Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Foscarbidopa and Foslevodopa (VYALEV)	MP-RX-FP-164-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Vyalev, a combination of foscarbidopa (an aromatic amino acid decarboxylation inhibitor) and foslevodopa (an aromatic amino acid) approved by the Food and Drug Administration (FDA) for the treatment of motor fluctuations in adults with advanced Parkinson's disease.

VYALEV (Foscarbidopa and Foslevodopa) is approved for subcutaneous administration only, preferably in the abdomen, via the VYAFUSER pump.

Background Information

Parkinson's disease (PD) is a prevalent neurodegenerative movement disorder that affects millions worldwide. It is characterized by the progressive loss of dopamine-producing neurons in the substantia nigra, leading to a classic symptom triad of tremor, rigidity, and bradykinesia, along with various nonmotor and neuropsychiatric symptoms that impair function and quality of life. PD is not limited to dopamine depletion, as cell loss and biochemical changes occur in multiple brain regions beyond the basal ganglia.

Management of PD involves personalized treatment based on the patient's symptoms, disease stage, functional status, and activity level. Therapeutic options include pharmacologic, nonpharmacologic, and surgical interventions aimed at optimizing motor function, alleviating nonmotor symptoms, and improving quality of life throughout the disease course.

As PD advances, degeneration of nigrostriatal dopaminergic neurons impairs the storage and conversion of levodopa to dopamine, diminishing the effectiveness of standard levodopa immediate-release formulations. The short half-life of levodopa (approximately 90 minutes) results in fluctuating dopamine levels, narrowing the therapeutic window over time. Factors such as impaired gastric emptying, slow intestinal transit, dietary protein interference, and small intestinal bacterial overgrowth further impact levodopa absorption.

Advanced PD is associated with complications like motor fluctuations and dyskinesia, where patients transition between "on" states (well-controlled symptoms) and "off" states (reappearance of symptoms like tremor and stiffness). Dyskinesia, involving involuntary movements, can significantly hinder daily activities. These complications typically emerge within two to five years after diagnosis in 50% of patients, and in nearly all patients after 10 years.

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Various pharmacologic strategies, device-assisted therapies, and surgical treatments are available to manage motor complications in advanced PD, especially when symptoms are not adequately controlled by medical therapy. These interventions include deep brain stimulation (DBS), focused ultrasound therapy (FUS), continuous levodopa-carbidopa intestinal gel (LCIG) infusion, and continuous subcutaneous apomorphine infusion (CSAI).

On October 17, 2024, the U.S. Food and Drug Administration (FDA) approved Vyalev (foscarbidopa and foslevodopa), the first 24-hour subcutaneous levodopa-based infusion therapy for managing motor fluctuations in adults with advanced Parkinson's disease (PD). The continuous delivery system ensures steady plasma levels of levodopa, leading to improved 'on' time without troublesome dyskinesia. The approval was supported by a pivotal 12-week, Phase 3 randomized, double-blind study comparing the efficacy of continuous subcutaneous Vyalev infusion to oral immediate-release carbidopa/levodopa (CD/LD IR), as well as data from a 52-week open-label trial evaluating the long-term safety and efficacy of Vyalev.

The Phase 3 trial enrolled approximately 130 adults with advanced PD across 80 sites in the U.S. and Australia. Patients were randomized to receive either continuous subcutaneous Vyalev plus oral placebo capsules or oral CD/LD IR capsules plus subcutaneous placebo. The primary endpoint was the change in "on" time without troublesome dyskinesia over 12 weeks, normalized to a 16-hour waking period. Vyalev demonstrated a significant increase in "on" time without troublesome dyskinesia (2.72 hours) compared to CD/LD IR (0.97 hours; p=0.0083), with improvements observed from the first week and maintained throughout the study. Most adverse reactions with Vyalev were non-serious and mild to moderate in severity, including infusion site events, hallucinations, and dyskinesia.

In the separate 52-week open-label study, 244 patients with levodopa-responsive PD and at least 2.5 hours of daily "off" time received 24-hour Vyalev infusion. The primary endpoint was safety and tolerability, with secondary endpoints assessing motor symptoms, quality of life, and functional outcomes. At week 52, "on" time without troublesome dyskinesia improved by 3.8 hours and "off" time decreased by 3.5 hours. The percentage of patients experiencing morning akinesia dropped from 77.7% at baseline to 27.8%. Improvements were also seen in sleep quality and quality of life measures. Most adverse events were mild or moderate, with infusion site reactions being the most common.

