foscarbidopa/foslevodopa injection (Vyalev™‡)

Medicare Advantage Medical Policy #MA-130
Original Effective Date: 10/01/2025
Current Effective Date: 10/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider Vyalev™‡ (foscarbidopa/ foslevodopa injection) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Vyalev (foscarbidopa/ foslevodopa injection) will be considered when the following criteria are met:

- Initial
  - Patient is diagnosed with advanced Parkinson's disease; AND
  - Patient is experiencing "off" episodes such as muscle stiffness, slow movements, or difficulty starting movements; AND
  - Patient has tried an oral carbidopa/levodopa therapy and meets ONE of the following:
    - Patient had significant intolerance, according to the prescriber; OR
    - Patient had inadequate efficacy, according to the prescriber; AND
  - Daily dose does not exceed 3525 mg of the foslevodopa component (equivalent to approximately 2500 mg levodopa).
- Continuation
  - Patient has received an initial authorization for Vyalev from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
  - According to the prescriber, the patient continues to benefit from therapy with Vyalev (e.g., stabilization in clinical signs and symptoms of disease, increase of "on"-time, or decrease in the number of "off" episodes compared to baseline); AND
  - Daily dose does not exceed 3525 mg of the foslevodopa component (equivalent to approximately 2500 mg levodopa).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of Vyalev (foscarbidopa/ foslevodopa injection) when the patient has not tried and failed and oral carbidopa/levodopa therapy to be **not medically necessary.****

Based on review of available data, the Health Plan considers the continued use of Vyalev (foscarbidopa/ foslevodopa injection) when the patient has not demonstrated a beneficial response to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers Vyalev (foscarbidopa/ foslevodopa injection) for the treatment of any indication other than "off" episodes in Parkinson disease to be **investigational.***

Based on the review of available data, the Health Plan considers Vyalev in daily doses that exceed 3525 mg of the foslevodopa component (equivalent to approximately 2500 mg levodopa) to be **investigational.***

Background/Overview

Vyalev is a combination of foscarbidopa (an aromatic amino acid decarboxylation inhibitor) and foslevodopa (an aromatic amino acid) indicated for the treatment of motor fluctuations in adults with advanced Parkinson's disease. Vyalev is administered as a subcutaneous infusion, preferably in the abdomen, via the Vyafuser™ pump. Patients selected for treatment with Vyalev should be capable of understanding and using the delivery system themselves or with assistance from a caregiver. Vyalev is available as an injection at a concentration of 120 mg foscarbidopa and 2,400 mg foslevodopa per 10 mL (12 mg foscarbidopa and 240 mg foslevodopa per mL). Dosing of Vyalev is determined by the total levodopa dosage (TLD) for the levodopa-containing medication that Vyalev is replacing and the number of hours the patient is typically awake. The maximum recommended daily dosage of Vyalev is 3,525 mg of foslevodopa (approximately 2,500 mg levodopa).

Parkinson disease is a progressive neurodegenerative disease in which dopamine depletion from the basal ganglia results in disruptions in the connections to the thalamus and motor cortex. For most patients, first line therapy involves supplementation of dopamine via levodopa/carbidopa. As the disease progresses, periods of increased symptoms known as "off" episodes can occur when levodopa/carbidopa begins to wear off between doses. Initially, these episodes may be managed by adjusting the levodopa/carbidopa dose and schedule, but this may not be sufficient if the patient is experiencing adverse effects of the levodopa/carbidopa (such as dyskinesia). There are four classes of drugs indicated as adjunctive therapy to manage "off" episodes with levodopa/carbidopa: dopamine agonists, catecholamine-O-methyltransferase (COMT) inhibitors, MAO-B inhibitors, and adenosine receptor antagonists. Dopamine agonists such as pramipexole or ropinirole can be effective at prolonging symptom-free periods, but patients must be monitored for excessive dopaminergic effects (hallucinations, confusion, somnolence). The COMT inhibitors entacapone and tolcapone prolong and potentiate the levodopa effect by preventing its degradation. MAO-B inhibitors also prevent the degradation of levodopa by blocking its catabolism. There are three available MAO-B inhibitors: rasagiline, safinamide, and selegiline. Both rasagiline and safinamide have demonstrated consistent efficacy in reducing motor complications in combination with levodopa/carbidopa, but the clinical benefit of selegiline appears to be relatively mild. Nourianz is a

first-in-class adenosine receptor antagonist that appears to have similar efficacy and safety to other treatment options for this indication. Inbrija provides an additional therapy option of supplemental doses of levodopa when the patient notices an "off" episode beginning.

