

Rebif (interferon beta-1a)

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).

Rebif (interferon beta-1a) is a first-generation DMT indicated for relapsing forms of MS, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. It is administered via subcutaneous injection three times per week. Rebif (interferon beta-1a) works by modulating the immune system and reducing inflammation in the central nervous system, though its exact mechanism of action in MS is not fully understood.

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" 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 Rebif (interferon beta-1a) 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. Rebif (interferon beta-1a) 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 Rebif); *AND*
5. Rebif (interferon beta-1a) is being prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature.
 - o *The recommended dose is 22 mcg or 44 mcg injected subcutaneously three times per week.*
 - i. *Rebif 22 mcg/0.5 mL: 6 mL (12 syringes or autoinjectors) per 28 days.*
 - ii. *Rebif 44 mcg/0.5 mL: 6 mL (12 syringes or autoinjectors) per 28 days.*

If the above prior authorization criteria are met, the requested product 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

Rebif (interferon beta-1a) 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 in combination with other disease-modifying therapies for multiple sclerosis.
- Treatment of non-relapsing forms of multiple sclerosis (e.g., primary progressive MS without active disease).
- Use for the treatment of other neurological conditions not related to multiple sclerosis.
- Use as a treatment for cancer or as an adjunct to cancer therapies.
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- Use for the treatment of viral infections, including chronic viral hepatitis.
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- Use in pediatric members under 18 years of age.

Use in the management of other autoimmune disorders not related to multiple sclerosis.

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. Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. *Am J Med*. 2020 Dec;133(12):1380-1390.e2. doi: 10.1016/j.amjmed.2020.05.049. Epub 2020 Jul 17.
3. 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
4. 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.
5. Multiple Sclerosis Society of Canada. Disease-modifying therapies. <https://mssociety.ca/managing-ms/treatments/medications/disease-modifying-therapies-dmts>.
6. 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>.
7. Panitch H, Goodin D, Francis G, et al,. Benefits of high-dose, high-frequency interferon beta-1a in relapsing-remitting multiple sclerosis are sustained to 16 months: final comparative results of the EVIDENCE trial. *J Neurol Sci*. 2005 Dec 15;239(1):67-74. doi: 10.1016/j.jns.2005.08.003. Epub 2005 Sep 19.
8. PRISMS Study Group and the University of British Columbia MS/MRI Analysis Group.. PRISMS-4: Long-term efficacy of interferon-beta-1a in relapsing MS. *Neurology*. 2001 Jun 26;56(12):1628-36. doi: 10.1212/wnl.56.12.1628. Erratum in: *Neurology* 2001 Sep 25;57(6):1146.
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. Randomised double-blind placebo-controlled study of interferon beta-1a in relapsing/remitting multiple sclerosis. PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) Study Group. *Lancet*. 1998 Nov 7;352(9139):1498-504. Erratum in: *Lancet* 1999 Feb 20;353(9153):678.
11. Rebif (interferon beta-1a) [prescribing information]. Rockland, MA: EMD Serono Inc; July 2023.
12. Reich DS, Lucchinetti CF, Calabresi PA. 2018. Multiple sclerosis. *New England Journal of Medicine* 378(2):169-180
13. Schwid SR, Panitch HS. Full results of the Evidence of Interferon Dose-Response-European North American Comparative Efficacy (EVIDENCE) study: a multicenter, randomized, assessor-blinded comparison of low-dose weekly versus high-dose, high-frequency interferon beta-1a for relapsing multiple sclerosis. *Clin Ther*. 2007 Sep;29(9):2031-48. doi: 10.1016/j.clinthera.2007.09.025.
14. 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/>.
15. 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.
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>.

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