Vumerity (diroximel fumarate)

Summary

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. It typically presents in young adults (generally diagnosed before 50 years of age) with symptoms such as vision problems, muscle weakness, numbness, and difficulty with balance and coordination. The most common form is relapsing-remitting MS (occurring in about 85% of patients), characterized by acute attacks followed by periods of remission. Treatment goals include reducing relapses, slowing disability progression, and managing symptoms. Disease-modifying therapies are the primary treatment approach and include injectable medications (e.g., interferons, glatiramer acetate), oral medications (e.g., dimethyl fumarate, fingolimod, teriflunomide, etc.), and infusion therapies (e.g., natalizumab, ocrelizumab).

Vumerity (Diroximel fumarate) is an oral medication used to treat relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. It's a fumaric acid derivative that, like dimethyl fumarate (Tecfidera), is metabolized to monomethyl fumarate (MMF), the active compound responsible for its immunomodulatory and disease-modifying effects, though its exact mechanism in MS is not fully understood. The efficacy of diroximel fumarate is based on its bioequivalence to dimethyl fumarate, which has been shown in clinical trials to significantly reduce relapse rates and the development of new or enlarging T2 lesions in MS patients compared to placebo. While expected to have a similar efficacy and safety profile to dimethyl

fumarate, diroximel fumarate has also undergone its own phase 3 safety and tolerability studies in patients with relapsing-remitting MS.

Definitions

"Bioequivalence" refers to the absence of a significant difference in the rate and extent to which the active ingredient becomes available at the site of drug action when administered at the same molar dose under similar conditions.

"Clinically isolated syndrome" refers to a first episode of neurologic symptoms lasting at least 24 hours caused by inflammation or demyelination in the central nervous system.

"Disease-modifying therapy" is a medication that modifies the course of MS by reducing relapses and slowing disability progression.

"Multiple sclerosis" is a chronic autoimmune disease of the central nervous system characterized by inflammation, demyelination, and neurodegeneration.

"Primary progressive MS" refers to worsening neurologic function from the onset of symptoms, without early relapses or remissions.

"Relapse" is defined as the appearance of new symptoms or the worsening of existing symptoms lasting at least 24 hours in the absence of fever or infection.

"Relapsing-remitting MS" refers to a disease course characterized by clearly defined attacks of new or increasing neurologic symptoms followed by periods of partial or complete recovery.

"Secondary progressive MS" is a disease course following relapsing-remitting MS that is characterized by a progressive worsening of neurologic function over time with or without relapses.

Medical Necessity Criteria for Initial Authorization

The Plan considers Vumerity (diroximel fumarate) medically necessary when recent (within the last 3 months) clinical chart documentation provided indicates the member meets ALL of the following:

1. Prescribed by or in consultation with a neurologist or physician who specializes in the treatment of multiple sclerosis; *AND*
2. Is 18 years of age or older; *AND*
3. Has ONE of the following forms of multiple sclerosis:
    a. relapsing-remitting (RRMS)*; or*
    b. active secondary progressive disease (SPMS)*; or*

c. clinically isolated syndrome (CIS); *AND*

4. Is unable to use, or has tried and failed at least TWO of the following:
    a. An interferon beta product (Avonex, Betaseron, Plegridy, or Rebif)*; and/or*
    b. Dimethyl Fumarate (generic Tecfidera)*; and/or*
    c. Fingolimod (generic Gilenya)*; and/or*
    d. Glatiramer acetate (Copaxone)*; and/or*
    e. Teriflunomide (generic Aubagio); *AND*
5. Vumerity (diroximel fumarate) will be used as monotherapy for multiple sclerosis (i.e., member is not using and will not use other disease-modifying MS therapies while on Vumerity); *AND*
6. Vumerity (diroximel fumarate) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.
    - *Initial: 231 mg orally twice daily for 7 days*
    - *Maintenance (after the first 7 days): 462 mg orally twice daily*
        i. *240 capsules per 30 days*

<u>If the above prior authorization criteria are met, the requested medication will be authorized for up to 12 months.</u>

Medical Necessity Criteria for Reauthorization

Reauthorization for up to 12 months will be granted if the member has recent (within the last 6-months) clinical documentation showing BOTH of the following:

1. The requested medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of multiple sclerosis; *AND*
2. The member has experienced at least ONE of the following:
    a. Improvement in at least ONE objective measure, such as:
        i. Reduced disease activity on MRI*; and/or*
        ii. Improved or stable disability scores*; and/or*
        iii. Reduced relapse rate*; and/or*
        iv. Improved fatigue or walking assessments; *AND/OR*
    b. The member has shown stabilization or improvement in at least ONE MS symptom, such as:
        i. Motor function*; and/or*
        ii. Fatigue*; and/or*
        iii. Vision*; and/or*
        iv. Bowel/bladder function*; and/or*
        v. Spasticity*; and/or*
        vi. Walking/gait*; and/or*
        vii. Pain/numbness/tingling.

