

glatiramer acetate (Copaxone[®])

Policy # 00760

Original Effective Date: 01/01/2022

Current Effective Date: 10/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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 glatiramer acetate (Copaxone[®])[‡] for the treatment of relapsing forms of multiple sclerosis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for glatiramer acetate (Copaxone) will be considered when the following criterion is met:

- Patient has a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease, active secondary progressive disease); AND
- The patient has tried and failed (e.g., intolerance or inadequate response) a GENERIC glatiramer acetate product (e.g. glatiramer acetate or Glatopa[®])[‡] unless there is clinical evidence or patient history that suggest the use of the generic will be ineffective or cause an adverse reaction to the patient.

*(Note: This specific patient 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 brand Copaxone when the patient has not tried and failed a GENERIC equivalent 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 glatiramer acetate (Copaxone) when the patient selection criterion is not met to be **investigational**.*

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Background/Overview

Copaxone is an injectable therapy indicated for the treatment of relapsing forms of multiple sclerosis. Although its mechanism of action is unknown, it is thought to act by modifying immune processes that are believed to be responsible for the pathogenesis of multiple sclerosis. It is available in both brand and generic formulations, both of which may be dosed as 20 mg/mL administered subcutaneously once per day or 40 mg/mL administered 3 times per week and at least 48 hours apart.

Multiple sclerosis (MS) is believed to have an immunologic mechanism that is characterized by demyelination in the brain and spinal cord. This is often expressed by symptoms such as visual and oculomotor abnormalities, weakness, urinary dysfunction, and mild cognitive impairment. In the most common forms of MS, patients experience remissions and exacerbations. Treatment includes corticosteroids for acute exacerbations and immunomodulatory (disease modifying) drugs to prevent exacerbations. Disease modifying drugs include oral products such as fingolimod (Gilenya[®])[‡], ponesimod (Ponvory[™])[‡], siponimod (Mayzent[®])[‡], ozanimod (Zeposia[®])[‡], dimethyl fumarate (Tecfidera[®], generics)[‡], diroximel fumarate (Vumerity[®])[‡], teriflunomide (Aubagio[®])[‡], and cladribine (Mavenclad[®])[‡]; subcutaneous and intramuscular injectable products such as glatiramer acetate (Copaxone, generics), interferon beta-1a (Avonex[®], Rebif[®])[‡], interferon beta-1b (Extavia[®], Betaseron[®])[‡], peginterferon beta-1a (Plegridy[®])[‡], and ofatumumab (Kesimpta[®])[‡]; and intravenous infusions such as ocrelizumab (Ocrevus[®])[‡], natalizumab (Tysabri[®])[‡], and alemtuzumab (Lemtrada[®])[‡].

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Copaxone is approved for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

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.

Copaxone was approved based on five placebo-controlled trials, four of which used a dose of 20 mg per mL per day and one of which used a dose of 40 mg per mL three times per week.

Copaxone 20 mg per mL per day

Study 1 was performed at a single center. Fifty patients were enrolled and randomized to receive daily doses of either Copaxone 20 mg per mL subcutaneously (n=25) or placebo (n=25). Patients were diagnosed with RRMS by standard criteria and had at least 2 exacerbations during the 2 years immediately preceding enrollment. Patients were examined every 3 months for 2 years, as well as within several days of a presumed exacerbation. To confirm an exacerbation, a blinded neurologist had to document objective neurologic signs, as well as the existence of other criteria (e.g., the

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persistence of the neurological signs for at least 48 hours). The primary outcome measure was the proportion of patients in each treatment group who remained exacerbation free for the 2 years of the trial, but the frequency of attacks during the trial and the change in number of attacks compared to the previous 2 years were also evaluated. In the Copaxone group, 56% were relapse free after 2 years compared to 28% in the placebo group ($p=0.085$), the mean relapse frequency was 0.6 compared to 2.4 years in the placebo group ($p=0.005$), and the reduction in relapse rate was 3.2 compared to 1.6 in the placebo group ($p=0.025$).

Study 2 was a multicenter trial of similar design which was performed in 11 US centers. A total of 251 patients (Copaxone $n=125$; placebo $n=126$) were enrolled. The primary outcome measure was the mean 2-year relapse rate. In the Copaxone group, the rate was 1.19 compared to 1.68 in the placebo group ($p=0.055$).

In Study 3, 481 patients who had recently (within 90 days) experienced an isolated demyelinating event and who had lesions typical of MS on brain MRI were randomized to receive either Copaxone 20 mg per mL ($n=243$) or placebo ($n=238$). The primary outcome measure was time to development of a second exacerbation. Patients were followed for up to 3 years or until they reached the primary endpoint. This time to development of a second exacerbation was significantly delayed in patients treated with Copaxone compared to placebo (hazard ratio=0.055; 95% confidence interval 0.4-0.77).

Study 4 was a multinational study in which MRI parameters were used both as primary and secondary endpoints. A total of 239 patients with RRMS (Copaxone $n=119$; and placebo $n=120$) were randomized. Inclusion criteria were similar to those in the second study with the additional criterion that patients had to have at least one Gd-enhancing lesion on the screening MRI. The patients were treated in a double-blind manner for nine months, during which they underwent monthly MRI scanning. The primary endpoint was the total cumulative number of T1 Gd-enhancing lesions over the nine months. In the Copaxone group, the median was 11 lesions, and in the placebo group the median was 17 lesions ($p=0.003$).

Copaxone 40 mg per mL three times per week

Study 5 was a double-blind, placebo-controlled, multinational study with a total of 1404 patients with RRMS randomized in a 2:1 ratio to receive either Copaxone 40 mg/mL ($n=943$) or placebo ($n=461$) three times a week for 12 months. Patients had a median of 2 relapses in the 2 years prior to screening and had not received any interferon-beta for at least 2 months prior to screening. Neurological evaluations were performed at baseline, every 3 months, and at unscheduled visits for suspected relapse or early termination. The primary outcome measure was the total number of confirmed relapses (persistence of neurological symptoms for at least 48 hours confirmed on examination with objective signs). The adjusted mean estimate for the Copaxone group was found to be 0.331 compared to 0.505 in the placebo group ($p<0.0001$).

References

1. Copaxone [package insert]. Teva Neuroscience. Parsippany, NJ. Updated July 2020.

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10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. New policy.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/03/2024	Medical Policy Committee review
10/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/02/2025	Medical Policy Committee review
10/08/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/09/2026	Pre Pharmacy & Therapeutics Committee review.
09/16/2026	Pharmacy & Therapeutics Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 09/2027

*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;

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- 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 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.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.