The American Academy of Neurology guidelines for the treatment of Parkinson disease with motor fluctuations and dyskinesia were published in 2006, prior to the approval of Xadago, Inbrija, Nourianz, or Ongentys. These guidelines recommend that rasagiline, pramipexole, ropinirole, apomorphine (i.e., Apokyn), and tolcapone should be considered to reduce "off" time. It should be noted that tolcapone is associated with liver injury and is therefore rarely used.

Additional guidance was published in 2018 by the International Parkinson and Movement Disorder Society which recommends that treatment approaches be individualized to the patient based on the evaluation of side effect profiles, patient specific characteristics as well as cost and availability. There are currently no studies to suggest superiority of one drug class over another in symptom management. For patients with motor fluctuations, dopamine agonists (pramipexole, ropinirole, apomorphine intermittent injections), levodopa ER, COMT inhibitors (entacapone, Ongentys [opicapone]), and MAO-B inhibitors (rasagiline, zonisamide, Xadago [safinamide]) are considered to be clinically useful. Possibly useful treatments include Nourianz (istradefylline) and tolcapone. For dyskinesia, treatment with amantadine and clozapine is determined to be efficacious and clinically useful. The availability of clinically efficacious generic products in this treatment category lends itself to be a more economical option versus the branded products available on the market.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Vyalev was approved in October 2024 for the treatment of motor fluctuations in adults with advanced Parkinson's disease.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Vyalev was established in a 12-week, randomized, double-blind, double-dummy, active-controlled, multicenter study which enrolled patients with advanced Parkinson's disease (PD) who were responsive to levodopa treatment, had motor fluctuations inadequately controlled by their current medications, and who experienced a minimum of 2.5 hours of "Off" time per day as assessed by PD diaries. A total of 141 patients were randomized in 1:1 ratio and received either 24-hour/day continuous subcutaneous administration of Vyalev plus oral placebo capsules (N=74) or 24-hour/day

continuous subcutaneous administration of placebo solution plus oral encapsulated carbidopa/levodopa immediate-release (IR) tablets (N=67). The primary clinical outcome measure was the mean change from baseline to Week 12 in the total daily mean "On" time without troublesome dyskinesia (defined as "On" time without dyskinesia plus "On" time with non-troublesome dyskinesia) based on PD diary. The key secondary clinical outcome measure was the mean change from baseline to Week 12 in the total daily mean "Off" time. The "On" and "Off" time were normalized to a daily 16-hour awake period. Daily normalized "Off" and "On" times are averaged over valid PD diary days for each visit to obtain the average daily normalized times. Vyalev demonstrated statistically significant improvements from baseline to Week 12 in "On" time without troublesome dyskinesia compared with the oral IR carbidopa-levodopa group ($p = 0.0083$). Vyalev also demonstrated statistically significant improvements from baseline to Week 12 in "Off" time compared with the oral IR carbidopa-levodopa group ($p = 0.0054$).

References

1. Pahwa R, Factor SA, Lyons KE, et al. Practice parameter: treatment of Parkinson disease with motor fluctuations and dyskinesia (an evidence-based review). Report of the quality standards subcommittee of the American Academy of Neurology. Neurology. 2006;66:983-995.
2. Fox, S. H., Katzenschlager, R., Lim, S., Barton, B., De Bie, R. M. A., Seppi, K., Coelho, M., & Sampaio, C. (2018). International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Movement Disorders, 33(8), 1248–1266. https://doi.org/10.1002/mds.27372
3. Vyalev [package insert]. AbbVie, Inc. North Chicago, Illinois. Updated October 2024.

Policy History

Original Effective Date: 10/01/2025
Current Effective Date: 10/01/2025
07/15/2025 UM Committee review and approval. New policy.
Next Scheduled Review Date: 07/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J7356
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.