

Dimethyl Fumarate (Tecfidera)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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 (DMTs) 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).

Dimethyl fumarate (Tecfidera) is an oral fumarate DMT approved for the treatment of relapsing forms of MS (to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease) in adults. It has immunomodulatory and neuroprotective effects, though its exact mechanism in MS is not fully understood. Clinical trials have demonstrated that dimethyl fumarate reduces relapse rates, disability progression, and MRI lesion activity compared to placebo. It is generally considered a moderate-efficacy therapy with a favorable safety profile, though it carries risks of lymphopenia, liver injury, and progressive multifocal leukoencephalopathy (PML) in rare cases.

Definitions

"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 (DMT)" 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.

"Progressive multifocal leukoencephalopathy (PML)" is an opportunistic viral infection of the brain that can result in severe disability or death.

"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 Dimethyl Fumarate (Tecfidera) 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. For Brand name Tecfidera ONLY - member is unable to use, or has tried and failed BOTH of the following:
 - a. generic dimethyl fumarate from at least two different manufacturers; *and*
 - b. at least TWO of the following:

- i. An interferon beta product (Avonex, Betaseron, Plegridy, or Rebif); *and/or*
 - ii. Fingolimod (generic Gilenya); *and/or*
 - iii. Glatiramer acetate (Copaxone); *and/or*
 - iv. Teriflunomide (generic Aubagio); *AND*
- 5. Dimethyl fumarate (Tecfidera) 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 dimethyl fumarate); *AND*
- 6. Dimethyl fumarate (Tecfidera) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.
 - o *Initial:*
 - i. *Dimethyl fumarate 120 mg capsule orally twice daily*
 - 1. *14 capsules per 7 days (for initial titration only)*
 - o *Maintenance (after the first 7 days):*
 - i. *Dimethyl fumarate 240 mg capsule orally twice daily*
 - 1. *60 capsules per 30 days*

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

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

Dimethyl Fumarate (Tecfidera) 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. Baharnoori M, Gonzalez CT, Chua A, Diaz-Cruz C, Healy BC, Stankiewicz J, Weiner HL, Chitnis T. Predictors of hematological abnormalities in multiple sclerosis patients treated with fingolimod and dimethyl fumarate and impact of treatment switch on lymphocyte and leukocyte count. *Mult Scler Relat Disord*. 2018 Feb;20:51-57. doi: 10.1016/j.msard.2017.12.003. Epub 2017 Dec 14. PMID: 29304497.
3. Fox RJ, Miller DH, Phillips JT, et al,. Placebo-controlled phase 3 study of oral BG-12 or glatiramer in multiple sclerosis. *N Engl J Med*. 2012 Sep 20;367(12):1087-97. doi: 10.1056/NEJMoa1206328. Erratum in: *N Engl J Med*. 2012 Oct 25;367(17):1673.
4. Gold R, Arnold DL, Bar-Or A, et al,. Long-term safety and efficacy of dimethyl fumarate for up to 13 years in patients with relapsing-remitting multiple sclerosis: Final ENDORSE study results. *Mult Scler*. 2022 Apr;28(5):801-816. doi: 10.1177/13524585211037909. Epub 2021 Sep 1.
5. Gold R, Arnold DL, Bar-Or A, et al,. Long-term effects of delayed-release dimethyl fumarate in multiple sclerosis: Interim analysis of ENDORSE, a randomized extension study. *Mult Scler*. 2017 Feb;23(2):253-265. doi: 10.1177/1352458516649037. Epub 2016 Jul 11.
6. 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.
7. 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>.
8. Mao-Draayer Y, Bar-Or A, Balashov K, et al,. Real-World Safety and Effectiveness of Dimethyl Fumarate in Patients with MS: Results from the ESTEEM Phase 4 and PROCLAIM Phase 3 Studies with a Focus on Older Patients. *Adv Ther*. 2025 Jan;42(1):395-412. doi: 10.1007/s12325-024-03047-w. Epub 2024 Nov 21.
9. 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
10. Mehta D, Miller C, Arnold DL, et al. Effect of dimethyl fumarate on lymphocytes in RRMS: Implications for clinical practice. *Neurology*. 2019;92(15):e1724-e1738. doi: 10.1212/WNL.0000000000007262.
1. Montalban X, Gold R, Thompson AJ, et al.ECTRIMS/EAN guideline on the pharmacological treatment of people with multiple sclerosis [published correction appears in *Eur J Neurol*. 2018;25(3):605]. *Eur J Neurol*. 2018;25(2):215-237. doi:10.1111/ene.13536.
11. Multiple Sclerosis Society of Canada. Disease-modifying therapies. <https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts>.

12. 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>.
13. 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.
14. Reich DS, Lucchinetti CF, Calabresi PA. 2018. Multiple sclerosis. *New England Journal of Medicine* 378(2):169-180.
1. Rindi LV, Zaçe D, Braccialarghe N, Massa B, Barchi V, Iannazzo R, Fato I, De Maria F, Kontogiannis D, Malagnino V, Sarmati L, Iannetta M. Drug-Induced Progressive Multifocal Leukoencephalopathy (PML): A Systematic Review and Meta-Analysis. *Drug Saf*. 2024 Apr;47(4):333-354. doi: 10.1007/s40264-023-01383-4. Epub 2024 Feb 7.
15. Tecfidera (dimethyl fumarate) [prescribing information]. Cambridge, MA: Biogen Inc; March 2024.
16. 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/>.
17. 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.
18. 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>.
19. Yeh WZ, Widyastuti PA, Van der Walt A, et al; MSBase Study Group. Natalizumab, fingolimod and dimethyl fumarate use and pregnancy-related relapse and disability in women with multiple sclerosis. *Neurology*. 2021;96(24):e2989-e3002. doi:10.1212/WNL.0000000000012084.

Clinical Guideline Revision / History Information

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