Oscar Clinical Guideline: Briumvi (ublituximab) (PG134, Ver. 6)

Briumvi (ublituximab)

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 (CNS).. 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).

MS is a progressive disease, meaning that symptoms tend to worsen over time, and it can be classified into several types, including relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).

Currently, there is no cure for MS, but various treatment options are available to manage symptoms, slow the progression of the disease, and improve quality of life.

- Disease-modifying therapies (DMTs) are a class of medications that target the immune system to reduce inflammation and slow down the progression of the disease. The type of DMT prescribed will depend on the type and severity of MS, as well as the individual's medical history and preferences. Some common DMTs include interferon beta, glatiramer acetate, dimethyl fumarate, and fingolimod.
- High dose corticosteroids, such as high dose intravenous methylprednisolone or oral prednisone can be prescribed to reduce inflammation during acute MS relapses.
- Symptomatic treatments are also available to manage specific symptoms of MS, such as muscle spasms, bladder problems, and depression. Physical therapy, occupational therapy, and speech therapy can help individuals with MS maintain mobility, independence, and communication skills.

Briumvi (ublituximab), a recombinant human anti-CD20 monoclonal antibody, is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Briumvi (ublituximab) is an intravenous infusion administered every 24 weeks, following an initial dosing schedule (150 mg administered intravenously, followed by an infusion of 450 mg two weeks after the first infusion).

Definitions

"CIS" or "clinically isolated syndrome" refers to the first symptomatic episode lasting at least 24 hours caused by inflammation and demyelination in the central nervous system. This episode is characteristic of multiple sclerosis but does not always result in a person developing MS. Early treatment of CIS has been shown to delay the onset of MS.

"Compendia" are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Clinical pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex
5. United States Pharmacopeia-National Formulary (USP-NF)

"Disease modifying therapy" refers to treatments found to reduce the number of relapses, delay progression of disability, and limit new disease activity according to research and clinical trials.
"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"MRI" or "Magnetic Resonance Imaging" refers to a medical imaging technique that creates detailed three-dimensional (3D) images of the organs and tissues in your body. A brain MRI can reveal areas of active MS disease called lesions within the central nervous system.

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

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

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

"Relapse" refers to an attack or exacerbation of MS (also known as a flare-up) resulting in the occurrence new symptoms or the worsening of old symptoms.

"RRMS" or "relapsing-remitting MS" refers to the most common type of MS in which there are clearly defined attacks or relapses of increasing neurologic symptoms followed by periods of partial or complete recovery or remissions.

"[s]" indicates state mandates may apply.

"SPMS" or "secondary progressive MS" refers to a version of disease progression that can follow an initial relapsing-remitting course in which there is a worsening of neurologic function and increased disability over time.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Briumvi (ublituximab) medically necessary when ONE of the following criteria are met:

1. Authorization may be granted for pediatric members less than 18 years of age with multiple sclerosis when there is documentation that the benefits outweigh the risks*; OR*
   Note: If approved, the requested product will be authorized for up until the member reaches 18 years of age.
2. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Multiple Sclerosis - Adults

The Plan considers Briumvi (ublituximab) 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. The member is 18 years of age or older*; AND*
3. The member has ONE (1) of the following forms of multiple sclerosis:
   a. Relapsing-remitting (RRMS)*; or*
   b. Active secondary progressive (SPMS)*; or*
   c. Clinically isolated syndrome (CIS)*; AND*
4. The member meets ONE (1) of the following:
   a. Documentation of highly active or aggressive disease, as demonstrated by at least ONE (1) of the following:
      i. Frequent relapses (≥2 in the past year)*; or*
      ii. At least 1 relapse with incomplete recovery and MRI activity*; or*
      iii. Rapidly advancing disability or cognitive impairment*; or*
      iv. Disabling relapse with suboptimal response to corticosteroids*; or*
      v. MRI findings showing high disease activity (e.g., new/enlarging T2 lesions, enhancing lesions)*; or*
   b. The member is is unable to use, or has tried and failed ONE (1) of the following[s]:

i. Dimethyl Fumarate (generic Tecfidera)*; or*
ii. Fingolimod (generic Gilenya); *or*
iii. Teriflunomide (generic Aubagio); *AND*

