhibitor
- ☐ Hypersensitivity to levodopa, carbidopa, or any component of the formulation

Inclusion Criteria *The answers to one of the following must be fulfilled in order to meet criteria.*

Clinical diagnosis of Parkinson's disease (PD), post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication AND must have demonstrated lack of efficacy, have obtained maximal clinical benefit or contraindications to ALL of the following medications

- ☐ COMT inhibitors (either tolcapone or entacapone)
- ☐ Dopamine agonist (either pramipexole, ropinirole or rotigotine)
- ☐ MAO B inhibitor (either rasagiline or selegiline)
- ☐ Combination therapy of carbidopa/levodopa IR with carbidopa/levodopa CR

- **AND must have the following motor complications**
  - ☐ Fluctuations ("wearing off') that requires dosing of dopaminergic medications at intervals ≤every 4 hours

Dosage and Administration

- Dose conversions from carbidopa/levodopa IR should be based on the total daily dose of levodopa that a patient is receiving. For patients receiving carbidopa/levodopa IR please refer to Table 1.
- Dose conversions from carbidopa/levodopa CR have not been studied in clinical trials. Based on bioavailability, a conversion using a 30% lower dose than the IR product could be used.
- Dose conversion for patients on entacapone will require higher doses of levodopa. Increasing the total levodopa daily dose by 25 % can serve as a guide.
- Some patients may require more than three times daily dosing. This is especially true for treatment experienced patients who may be using treatment intervals of every 3 hrs or less. While the goal is to transition a patient to the lowest dosing frequency patients may require up to five doses of CLERC daily.
- May be taken with or without food. There may be a delay by 2 hours in the absorption of levodopa if taken with a high-fat, high-calorie meal. Protein may also cause a decrease in the absorption of levodopa.
- Do not chew, divide or crush capsules.
- For patients who have difficulty swallowing intact capsules, administer by carefully opening the capsule, sprinkling the entire contents on a small amount of applesauce (1 to 2 tablespoons), and consuming immediately.
- Withdrawal-Emergent Hyperpyrexia and Confusion can occur with rapid discontinuation or sudden dose reduction. This symptom may appear similar to neuroleptic malignant syndrome. Do not abruptly discontinue therapy, a dose taper is suggested.

Monitoring

- Prescribing provider should assess patient for efficacy and safety within 12 weeks and then again every six months. Ensure documentation on patient outcomes prior to continuation of therapy. This monitoring should be specific and operationalized in clinical care.
- Monitor the usefulness of the medication by asking patients how much OFF-time they typically have in a waking day.

- Assessment of efficacy using the Unified Parkinson's Disease Rating Scale (UPDRS) prior to initiating therapy and periodically thereafter.
- Therapy should be stopped if there is no improvement in OFF time or patient has develops worsening dyskinesia, hallucinations, or causes other side effects, despite appropriate dose adjustments.
- Warnings/precautions:
  - Somnolence (falling asleep during activities of daily living)
  - Cardiovascular ischemic events may occur in patients with history of ischemic heart disease or risk factors for ischemic heart disease.
  - Hallucinations and psychosis can occur shortly after beginning CLERC, patients with major psychiatric disorders should not be treated with CLERC
  - Impulse Control/Compulsive behaviors can develop
  - Dyskinesia's may occur and require a dose reduction of CLERC
  - Peptic Ulcer Disease, treatment with CLERC may increase the risk for upper gastrointestinal hemorrhage
  - Glaucoma and/or intraocular pressure may increase
  - Parkinson's patients are at a higher risk for developing melanoma, it is unknown as to whether it is caused by medication or other factors

Table 1: Conversion from Immediate-Release Carbidopa-Levodopa to RYTARY

Total Daily Dose of Levodopa in Immediate-Release Carbidopa-Levodopa	Recommended Starting Dosage of RYTARY	
	Total Daily Dose of Levodopa in RYTARY	RYTARY Dosing Regimen
400 mg to 549 mg	855 mg	3 capsules RYTARY 23.75 mg / 95 mg taken TID[a]
550 mg to 749 mg	1140 mg	4 capsules RYTARY 23.75 mg / 95 mg taken TID
750 mg to 949 mg	1305 mg	3 capsules RYTARY 36.25 mg / 145 mg taken TID
950 mg to 1249 mg	1755 mg	3 capsules RYTARY 48.75 mg / 195 mg taken TID
Equal to or greater than 1250 mg	2340 mg or	4 capsules RYTARY 48.75 mg / 195 mg taken TID or
	2205 mg	3 capsules RYTARY 61.25 mg / 245 mg taken TID

[a] TID: three times a day

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