

## Carbidopa/ Levodopa Enteral Suspension (Duopa)

### Criteria for Use

March 2016

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](http://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 Intestinal Gel*

- Treatment of any indication other than idiopathic 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
- Narrow angle glaucoma
- Patient is not an appropriate candidate for PEG J placement. Contraindications include: known or suspected intestinal obstruction, serious coagulation disorders, sepsis or active peritonitis. Relative contraindications include; ascites and neoplastic, inflammatory and infiltrative disease of the gastric and abdominal walls.
- Less than 2 hours of "off time" daily, despite optimization of medical therapy.
- Patient who has not demonstrated a response to prior levodopa use
- Dosing frequency for levodopa less than 4 times daily.

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

Diagnosis of Idiopathic Parkinson's disease. Care managed by a VA Neurologist or Movement Disorder Specialist

#### AND

Patient must have been tried on at least two agents from the following classes of therapies with documentation of lack of efficacy and/or poor tolerability/side effects:

- Dopamine agonists (pramipexole, ropinirole, rotigotine)
- COMT inhibitors (entacapone, tolcapone)
- Oral levodopa formulations (any carbidopa/levodopa in any formulation)
- Amantadine
- MAO-B Inhibitors (selegiline, rasagiline)

#### AND must have the following motor complications

Fluctuations ("wearing off") that requires dosing of dopaminergic medications at intervals  $\leq$  every 4 hours

### Dosage and Administration

- Carbidopa/levodopa enteral suspension (CLES) is delivered by a pump and the cartridge containing the suspension and is changed daily. Each cartridge contains 2 g of levodopa and 500 mg carbidopa, sufficient for most patients' daily requirements. A modified percutaneous gastrostomy tube is inserted endoscopically. An inner jejunostomy tube is then inserted through the percutaneous gastrostomy into the jejunum. The pump is attached to the inner tube and the suspension is infused directly into the jejunum
- Treatment with CLES is initiated in 3 steps
  - Conversion of patients to oral immediate-release carbidopa-levodopa tablets
  - Calculation and administration of the CLES starting dose (Morning Dose and Continuous Dose) for Day 1. (See Appendix A)
  - Titration of the dose as needed based on individual clinical response and tolerability.
- MAO Inhibitors: Levodopa may enhance the adverse/toxic effect of MAO Inhibitors. Of particular concern is the development of hypertensive reactions when levodopa is used with nonselective MAOI. Management: The concomitant use of nonselective monoamine oxidase inhibitors (MAOIs) and levodopa is contraindicated. Discontinue the nonselective MAOI at least two weeks prior to initiating levodopa. Monitor patients taking a selective MAOIs and lev May decrease the serum concentration of Levodopa.
- Oral iron preparations may decrease the serum concentration of levodopa. Consider separating doses of the agents

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by 2 or more hours to minimize the effects of this interaction. Monitor for decreased therapeutic effects of levodopa during concomitant therapy, particularly if doses cannot be separated. Exceptions: Ferric Carboxymaltose; Ferric Gluconate; Ferric Pyrophosphate Citrate; Ferumoxytol; Iron Dextran Complex; Iron Sucrose

### Issues for Consideration

- Generalized polyneuropathy has been reported in patients receiving CLES. Assess patients for the signs and symptoms of peripheral neuropathy before and periodically after starting CLES, especially patients with pre-existing neuropathy, patients taking medications, or those who have medical conditions associated with neuropathy. The presence of hyperhomocysteinaemia may also contribute to neuropathy.
- Myocardial infarction and arrhythmia were reported in patients taking carbidopa-levodopa. Ask patients about symptoms of ischemic heart disease and arrhythmia, especially those with a history of myocardial infarction or cardiac arrhythmias.
- CLES may increase the risk for elevated blood urea nitrogen (BUN) and creatine phosphokinase (CPK). Patients taking levodopa may have increased levels of catecholamines and their metabolites in plasma and urine, giving false positive results that suggest the diagnosis of pheochromocytoma.
- Dopamine agonists used for Parkinson disease have been associated with compulsive behaviors and/or loss of impulse control, which has manifested as pathological gambling, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges. Dose reduction or discontinuation of therapy has been reported to reverse these behaviors in some, but not all cases
- Dopaminergic agents have been associated with a syndrome resembling neuroleptic malignant syndrome on abrupt withdrawal, rapid dose reduction, significant dosage reduction after long-term use, or changes in dopaminergic therapy. Avoid sudden discontinuation or rapid dose reduction; taper dose to reduce the risk of hyperpyrexia and confusion
- Levodopa may cause orthostatic hypotension; Parkinson disease patients appear to have an impaired capacity to respond to a postural challenge. Use with caution in patients at risk of hypotension (such as those receiving antihypertensive drugs) or where transient hypotensive episodes would be poorly tolerated (cardiovascular disease or cerebrovascular disease). Parkinson patients being treated with dopaminergic agonists ordinarily require careful monitoring for signs and symptoms of postural hypotension, especially during dose escalation, and should be informed of this risk

### Monitoring

- 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 CLES , patients with major psychiatric disorders should not be treated with CLES
  - Impulse Control/Compulsive behaviors can develop
  - Dyskinesia’s may occur and require a dose reduction of CLES
  - Peptic Ulcer Disease, treatment with CLES 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

Appendix A

**Step 1: Calculate and administer the DUOPA Morning Dose for Day 1**

- Determine the total amount of levodopa (in milligrams) in the first dose of oral immediate-release carbidopa-levodopa that was taken by the patient on the previous day.
- Convert the oral levodopa dose from milligrams to milliliters by multiplying the oral dose by 0.8 and dividing by 20 mg/mL. This calculation will provide the Morning Dose of DUOPA in milliliters.
- Add 3 milliliters to the Morning Dose to fill (prime) the intestinal tube to obtain the Total Morning Dose.
- The Total Morning Dose is usually administered over 10 to 30 minutes.

**Step 2: Calculate and administer the DUOPA Continuous Dose for Day 1**

- Determine the amount of oral immediate-release levodopa that the patient received from oral immediate-release carbidopa levodopa doses throughout the previous day (16 waking hours), in milligrams. Do not include the doses of oral immediate-release carbidopa-levodopa taken at night when calculating the levodopa amount.
- Subtract the first oral levodopa dose in milligrams taken by the patient on the previous day (determined in Step 1 (a)) from the total oral levodopa dose in milligrams taken over 16 waking hours (determined in Step 2 (a)). Divide the result by 20 mg/mL. This is the dose of DUOPA administered as a Continuous Dose (in mL) over 16 hours.
- The hourly infusion rate (mL per hour) is obtained by dividing the Continuous Dose by 16 (hours). This value will be programmed into the pump as the continuous rate.
- If persistent or numerous "Off" periods occur during the 16-hour infusion, consider increasing the Continuous Dose or using the Extra Dose function. If dyskinesia or DUOPA-related adverse reactions occur, consider decreasing the Continuous Dose or stopping the infusion until the adverse reactions subside.

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