November 22, 2024

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**Subject: LCD Reconsideration Request - L33794 - External Infusion Pumps: Addition of VYALEV™ (foscarbidopa/foslevodopa)**

Dear Drs. Ballyamanda, Hoover, Jenny, and Lalla,

On behalf of AbbVie, we are writing to formally request reconsideration of External Infusion Pumps Local Coverage Determination (LCD) (L33794) to include coverage for our product, VYALEV™ (foscarbidopa/foslevodopa), for subcutaneous injection for patients with advanced Parkinson's Disease (PD).

Parkinson's disease is a progressive neurological disorder characterized by a gradual loss or degeneration of dopaminergic neurons.[1] Most patients initially respond well to therapies like oral carbidopa/levodopa; however, as the disease progresses, due to factors like the progressive loss of neurons, short half-life of oral levodopa (resulting in fluctuating plasma levels and dyskinesia), and erratic gastric emptying, oral carbidopa/levodopa effectiveness diminishes over time, resulting in uncontrolled motor fluctuations.[2,3] Patients uncontrolled on oral therapy experiencing fluctuations have been shown to have higher disease burden, poorer quality of life, and higher dissatisfaction with their treatment.[4,5,6,7] The burden on care partners also increases significantly as the disease progresses.[8] Previously, when patients were uncontrolled on oral treatment regimens, treatment options were limited to surgical options such as carbidopa/levodopa enteral suspension (DUOPA™) or deep brain stimulation. On October 16, 2024, the Food and Drug Administration (FDA) approved VYALEV™ (foscarbidopa/foslevodopa) injection for subcutaneous use for the treatment of motor fluctuations in patients with advanced Parkinson's Disease.[9] VYALEV™ is the first and only non-surgical subcutaneous option for 24-hour continuous, levodopa-based therapy titratable for individualized treatment. VYALEV™ consists of levodopa and carbidopa prodrugs that are delivered continuously via an external infusion pump. In the registrational trial for VYALEV™, patients were included in the study if they had uncontrolled motor fluctuations despite their current treatment regimen (an average of 2.5 hours of "Off" time per day and at least 400 mg of levodopa equivalents/day).[10] HCPs and patients have been waiting for treatment that would address this unmet need.

**We respectfully request that the DME MACs establish coverage for VYALEV™ consistent with its FDA label and published clinical evidence.** Below we include the requested coverage criteria for your consideration, and attached to this letter, you will find the following information:

1) FDA approval letter and prescribing information for VYALEV™ (foscarbidopa/foslevodopa) subcutaneous injection
2) Publications for the pivotal trials

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**Proposed coverage criteria for VYALEV™ (foscarbidopa/foslevodopa) subcutaneous injection**

In updating L33794, we recommend the following coverage criteria for VYALEV™ (foscarbidopa/foslevodopa) for the treatment of motor fluctuations in adults with Parkinson's disease:[10]

- Diagnosed with levodopa-responsive idiopathic PD
- Currently taking ≥400 mg/day of levodopa equivalents
- Motor fluctuations that are inadequately controlled with carbidopa/levodopa therapy
- Minimum daily average "Off" time of 2.5 hours per day

**Clinical background on Parkinson's Disease and VYALEV™ (foscarbidopa/foslevodopa) subcutaneous injection**

Parkinson's Disease

Parkinson's Disease is a progressive and chronic neurological disorder characterized by tremor, muscle rigidity, slowness of movement, and difficulty with balance.[11] The motor symptoms of PD result from the loss of dopamine-producing brain cells and begin when approximately 60-80 percent of these cells are lost.[12] Symptoms continue to worsen slowly over the course of time.[13] While there is no known cure for the disease, there are treatments available to help reduce symptoms.[14]

As PD progresses, patients experience motor complications, including motor and non-motor fluctuations and dyskinesia (involuntary movements) which can significantly hinder daily activities. Patients report switching from an "on" state (when symptoms are generally well controlled) to an "off" state, during which symptoms such as tremor and stiffness may reappear, and patients have more difficulty in moving.[15] Neuronal degeneration and fluctuating plasma levodopa levels are responsible for the onset of these motor complications, with 50 percent of patients reporting them two to five years after diagnosis and approximately 80-100 percent of patients presenting with them after 10 years.[16]

There is unmet need for treatment options for patients with PD whose motor symptoms are not controlled by current therapy. As the disease progresses, it can be difficult to control motor fluctuations. Once oral options are not as effective, there are only surgical options available in the US, such as deep brain stimulation and DUOPA™ (carbidopa and levodopa) enteral suspension. AbbVie currently manufactures DUOPA™ (carbidopa and levodopa) for the treatment of motor fluctuations for people with advanced PD. DUOPA™ is administered using a portable infusion pump that delivers carbidopa and levodopa directly into the small intestine for 16 continuous hours via a surgically placed tube. Limitations of DUOPA™ include requirement of a surgery and inability to control symptoms overnight, which can lead to sleep disturbances and morning akinesia. The External Infusion Pumps LCD (L33794) provides Medicare coverage for DUOPA™.

