ublituximab (Briumvi™)

Medicare Advantage Medical Policy #MNG-054
Original Effective Date: 01/01/2025
Current Effective Date: 01/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider ublituximab (Briumvi™)‡ for the treatment of multiple sclerosis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for ublituximab (Briumvi) will be considered when the following criteria are met:

- Patient has a diagnosis of a relapsing form of multiple sclerosis (i.e., clinically isolated syndrome, relapsing remitting disease, or active secondary progressive disease).

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of ublituximab (Briumvi) when the patient selection criteria are not met to be **investigational.***

Background/Overview

Briumvi is a CD20-directed cytolytic antibody that is indicated for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing remitting disease, and active secondary progressive disease in adults. It is unknown exactly how Briumvi exerts its therapeutic effects in multiple sclerosis. Briumvi is administered via intravenous infusion following premedication with methylprednisolone and an antihistamine. The initial dose is 150 mg followed by a 450 mg dose two weeks later. Subsequent infusions should be 450 mg administered 24 weeks after the first infusion and every 24 weeks thereafter.

Multiple sclerosis is believed to have an immunologic mechanism that is characterized by demyelination in the brain and spinal cord. This is often expressed by symptoms such as visual and oculomotor abnormalities, weakness, urinary dysfunction, and mild cognitive impairment. Often patients will experience remissions and exacerbations. Treatment can include corticosteroids for acute exacerbations and immunomodulatory (disease modifying) drugs to prevent exacerbations.

Disease modifying drugs for the treatment of relapsing forms of multiple sclerosis include oral products such as fingolimod (Gilenya®)‡, siponimod (Mayzent®)‡, dimethyl fumarate (Tecfidera®)‡, diroximel fumarate (Vumerity®)‡, teriflunomide (Aubagio®)‡, and cladribine (Mavenclad®)‡; subcutaneous and intramuscular injectable products such as glatiramer acetate (Copaxone®)‡, ofatumumab (Kesimpta®)‡, interferon beta-1a (Avonex®, Rebif®)‡, interferon beta-1b (Extavia®, Betaseron®)‡, and peginterferon beta-1a (Plegridy®)‡; and intravenous infusions such as ocrelizumab (Ocrevus®)‡, natalizumab (Tysabri®)‡, and alemtuzumab (Lemtrada®)‡.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Briumvi was approved in December 2022 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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Briumvi was demonstrated in two randomized, double-blind, double-dummy, parallel group, active comparator-controlled clinical trials of identical design, in patients with relapsing remitting multiple sclerosis treated for 96 weeks. Patients were randomized to receive either Briumvi, given as an IV infusion of 150 mg for the first infusion, 450 mg two weeks after the first infusion for the second infusion, and 450 mg every 24 weeks after the first infusion for subsequent doses with oral placebo administered daily; or teriflunomide, the active comparator, given orally as a 14 mg daily dose with IV placebo administered on the same schedule as Briumvi. Both studies enrolled patients who had experienced at least one relapse in the previous year, two relapses in the previous two years, or had the presence of a t1 gadolinium enhancing lesion in the previous year. Patients were also required to have an Expanded Disability Status Scale (EDSS) score from 0 to 5.5 at baseline. Neurological evaluations were performed at baseline every 12 weeks, and at the time of a suspected relapse. Brain MRI scans were performed at baseline and at Weeks 12, 24, 48, and 96.

The primary outcome of both studies was the annualized relapse rate (ARR) over the treatment period. In Study 1, 274 patients were randomized to Briumvi and 275 to teriflunomide. Of those randomized to Briumvi, 88% completed the 96-week treatment period; of those randomized to teriflunomide, 92% completed the 96-week treatment period. The ARR was statistically significantly lower in the Briumvi group (0.076) compared to the teriflunomide group (0.188) with a relative reduction of 59% ($p<0.001$). In Study 2, 272 patients were randomized to Briumvi and 273 to teriflunomide. Of those randomized to Briumvi, 93% completed the 96-week treatment period; of

those randomized to teriflunomide, 88% completed the 96-week treatment period. The ARR was statistically significantly lower in the Briumvi group (0.091) compared to the teriflunomide group (0.178) with a relative reduction of 49% (p=0.002).

References

1. Briumvi [package insert]. TG Therapeutics, Inc. Morrisville, NC. Updated January 2023.

Policy History

Original Effective Date: 01/01/2025
Current Effective Date: 01/01/2025
10/15/2024 UM Committee review
12/30/2024 Coding update
Next Scheduled Review Date: 10/2025

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J2329 Delete code effective 01/01/2025: C9399, J3490, J3590
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.