cladribine (Mavenclad®)

Policy # 00689
Original Effective Date: 09/11/2019
Current Effective Date: 11/11/2024

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 cladribine (Mavenclad®)‡ for the treatment of relapsing forms of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for cladribine (Mavenclad) will be considered when the following criteria are met:

- Patient has a relapsing form of multiple sclerosis (including relapsing remitting multiple sclerosis or active secondary progressive multiple sclerosis); AND
- Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE other disease modifying medication used to treat multiple sclerosis.

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 cladribine (Mavenclad) when patient selection criterion is not met to be **investigational.***

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Background/Overview

Mavenclad is a purine antimetabolite indicated for the treatment of relapsing forms of multiple sclerosis (MS). It is thought to reduce relapses in MS through its cytotoxic effects on B and T lymphocytes via impairment of DNA synthesis. While Mavenclad is an oral formulation of cladribine that is specifically approved for MS, cladribine is also available in a generic intravenous form for the treatment of hairy cell leukemia. The recommended cumulative dosage of Mavenclad for MS is 3.5 mg/kg given orally and divided into two yearly treatment courses (1.75 mg/kg per course). Each treatment course is divided into two treatment cycles. The first cycle can be started any time and consists of one or two 10 mg tablets once daily for 4 or 5 days. The second cycle should be given 23 to 27 days after the last dose of the first cycle. The second course should be started at least 43 weeks after the last dose of the first course and also consists of two 4-5 day treatment cycles. There is data suggesting that the benefit of Mavenclad extends for at least 2 years after the last dose, but it is not known how to provide additional management of MS beyond the 4-year timeframe in which Mavenclad has established efficacy. Mavenclad carries a black box warning for an increased risk of malignancy in patients taking it. In addition, it is a known teratogen and may cause lymphopenia and increase the occurrence of infections. Because of its safety profile, Mavenclad should be reserved for patients who have had an inadequate response to or are unable to tolerate an alternate drug for the treatment of MS.

Multiple sclerosis 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®, generics)‡, diroximel fumarate (Vumerity®)‡, teriflunomide (Aubagio®)‡, cladribine (Mavenclad), siponimod (Mayzent®)‡, ozanimod (Zeposia®)‡, and ponesimod (Ponvory™)‡; subcutaneous and intramuscular injectable products such as glatiramer acetate (Copaxone®, generics)‡, ofatumumab (Kesimpta®)‡, interferon beta-1a (Avonex®, Rebif®)‡, interferon beta-1b (Extavia®, Betaseron®)‡, and peginterferon beta-1a (Plegridy®)‡; and intravenous infusions such as ocrelizumab (Ocrevus®)‡, natalizumab (Tysabri®)‡, and alemtuzumab (Lemtrada®)‡.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Mavenclad was approved in March 2019 for the treatment of relapsing forms of multiple sclerosis including relapsing-remitting disease and active secondary progressive disease in adults. Because of its safety profile, use of Mavenclad is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of multiple sclerosis.

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.

The efficacy of Mavenclad was established in the CLARITY trial, a 96-week, randomized, double-blind, placebo-controlled study in patients with relapsing forms of MS. Included patients were required to have at least 1 relapse in the previous 12 months. A total of 1,326 patients were randomized to receive either placebo (n=437) or a cumulative oral dosage of Mavenclad 3.5 mg per kg (n=433) or 5.25 mg per kg body weight (n=456) over the 96-week study period in 2 treatment courses. Patients randomized to the 3.5 mg per kg received a first treatment course at Weeks 1 and 5 of the first year and a second treatment course at Weeks 1 and 5 of the second year. Patients randomized to the 5.25 mg per kg group received additional treatment at Weeks 9 and 13 of the first year. Higher cumulative doses did not add any clinically meaningful benefit, but were associated with a higher incidence in grade 3 lymphopenia or higher (44.9% in the 5.25 mg per kg group vs 25.6% in the 3.5 mg per kg group).

The primary outcome of the study was the annualized relapse rate (ARR) which was statistically significantly lower in the Mavenclad 3.5 mg per kg group vs placebo (0.14 vs 0.33, corresponding to a 58% relative reduction).

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References

1. Mavenclad [package insert]. EMD Serono, Inc. Rockland, MA. Updated April 2019.
2. Mavenclad Drug Evaluation. Express Scripts. Updated April 2019.

Policy History

Original Effective Date: 09/11/2019
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09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. New policy.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. Removed age and dosing requirements from criteria.
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.

Next Scheduled Review Date: 10/2025

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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 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.

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.