ponesimod (Ponvory™)

Policy # 00749
Original Effective Date: 07/12/2021
Current Effective Date: 07/12/2021

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 ponesimod (Ponvory™)‡ for the treatment of relapsing forms of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for ponesimod (Ponvory) will be considered when the following criteria are met:

- Patient has a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease, active secondary progressive disease); AND
- Patient is greater than or equal to 18 years of age.

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 ponesimod (Ponvory) when patient selection criteria are not met to be **investigational.***

Background/Overview

Ponvory is a sphingosine 1 (S1P) receptor modulator indicated for the treatment of relapsing forms of multiple sclerosis including clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in adults. It is the first S1P receptor modulator to bind with high

affinity to S1P receptor 1 only and works by reducing the number of lymphocytes in the peripheral blood. It is the fourth S1P receptor modulator to be approved with the others being fingolimod (Gilenya®)‡, siponimod (Mayzent®)‡, and ozanimod (Zeposia®)‡. Each of these products has various advantages and disadvantages relative to the others. Gilenya is indicated in patients as young as 10 years of age and binds to S1P receptors 1, 3, 4, and 5. Dose titration is not required for Gilenya, but all patients must be monitored for bradycardia for at least 6 hours after receiving their first dose. Mayzent binds to S1P receptors 1 and 5 and is indicated in adults. It does not require first-dose monitoring but does require genetic testing for the CYP2C9 variants prior to treatment. Zeposia binds to S1P receptors 1 and 5 and does not require first-dose monitoring or genetic testing. Mayzent, Zeposia, and Ponvory all require dose titration to the target dose. Ponvory and Mayzent have shorter half lives than the others to allow for more rapid discontinuation if needed. The target dose of Ponvory is 20 mg by mouth once daily after a 14-day titration period. If more than 4 consecutive doses are missed, the treatment should be re-initiated with a new titration period.

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), dimethyl fumarate (Tecfidera®)‡, teriflunomide (Aubagio®)‡, cladribine (Mavenclad®)‡, and siponimod (Mayzent); subcutaneous and intramuscular injectable products such as glatiramer acetate (Copaxone®, Glatopa®)‡, 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)

Ponvory was approved in March 2021 for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

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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, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Ponvory was demonstrated in a randomized, double-blind, parallel group, active-controlled superiority study in 1133 patients with relapsing forms of MS. Patients were treated for 108 weeks. This study included patients who had an Expanded Disability Status Scale (EDSS) score of 0 to 5.5 at baseline, had experienced at least one relapse within the year prior, or two relapses within the prior two years, or who had at least one gadolinium-enhancing (Gd-enhancing) lesion on a brain MRI within the prior 6 months or at baseline. Patients with primary progressive MS were excluded. Patients were randomized 1:1 to receive either once daily Ponvory, beginning with a 14-day dose titration or teriflunomide (Aubagio) 14 mg.

The primary endpoint was the annualized relapse rate (ARR) over the study period. In the Ponvory group, the ARR was statistically significantly lower than in the Aubagio group (0.202 vs 0.290, p=0.0003).

References

1. Ponvory [package insert]. Janssen Pharmaceuticals, Inc. Titusville, NJ. Updated April 2021.

Policy History

Original Effective Date: 07/12/2021
Current Effective Date: 07/12/2021
06/03/2021 Medical Policy Committee review
06/09/2021 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 06/2022

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*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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated 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.

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‡ 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.