VYALEV™ (foscarbidopa/foslevodopa) subcutaneous injection

VYALEV™ is the first and only subcutaneous 24-hour continuous infusion of levodopa-based therapy for the treatment of motor fluctuations in advanced Parkinson's disease. VYALEV™ works by delivering foslevodopa and foscarbidopa prodrugs into the subcutaneous space, which are converted to the active forms of levodopa-carbidopa. AbbVie has focused on maximizing the solubility and concentration of the prodrugs to make it practical to deliver a broader dose range to meet the needs of PD patients whose motor symptoms are not controlled by current therapy via a portable pump. Results from pharmacokinetic studies showed that 24 hour/day continuous delivery of foscarbidopa-foslevodopa provided stable levodopa exposures. Adults treated with VYALEV™ reported superior improvement in "on" time without troublesome dyskinesia, compared to oral immediate-release carbidopa/levodopa. VYALEV™ allows for personalized dosing based on individual needs, morning, day and night.

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**Published Evidence in Support of Coverage of VYALEV™**

The data from published, peer-reviewed literature support coverage of VYALEV™ for its FDA-approved indication. The FDA approval is based primarily on data from the M15-736 study, a Phase 3 randomized, double-blind, double-dummy, active-controlled study. Approximately 145 adult participants with PD, whose motor symptoms were no longer adequately controlled by their current medications, were enrolled in the study across 65 sites in the U.S. and Australia, and the study demonstrated statistically superior efficacy of VYALEV™ compared to oral immediate-release CD/LD in improving "on" time without troublesome dyskinesia and decreasing "off" time for patients.[17]

The primary efficacy endpoint was the change from baseline to Week 12 in average daily normalized "on" time without troublesome dyskinesia, defined as the sum of "on" time with no dyskinesia and "on" time with non-troublesome dyskinesia. A significant and clinically meaningful improvement from baseline in "on" time without troublesome dyskinesia was demonstrated during treatment with VYALEV™ compared to oral CD/LD at Week 12, with 2.8 times the increase in "on" time without troublesome dyskinesia (least squares mean [LSM] change [hours]: 2.72 vs. 0.97, respectively; p=0.0083).[17]

Patients treated with VYALEV™ experienced statistically significant and clinically meaningful improvements in normalized "off" time compared to oral CD/LD at Week 12, with 2.9 times as much reduction (LSM change [hours]: –2.75 vs. –0.96; p=0.0054).[17]

VYALEVTM was generally safe and well-tolerated. The majority of adverse events (AEs) were non-serious and mild or moderate in severity. There was one patient with a treatment-emergent AE leading to death in the oral CD/LD group and none in the VYALEVTM group. The most common AEs reported for VYALEV™ (VYALEV™ incidence at least 10% and greater than oral carbidopa-levodopa incidence) were infusion/catheter site reactions, infusion/catheter site infections, hallucinations, and dyskinesia.[10,17] The efficacy and safety profile were consistent following long-term use with VYALEV™ therapy (i.e. >2 years).[18,19*]

**Proposed coverage criteria for VYALEV™ (foscarbidopa/foslevodopa) subcutaneous injection**

In updating L33794, we recommend the following coverage criteria for VYALEV™ (foscarbidopa/foslevodopa) for the treatment of motor fluctuations in adults with Parkinson's disease:[10]

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In the associated LCD-related Policy Article, A52507, the following ICD-10 codes are considered aligned to label:

- G20.A2 (Parkinson's disease without dyskinesia, with fluctuations)
- G20.B1 (Parkinson's disease with dyskinesia, without mention of fluctuations)
- G20.B2 (Parkinson's disease with dyskinesia, with fluctuations)

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Based on the clinical evidence and publications set forth above and attached hereto, we respectfully urge the DME MACs to revise the External Infusion Pumps LCD (L33794) to allow for coverage of VYALEV™ (foscarbidopa/foslevodopa) with the proposed coverage criteria above.

Thank you again for the opportunity to submit this reconsideration request for the addition of VYALEV™ (foscarbidopa/foslevodopa) injection for subcutaneous use within the LCD - External Infusion Pumps (L33794). If you have any questions or would like to meet to discuss, please do not hesitate to contact us.

Sincerely,

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*Manuscript in development.