5. The member has been screened for hepatitis B virus AND has no evidence of active hepatitis B infection; *AND*
6. Briumvi (ublituximab) 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 Briumvi [ublituximab])*; AND*
7. Briumvi (ublituximab) will be prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication.
    - *First dose: 150 mg administered by intravenous infusion.*
    - *Second dose: 450 mg administered by intravenous infusion 2 weeks after the first infusion.*
    - *Subsequent doses: 450 mg administered by intravenous infusion every 24 weeks after the first infusion.*

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.[5]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Multiple Sclerosis - Adults

The Plan considers Briumvi (ublituximab) medically necessary when recent (within the last 6-months) clinical chart documentation provided indicates the member meets 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 (1) of the following:
    a. Improvement in at least ONE (1) 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 (1) 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.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[5]

Experimental or Investigational / Not Medically Necessary[5]

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

- Treatment of non-relapsing forms of multiple sclerosis (e.g., primary progressive MS).
- Use in combination with other disease-modifying therapies for MS. There is limited knowledge about the use of combining DMTs for MS.

Applicable Billing Codes

Table 1	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
J2329	Injection, ublituximab-xiiy, 1mg

Table 2	
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
G35	Multiple Sclerosis
G35.A	Relapsing-remitting multiple sclerosis

G35.B0	Primary progressive multiple sclerosis, unspecified
G35.B1	Active primary progressive multiple sclerosis
G35.B2	Non-active primary progressive multiple sclerosis
G35.C0	Secondary progressive multiple sclerosis, unspecified
G35.C1	Active secondary progressive multiple sclerosis
G35.C2	Non-active secondary progressive multiple sclerosis
G35.D	Multiple sclerosis, unspecified

References

1. Benallegue N, Rollot F, Wiertlewski S, Casey R, Debouverie M, Kerbrat A, De Seze J, Ciron J, Ruet A, Labauge P, Maillart E, Zephir H, Papeix C, Defer G, Lebrun-Frenay C, Moreau T, Berger E, Stankoff B, Clavelou P, Heinzlef O, Pelletier J, Thouvenot E, Al Khedr A, Bourre B, Casez O, Cabre P, Wahab A, Magy L, Vukusic S, Laplaud DA; OFSEP (Observatoire Français de la Sclérose en Plaques) Investigators. Highly Effective Therapies as First-Line Treatment for Pediatric-Onset Multiple Sclerosis. JAMA Neurol. 2024 Mar 1;81(3):273-282.
2. Briumvi (ublituximab) [prescribing information]. Morrisville, NC: TG Therapeutics, Inc; August 2025.
3. Chitnis T, Tenembaum S, Banwell B, Krupp L, Pohl D, Rostasy K, Yeh EA, Bykova O, Wassmer E, Tardieu M, Kornberg A, Ghezzi A; International Pediatric Multiple Sclerosis Study Group. Consensus statement: evaluation of new and existing therapeutics for pediatric multiple sclerosis. Mult Scler. 2012 Jan;18(1):116-27.
4. Farez MF, Correale J, Armstrong MJ, et al. Practice guideline update summary: vaccine-preventable infections and immunization in multiple sclerosis: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. Neurology. 2019;93(13):584-594. doi:10.1212/WNL.0000000000008157.
5. Fox E, Lovett-Racke AE, Gormley M, et al,. A phase 2 multicenter study of ublituximab, a novel glycoengineered anti-CD20 monoclonal antibody, in patients with relapsing forms of multiple sclerosis. Mult Scler. 2021 Mar;27(3):420-429. doi: 10.1177/1352458520918375. Epub 2020 Apr 30.
6. He A, Merkel B, Brown JWL, et al. Timing of high-efficacy therapy for multiple sclerosis: a retrospective observational cohort study. Lancet Neurol. 2020 Apr;19(4):307-316. doi: 10.1016/S1474-4422(20)30067-3. Epub 2020 Mar 18.
7. Krysko KM, Graves JS, Rensel M, et al; US Network of Pediatric MS Centers. Real-World Effectiveness of Initial Disease-Modifying Therapies in Pediatric Multiple Sclerosis. Ann Neurol. 2020 Jul;88(1):42-55.
8. Krysko KM, Graves J, Rensel M, et al; US Network of Pediatric MS Centers. Use of newer disease-modifying therapies in pediatric multiple sclerosis in the US. Neurology. 2018 Nov 6;91(19):e1778-e1787.
9. Luzzio C, Dangond F. Multiple Sclerosis Guidelines. MedScape. 12 March 2024. Available at: https://emedicine.medscape.com/article/1146199-guidelines#g1. Accessed 20 January 2026.
10. Moloney E, Mashayekhi A, Sharma S, et al. Comparative efficacy and tolerability of ublituximab vs. other monoclonal antibodies in the treatment of relapsing multiple sclerosis: a systematic review and network meta-analysis of randomized trials. Front Neurol. 2024 Dec 6;15:1479476. doi: 10.3389/fneur.2024.1479476.

