LOUISIANA BLUE

Select Carbidopa/Levodopa Products

Policy # 00791
Original Effective Date: 06/13/2022
Current Effective Date: 01/13/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), 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 Company may consider Dhivy™‡ (carbidopa/levodopa) or Crexont®‡ (carbidopa/levodopa extended-release capsules) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Dhivy (carbidopa/levodopa) or Crexont (carbidopa/levodopa extended-release capsules) will be considered when the following criteria are met for the requested drug:

- For Dhivy requests:
  - Patient has a diagnosis of one of the following conditions:
    - Parkinson's disease; OR
    - Post-encephalitic parkinsonism; OR
    - Symptomatic parkinsonism following carbon monoxide intoxication or manganese intoxication; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC immediate release carbidopa/levodopa tablets OR GENERIC carbidopa/levodopa orally disintegrating tablets unless there is clinical evidence or patient history that suggests the generic products will be ineffective or cause an adverse reaction to the patient; OR
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- For Crexont requests:
  - Patient has a diagnosis of one of the following conditions:
    - Parkinson's disease; OR
    - Post-encephalitic parkinsonism; OR
    - Symptomatic parkinsonism following carbon monoxide intoxication or manganese intoxication; AND

- Patient has tried and failed (e.g., intolerance or inadequate response) one of the following GENERIC carbidopa/levodopa formulations: immediate release carbidopa/levodopa tablets, carbidopa/levodopa orally disintegrating tablets, OR extended-release carbidopa/levodopa unless there is clinical evidence or patient history that suggests the generic products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed (e.g., intolerance or inadequate response) Rytary (carbidopa/levodopa extended-release capsules) unless there is clinical evidence or patient history that suggests the use of this product will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Dhivy (carbidopa/levodopa) when patient has not tried and failed either the GENERIC carbidopa/levodopa tablets or the GENERIC carbidopa/levodopa orally disintegrating tablets to be **not medically necessary.****

Based on review of available data, the Company considers the use of Crexont (carbidopa/levodopa extended-release capsules) when the patient has not tried and failed one of the following GENERIC carbidopa/levodopa formulations: immediate release carbidopa/levodopa tablets, carbidopa/levodopa orally disintegrating tablets, OR extended-release carbidopa/levodopa AND Rytary (carbidopa/levodopa extended-release capsules) 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 Company considers the use of Dhivy (carbidopa/levodopa) or Crexont (carbidopa/levodopa extended-release capsules) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Both Dhivy and Crexont are indicated for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and symptomatic parkinsonism that may follow carbon monoxide intoxication or manganese intoxication. Dhivy is an immediate release tablet formulation of carbidopa and levodopa that is scored with 4 fractionated segments to allow for easier dosing adjustments. Each tablet contains 25 mg of carbidopa and 100 mg of levodopa and each segment contains 6.25 mg of

carbidopa and 25 mg of levodopa. The recommended starting dosage of immediate release carbidopa/levodopa is 25 mg/100 mg given three times daily for a total carbidopa dose of 75 mg per day. Studies have shown that approximately 70-100 mg of carbidopa are needed per day to saturate the peripheral dopa decarboxylase enzyme. Patients receiving less than this amount of carbidopa are more likely to experience nausea and vomiting. Additionally, there is limited experience with using total daily dosages of carbidopa greater than 200 mg. Dhivy was approved based on bioavailability studies comparing it to generically available immediate release carbidopa/levodopa tablets. Thus, the generically available products likely represent equally efficacious and more cost-effective treatment options for patients with the indicated conditions. Crexont is an extended-release formulation of carbidopa/levodopa and is available as 35 mg/140 mg, 52.5 mg/210 mg, 70 mg/280 mg, and 87.5 mg/350 mg extended-release capsules. The recommended starting dosage of Crexont in levodopa-naïve patients is 35 mg carbidopa/140 mg levodopa taken orally twice daily for the first three days. Thereafter, the dosage may be increased gradually as needed to a maximum daily dosage of 525 mg carbidopa/2100 mg levodopa divided up to four times daily. The dosages of immediate-release carbidopa-levodopa products are not substitutable on a 1:1 basis with the dosages of Crexont. A conversion chart is available in the package insert to determine the dosage in patients switching from immediate-release carbidopa-levodopa. In addition to Crexont, several other extended-release carbidopa/levodopa products are available including more cost-effective generic tablet formulations, and an additional branded capsule product, Rytary. There have been no head-to-head studies conducted comparing the extended-release products to suggest superiority of one product over another.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Dhivy was approved in November of 2021 for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and symptomatic parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.

Crexont was approved in August of 2024 for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and symptomatic parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.

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 federal regulations, other plan medical policies, and accredited national guidelines.

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Patient selection criteria presented in this policy take into account clinical evidence or patient history that suggest that the alternative treatment agents for Parkinson's disease or parkinsonism caused by encephalopathy or intoxication, generic formulations of carbidopa/levodopa products or Rytary (carbidopa/levodopa extended-release capsules), are contraindicated, ineffective, or will cause an adverse reaction to the patient. Based on review of available data, in the absence of the above-mentioned caveats, there is no advantage of using Dhivy or Crexont over the available generic carbidopa/levodopa products or Rytary.

References

1. Dhivy [package insert]. Avion Pharmaceuticals, LLC. Alpharetta, GA. Updated February 2022.
2. Crexont [package insert]. Amneal Pharmaceuticals, LLC. Bridgewater, NJ. Updated August 2024.

Policy History

Original Effective Date: 06/13/2022
Current Effective Date: 01/13/2025

05/05/2022	Medical Policy Committee review
05/11/2022	Medical Policy Implementation Committee approval. New policy.
05/04/2023	Medical Policy Committee review
05/10/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/02/2024	Medical Policy Committee review
05/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Title changed from "Dhivy™ (carbidopa/levodopa)" to "Select Carbidopa/Levodopa Products." Added new product, Crexont, to the policy with relevant criteria and background information.

Next Scheduled Review Date: 12/2025

*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.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA 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 Company 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.