



Louisiana

diroximel fumarate (Vumerity®)

Policy # 00719

Original Effective Date: 10/12/2020

Current Effective Date: 10/12/2020

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 diroximel fumarate (Vumerity®)‡ for the treatment of relapsing forms of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for diroximel fumarate (Vumerity) will be considered when the following criteria are met:

- Patient has a diagnosis of a relapsing form of multiple sclerosis, to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease; AND
- Patient is 18 years of age or older; AND
- Patient has tried and failed (e.g. intolerance or inadequate response) TWO ORAL disease modifying agents for the treatment of multiple sclerosis. Oral disease modifying agents include dimethyl fumarate (Tecfidera®)‡, teriflunomide (Aubagio®)‡, fingolimod (Gilenya®)‡, and siponimod (Mayzent®)‡

*(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 diroximel fumarate (Vumerity) when the patient has not tried and failed at least TWO ORAL disease modifying agents for the treatment of multiple sclerosis to be **not medically necessary.****

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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 diroximel fumarate (Vumerity) when patient selection criteria are not met (except those noted to be **not medically necessary****) to be **investigational.***

Background/Overview

Vumerity is a prodrug of monomethyl fumarate that is indicated to treat relapsing forms of multiple sclerosis. Although its exact mechanism of action is unknown, monomethyl fumarate has been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway which is involved in the cellular response to oxidative stress. Vumerity should be dosed at 231 mg twice daily for the first 7 days then increased to the maintenance dose of 462 mg twice daily.

Vumerity is now one of three products that act as monomethyl fumarate to treat relapsing forms of multiple sclerosis. Tecfidera is dimethyl fumarate which is also converted to monomethyl fumarate in the body, and Bafiertam^{TM†} is the active agent, monomethyl fumarate. When dimethyl fumarate (Tecfidera) is converted to monomethyl fumarate, methanol is also formed as a minor metabolite. This methanol formation may be related to the tolerability issues with Tecfidera, such as gastrointestinal issues and flushing. In comparison, diroximel fumarate (Vumerity) generates much less methanol when it is converted to monomethyl fumarate and this may result in fewer adverse events. However, the prescribing information for Vumerity notes that the adverse event profile with Vumerity is consistent with the experience in the placebo-controlled clinical trials with Tecfidera. It should also be noted that the GI events and flushing with Tecfidera tended to decrease over time in clinical trials.

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),

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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[®])[‡], and peginterferon beta-1a (Plegridy[®])[‡]; 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)

Vumerity was approved in October 2019 for the treatment of relapsing forms of multiple sclerosis 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, 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.

Vumerity was approved based on bioavailability studies comparing oral dimethyl fumarate delayed-release capsules (Tecfidera) to Vumerity delayed-release capsules. These studies established the bioequivalence of Vumerity to Tecfidera in healthy subjects and in patients with relapsing forms of multiple sclerosis. Bafiertam was also approved based on bioavailability studies comparing it to dimethyl fumarate. When available, these other products may provide a more economical and equally effective treatment option to Vumerity.

References

1. Vumerity [package insert]. Biogen, Inc. Cambridge, MA. Updated March 2020.
2. Vumerity Drug Evaluation. Express Scripts. Updated November 2019.
3. Bafiertam [package insert]. Banner Life Sciences LLC. High Point, NC. Updated April 2020.

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09/03/2020 Medical Policy Committee review

09/09/2020 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 09/2021

*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

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- 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.

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