11. Montalban X et al: ECTRIMS/EAN guideline on the pharmacological treatment of people with multiple sclerosis. Eur J Neurol. 25(2):215-37, 2018
12. Montalban X, Lebrun-Frénay C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. Lancet Neurol. 2025 Oct;24(10):850-865. doi: 10.1016/S1474-4422(25)00270-4. Erratum in: Lancet Neurol. 2025 Nov;24(11):e13. doi: 10.1016/S1474-4422(25)00355-2.
13. National Institute for Health and Care Excellence [NICE]. Multiple sclerosis in adults: management. NICE Guidelines [NG220]. 22 June 2022. Available at: https://www.nice.org.uk/guidance/ng220/chapter/Recommendations#ms-symptom-management-and-rehabilitation. Accessed 20 January 2026.
14. 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.
15. Rae-Grant A et al: Comprehensive systematic review 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. 90(17):789-800, 2018
16. Rae-Grant A 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. 90(17):777-88, 2018.
17. Rashid W, Ciccarelli O, Leary SM, et al. Using disease-modifying treatments in multiple sclerosis: Association of British Neurologists (ABN) 2024 guidance. Pract Neurol. 2025 Jan 16;25(1):18-24. doi: 10.1136/pn-2024-004228.
18. Sahraian MA, Emami S, Ataei S, Nasr Esfahani F, Ghalandari N. Secondary Autoimmune Dermatological Disorders Induced by Multiple Sclerosis Biological Immunotherapy Agents: A Systematic Review of Case Reports. Iran J Pharm Res. 2025 Dec 2;24(1):e166426. doi: 10.5812/ijpr-166426.
19. Samjoo IA, Drudge C, Walsh S, et al,. Comparative efficacy of therapies for relapsing multiple sclerosis: a systematic review and network meta-analysis. J Comp Eff Res. 2023 Jul;12(7):e230016. doi: 10.57264/cer-2023-0016. Epub 2023 Jun 2.
20. Scavone C, Cagnotta C, Sportiello L, et al. Hypogammaglobulinemia and infections in patients with multiple sclerosis treated with anti-CD20 monoclonal antibodies: a systematic review and meta-analysis of observational studies. Expert Opin Drug Saf. 2025 Oct 24:1-21. doi: 10.1080/14740338.2025.2574668. Epub ahead of print.
21. Sladowska K, Mocko P, Brzostek T, et al. Efficacy and safety of disease-modifying therapies in pediatric-onset multiple sclerosis: A systematic review of clinical trials and observational studies. Mult Scler Relat Disord. 2025. doi: 10.1016/j.msard.2025.106263
22. Steinman L, Fox E, Hartung HP, et al; ULTIMATE I and ULTIMATE II Investigators. Ublituximab versus teriflunomide in relapsing multiple sclerosis. N EnglJ Med. 2022;387(8):704-714. doi:10.1056/NEJMoa2201904.
23. Walsh R, Chitnis T. Therapeutic Advances in Pediatric Multiple Sclerosis. Children. 2025;12(3):259.

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