Experimental or Investigational / Not Medically Necessary

Vumerity (diroximel fumarate) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Use for the treatment of other neurological conditions not related to multiple sclerosis.
- Use for the treatment of primary progressive multiple sclerosis.
- Use in combination with other disease-modifying therapies for multiple sclerosis.
- Use in members under 18 years of age.

References

1. Bainbridge JL, Miravalle A, Wong PS. Multiple Sclerosis. In DiPiro JT, Yee GC, Posey LM, et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 11th ed. New York, NY: McGraw-Hill; 2019.
2. Gold R, Kappos L, Arnold DL, et al. Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. N Engl J Med. 2012 Sep 20;367(12):1098-107. doi: 10.1056/NEJMoa1114287. Erratum in: N Engl J Med. 2012 Dec 13;367(24):2362.
3. Hauser, S., & Cree, B. (2020). Treatment of Multiple Sclerosis: A Review.. The American journal of medicine. https://doi.org/10.1016/j.amjmed.2020.05.049.
4. Jiang T, Shanmugasundaram M, Božin I, et al. Comparative efficacy of diroximel fumarate, ozanimod and interferon beta-1a for relapsing multiple sclerosis using matching-adjusted indirect comparisons. J Comp Eff Res. 2024 Oct;13(10):e230161. doi: 10.57264/cer-2023-0161. Epub 2024 Aug 19.
5. McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and Treatment of Multiple Sclerosis: A Review. JAMA. 2021;325(8):765–779. doi:10.1001/jama.2020.26858
6. Multiple Sclerosis Society of Canada. Disease-modifying therapies. https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts.
7. Naismith RT, Wundes A, Ziemssen T, et al. Diroximel Fumarate Demonstrates an Improved Gastrointestinal Tolerability Profile Compared with Dimethyl Fumarate in Patients with Relapsing-Remitting Multiple Sclerosis: Results from the Randomized, Double-Blind, Phase III EVOLVE-MS-2 Study. CNS Drugs. 2020 Feb;34(2):185-196. doi: 10.1007/s40263-020-00700-0.
8. National MS Society. Disease-modifying therapies for MS (updated March 2022). Available from National MS Society website: https://nms2cdn.azureedge.net/cmssite/nationalmssociety/media/msnationalfiles/brochures/brochure-the-ms-disease-modifying-medications.pdf.
9. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90(17):777-788.
10. Reich DS, Lucchinetti CF, Calabresi PA. 2018. Multiple sclerosis. New England Journal of Medicine 378(2):169-180
11. Singer BA, Arnold DL, Drulovic J, et al. Diroximel fumarate in patients with relapsing-remitting multiple sclerosis: Final safety and efficacy results from the phase 3 EVOLVE-MS-1 study. Mult Scler. 2023 Dec;29(14):1795-1807. doi: 10.1177/13524585231205708. Epub 2023 Oct 31.
12. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence summary. Multiple Sclerosis Coalition. Available from the National MS Society Website: https://www.nationalmssociety.org/.
13. Tramacere I, Del Giovane C, Salanti G, et al. Immunomodulators and immunosuppressants for relapsing-remitting multiple sclerosis: a network meta-analysis. Cochrane Database Syst Rev 2015;9:CD011381.

14. Vumerity (diroximel fumarate) [prescribing information]. Cambridge, MA: Biogen Inc; March 2024.
15. Wehr A, Hard ML, Yu M, et al. Relative bioavailability of monomethyl fumarate after administration of ALKS 8700 and dimethyl fumarate in healthy subjects (P1.403). Neurology. 2018;90(Suppl. 15). https://n.neurology.org/content/90/15_Supplement/P1.403.
16. Yang, J., Rempe, T., Whitmire, N., Dunn-Pirio, A., & Graves, J. (2022). Therapeutic Advances in Multiple Sclerosis. Frontiers in Neurology, 13. https://doi.org/10.3389/fneur.2022.824926.

Clinical Guideline Revision / History Information

Original Date: 06/27/2024

Reviewed/Revised: 10/01/2025