IMPORTANT REMINDER
This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description
Carbidopa/levodopa (Duopa) is a self-administered enteral infusion indicated for the treatment of motor fluctuations in patients with advanced idiopathic Parkinson’s disease. It is administered as a continuous 16-hour daily infusion into the small intestine through a percutaneous endoscopic gastrostomy-jejunostomy (PEG-J) tube using a portable infusion pump.
Policy/Criteria

I. Most contracts require prior authorization approval of carbidopa/levodopa enteral infusion prior to coverage. Carbidopa/levodopa enteral infusion may be considered medically necessary when criteria A, B, C, and D below are met:

A. A diagnosis of idiopathic Parkinson’s disease when established by or in consultation with a specialist in neurology.

AND

B. There is clinical documentation that the patient is experiencing disabling motor fluctuations (“off time”) of greater than or equal to 6 hours per day while on a levodopa-containing product.

AND

C. Documentation that adequate trials of at least THREE adjunctive therapies from three different classes in combination with a levodopa-containing product, as specified in criteria a, b, AND c below, were either ineffective, not tolerated, or contraindicated:

a. Entacapone OR tolcapone (Tasmar).

AND

b. A dopamine agonist (such as pramipexole, ropinirole, or apomorphine). (See Appendix 1)

AND

c. Selegiline OR rasagiline mesylate (Azilect).

AND

D. Patient is responsive to levodopa therapy as supported by defined “on” periods of any duration when Parkinsonism symptoms are controlled while on a levodopa-containing product.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers carbidopa/levodopa enteral infusion to be a self-administered medication.

B. When prior authorization is approved, carbidopa/levodopa enteral infusion may be authorized in quantities of up to 30 cassettes per month.

C. Authorization shall be reviewed at least every six months to confirm that current medical necessity criteria are met and that the medication is effective.
III. Carbidopa/levodopa enteral infusion is considered investigational when used for all other conditions, including but not limited to:

A. Secondary Parkinsonism (e.g. drug-induced, neurodegenerative, post-encephalitic)
B. Atypical parkinsonian syndrome
C. Restless leg syndrome
D. Essential tremor

Position Statement

- Carbidopa/levodopa enteral infusion (Duopa) has been shown to be effective in reducing motor fluctuations in patients with advanced idiopathic Parkinson’s disease (PD); however, significant safety concerns undermine its net health benefit relative to oral and topical PD medications which have a more favorable safety profile.

- Carbidopa/levodopa enteral infusion (Duopa) was evaluated in patients who had a mean baseline “off” time of six hours while on an oral levodopa product and an adjunctive medication [i.e. dopamine agonist, catechol-O-methyl transferase (COMT) inhibitor, monoamine oxidase type B (MAO-B) inhibitor].

- Evidence-based guidelines recommend the use of adjunctive therapies from various classes, including dopamine agonists, COMT inhibitors, and MAO-B inhibitors for the symptomatic control of motor fluctuations in patients experiencing “off” time while on an oral levodopa product. [1,2]

- The safety and efficacy of carbidopa/levodopa enteral infusion (Duopa) has not been established in conditions other than advanced idiopathic PD.

Clinical Efficacy

- One fair confidence trial demonstrated that carbidopa/levodopa enteral infusion (Duopa) produces a modest reduction in “off” time relative to immediate release oral carbidopa/levodopa in patients with advanced idiopathic PD. [3]

  o Patients enrolled in this study had a mean baseline “off” time of six hours while on a levodopa product AND an adjunctive medication from the dopamine agonist, COMT inhibitor and/or MAO-B inhibitor class of medications. Mean difference in “off” time was approximately 2 hours relative to immediate release carbidopa/levodopa.

- Carbidopa/levodopa enteral infusion (Duopa) has not been compared to any other medication in the advanced PD setting.

- A high quality Cochrane systematic review concluded that there is insufficient evidence to demonstrate that one adjunctive therapy is clinically superior to another in terms of reducing motor fluctuations or improving functional outcomes. Evidence is limited to indirect comparisons of low to fair confidence placebo-controlled trials. [4]
Safety
- The overall safety profile of carbidopa/levodopa enteral infusion (Duopa) significantly lowers its net health benefit relative to existing alternatives.
  o Carbidopa/levodopa enteral infusion (Duopa) is associated with a high rate (92%) of clinically significant PEG-J tube related adverse events, some of which are serious and/or life threatening and include intestinal hemorrhage, intestinal obstruction, peritonitis, intestinal ischemia and post-operative wound infection. In addition, the 12-week duration of the pivotal trial may be insufficient to fully characterize the long term safety of carbidopa/levodopa enteral infusion (Duopa). [3]
  o In contrast, other oral and topical PD medications are generally well tolerated. Common adverse events include drowsiness, nausea, vomiting, and hypotension.

Dosing [5]
- The maximum total daily dose of carbidopa/levodopa enteral infusion (Duopa) is 2000 mg of the levodopa component (i.e. one cassette per day) administered over 16 hours.
- Cassettes are for single use only and should not be used for longer than 16 hours.

Appendix 1: Dopamine agonists

<table>
<thead>
<tr>
<th>apomorphine subcutaneous injection</th>
<th>ropinirole ER</th>
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<tbody>
<tr>
<td>bromocriptine mesylate</td>
<td>rotigotine transdermal patch (Neupro)</td>
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<tr>
<td>pramipexole</td>
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<tr>
<td>pramipexole ER</td>
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<td>ropinirole</td>
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<tr>
<th>Codes</th>
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<td>Idiopathic Parkinson’s disease</td>
</tr>
<tr>
<td>ICD-9</td>
<td>332.1</td>
<td>Secondary Parkinsonism</td>
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<tr>
<td>ICD-9</td>
<td>333.0</td>
<td>Atypical Parkinson’s disease</td>
</tr>
<tr>
<td>ICD-9</td>
<td>333.1</td>
<td>Essential and other specified forms of tremor</td>
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<tr>
<td>ICD-9</td>
<td>333.94</td>
<td>Restless leg syndrome</td>
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References