VYALEV (foscarbidopa and foslevodopa) is approved for subcutaneous administration only, preferably in the abdomen, using the VYAFUSER pump. According to the labeling information, patients prescribed VYALEV should be trained on the proper use of the delivery system and be able to operate it independently or with caregiver assistance.

Approved Indications

VYALEV is indicated for the treatment of motor fluctuations in adults with advanced Parkinson’s disease (PD).

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Other Uses

None.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J7799	Not otherwise classified, other than inhalation drugs, administered through DME (when specified as Vyalev)
Pump and Ancilliaries	
A4221	Infusion set, vial adapter
E1399	Durable Medical Equipment, muscellaneous

CPT Code	Description
96369	Subcutaneous infusion for therapy or prophylaxis initial (≤ 1 hour)
96370	Subcutaneous infusion for therapy or prophylaxis (> 1 hour)

ICD-10	Description
G20.B1	Parkinson's disease with dyskinesia, without mention of fluctuations
G20.B2	Parkinson's disease with dyskinesia and fluctuations
G20.A2	Parkinson's disease without dyskinesia, with fluctuations.

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Foscarbidopa and Foslevodopa (VYALEV)

A. Criteria For Initial Approval

i. Individual has a diagnosis of advanced idiopathic Parkinson's disease (PD) with motor fluctuations; **AND**

ii. Documentation is provided that the individual's condition is responsive to levodopa; **AND**

iii. Individual is using a minimum daily dose of 400 mg of oral levodopa (including combination products); **AND**

iv. Documentation is provided that individual is experiencing a minimum of 2.5 hours of "Off" time per day while using optimal medical therapy, which includes the following:
   A. Oral levodopa-carbidopa; **AND**
   B. Dopamine agonists; **AND**
   C. One agent from the following classes:
      1. Catechol-0-methyl transferase (COMT) inhibitor; **OR**
      2. Monoamine oxidase B (MAO B) inhibitor; **OR**
      3. Adenosine receptor antagonist (Nourianz); **AND**

v. Individual meets all of the following criteria:
   A. The individual will not use VYALEV in combination with a monoamine oxidase (MAO) inhibitor (including, but not limited to, phenelzine or tranylcypromine); **AND**
   B. If the individual is currently using a MAO inhibitor (including, but not limited to, phenelzine or tranylcypromine), it will be discontinued, and VYALEV will be initiated at least 2 weeks after discontinuation; **AND**

vi. VYALEV will be administered subcutaneously via the VYAFUSER pump.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Foscarbidopa and Foslevodopa (VYALEV) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when:
   A. Documentation is provided confirming that there has been clinically significant improvement or stabilization in clinical signs and symptoms of disease.

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C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Individual is receiving a nonselective MAO inhibitor (including but not limited to phenelzine or tranylcypromine); **OR**
ii. Individual has a diagnosis of atypical PD or secondary PD; **OR**
iii. When the above criteria are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Foscarbidopa and Foslevodopa (VYALEV)	The maximum recommended daily dosage of VYALEV is 3,525 mg of foslevodopa (approximately 2,500 mg levodopa), which equates to approximately 30 vials per month when administered during 16 awake hours.
Exceptions	
None	

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Reference Information

A. Soileau, M., et al. Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: a randomised, double-blind, active-controlled, phase 3 trial. *Lancet Neurol.* 2022 Dec;21(12):P1099-1109.
B. Aldred, J., et al. Continuous Subcutaneous Foslevodopa/Foscarbidopa in Parkinson's Disease: Safety and Efficacy Results From a 12-Month, Single-Arm, Open-Label, Phase 3 Study. *Neurol Ther.* 2023 Dec;12(6):1937-1958.
C. Ling, TW., et al. Medical Management Of Motor Fluctuations And Dyskinesia In Parkinson Disease. UpToDate. Last Updated Sept. 23, 2024.
D. Spindler M., et al. Initial pharmacologic treatment of Parkinson disease. Last Updated July 15, 2024.
E. Vyalev [package insert]. North Chicago, IL: AbbVie Inc.; October 2024.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	New Policy Creation	12/9/2024	12/17/2024

Revised: 10/25/2024