Medical Drug Clinical Criteria

Subject:	Briumvi (ublituximab)		
Document #:	CC-0227	**Publish Date:**	12/23/2024
Status:	Revised	**Last Review Date:**	11/15/2024

Table of Contents

Overview

This document addresses the use of Briumvi (ublituximab), a CD-20 directed monoclonal antibody approved by the Food and Drug Administration (FDA) to treat relapsing multiple sclerosis in adults, including clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease.

Multiple sclerosis is an autoimmune inflammatory demyelinating disease of the central nervous system. Common symptoms of the disease include fatigue, numbness, coordination and balance problems, bowel and bladder dysfunction, emotional and cognitive changes, spasticity, vision problems, dizziness, sexual dysfunction and pain. Multiple sclerosis can be subdivided into four phenotypes: clinically isolated syndrome (CIS), relapsing remitting (RRMS), primary progressive (PPMS) and secondary progressive (SPMS).

Relapsing multiple sclerosis (RMS) is a general term for all relapsing forms of multiple sclerosis including CIS, RRMS and active SPMS. The treatment goal for multiple sclerosis is to prevent relapses and progressive worsening of the disease. Currently available disease-modifying therapies (DMT) are most effective for the relapsing-remitting form of multiple sclerosis and less effective for secondary progressive decline. DMT include injectable agents, infusion therapies and oral agents. Briumvi is administered via intravenous infusion every 24 weeks.

The clinical efficacy of Briumvi was evaluated in two identically designed Phase III double-blind, double-dummy randomized controlled studies, ULTIMATE I and II. In the trials, 1094 study participants were randomized 1:1 to receive Briumvi plus placebo or Aubagio plus placebo. Notable inclusion criteria included diagnosis of multiple sclerosis according to the revised McDonald criteria, two documented clinical relapses within the last two years prior to screening or one clinical relapse or one gadolinium-enhancing lesion in the year prior to screening, neurologic stability for at least the past 30 days at baseline and expanded disability status scale (EDSS) score of 0-5.5. The primary endpoint in the studies was the annualized relapse rate. Secondary endpoints included the number of gadolinium-enhancing lesions and worsening of disability. In ULTIMATE I, the annualized relapse rate was 0.08 for Briumvi compared to 0.19 for Aubagio ($p<0.001$). In ULTIMATE II, the annualized relapse rate was 0.09 for Briumvi compared to 0.18 for Aubagio ($p=0.002$). The secondary endpoint of number of gadolinium-enhancing lesions was significantly lower in the Briumvi arms but no significant difference was detected in worsening of disability.

The American Academy of Neurology (AAN) guidelines suggest starting disease-modifying therapy in individuals with relapsing forms of multiple sclerosis with recent clinical relapses or MRI activity. The guidelines also suggest DMT for individuals who have experienced a single clinical demyelinating event and two or more brain lesions consistent with multiple sclerosis if the individual wishes to start therapy after a risks and benefits discussion. The guidelines do not recommend one DMT over another.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Briumvi (ublituximab)

Requests for Briumvi (ublituximab) may be approved if the following criteria are met:

I. Individual has a diagnosis of relapsing multiple sclerosis (RMS) (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease); **AND**

II. Individual is able to ambulate without aid or rest for at least 100 meters; **AND**
III. If initiating therapy, individual has experienced at least two relapses within the previous two years or one relapse within the previous year or at least one T1 gadolinium-enhancing lesion on MRI within the previous year.

Briumvi (ublituximab) may not be approved for the following:

I. Use in combination with other MS disease modifying agents (including Aubagio, Avonex, Bafiertam, Betaseron, Copaxone/Glatiramer/Glatopa, Extavia, Gilenya, Kesimpta, Lemtrada, Mavenclad, Mayzent, Ocrevus, Ocrevus Zunovo, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Tyruko, Tysabri, Vumerity and Zeposia); **OR**
II. Individual is using to treat non-active secondary progressive multiple sclerosis; **OR**
III. Individual is using to treat primary progressive multiple sclerosis; **OR**
IV. Individual has active hepatitis B or another active infection at initiation of therapy; **OR**
V. May not be approved when the above criteria are not met and for all other indications.

Quantity Limits

Briumvi (ublituximab) Quantity Limit

Drug	Limit
Briumvi (ublituximab) 150 mg/6 mL vial	450 mg (3 vials) every 24 weeks
Override Criteria	
Initiation of therapy for Briumvi: May approve 150 mg (1 vial) on day 1 and 450 mg (3 vials) two weeks after the first dose for initiation of therapy.	

Step Therapy

Note: When Briumvi (ublituximab) is deemed approvable based on the clinical criteria referenced above, the benefit plan may have additional criteria requiring the use of a preferred[1] agent or agents.

Briumvi Step Therapy

A list of the preferred products is available here.

Requests for Briumvi (ublituximab) may be approved when the following criteria are met:

I. Documentation is provided that individual has been on Briumvi (ublituximab);

OR

II. Documentation has been provided that individual has had a trial and inadequate response (including but not limited to clinical relapse, new or enlarged lesions on MRI or confirmed disability progression) or intolerance to the following:
   A. Preferred fumaric acid derivative;

OR

III. Documentation is provided that individual has high disease activity despite treatment with fingolimod (Gilenya, Tascenso ODT) defined as the following (AAN 2018, Devonshire 2012):
   A. At least one relapse in the previous year while on therapy; **AND**
   B. At least 9 T_2-hyperintense lesions in cranial MRI;

   OR
   C. At least one Gadolinium-enhancing lesion.

[1]Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J2329	Injection, ublituximab-xiiy, 1mg [Briumvi]

ICD-10 Diagnosis

G35	Multiple sclerosis

Document History

Revised: 11/15/2024
Document History:

- 11/15/2024 – Annual Review: Add Ocrevus Zunovo and Tyruko to exclusion for concurrent use with other disease modifying therapy criteria. Coding Reviewed: No changes.
- 03/01/2024 – Administrative update to add documentation.
- 11/17/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 03/01/2023 – Select Review: New clinical criteria and quantity limit for Briumvi. Coding Reviewed: Added HCPCS J3490, J3590. All diagnoses pend. Add step therapy table. Effective 7/1/2023 Added HCPCS J2329. Added ICD-10-CM G35. Deleted HCPCS J3490, J3590.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 22, 2024.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Expanded Disability Status Scale (EDSS). Department of Veterans Affairs: Multiple Sclerosis Centers for Excellence. Last updated: March 18, 2021. Available at: https://www.va.gov/MS/Professionals/diagnosis/Kurtzke_Expanded_Disability_Status_Scale.asp. Accessed: October 27, 2024.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
5. Olek MJ, Howard J. Clinical presentation, course and prognosis of multiple sclerosis in adults. Last updated: April 26, 2024. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: October 27, 2024.
6. 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: 777-788. Available from: https://www.aan.com/Guidelines/home/GuidelineDetail/898. Accessed: October 27, 2024.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

CC-0227 Briumvi

Commercial

Effective Date	Preferred Agents	Non-Preferred Agents
01/17/2023	Fumaric acid derivative: generic dimethyl fumarate	Briumvi

Medicaid

Effective Date	Preferred Agents	Non-Preferred Agents
N/A	N/A	N/A

Medicare

Effective Date	Preferred Agents	Non-Preferred Agents
N/A	N/A	N/A