Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Ublituximab-xiiy (Briumvi®)	MP-RX-FP-151-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drug

Service Description

This document addresses the use of Ublituximab-xiiy (Briumvi®), a CD20-directed cytolytic antibody approved by the Food and Drug Administration (FDA) 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.

Background Information

Ublituximab is a CD20-directed cytolytic antibody that targets the CD20-expressing B-cells and binds to them resulting in cellular death.

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.

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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.

Approved Indications

Briumvi 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.

Other Uses

None.

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

ICD-10	Description
G35	Multiple sclerosis

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Medical Necessity Guidelines

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.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Ublituximab-xiiy (Briumvi®)

A. Criteria For Initial Approval

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.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Ublituximab-xiiy (Briumvi®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) if the following information is provided:

A. Documentation of the patient's response to treatment showing no severe or life-threatening infusion reaction

C. Authorization Duration

i. Initial Approval Duration: Up to 12 months

ii. Reauthorization Approval Duration: Up to 12 months

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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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, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, 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.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Recommended Dosing Schedule	Dose (mg) and Volume (ml)
First Infusion	150 mg (6ml)
Second Infusion – 2 weeks after first infusion	450 mg (18ml)
Subsequent Infusions – 24 weeks after the first infusion and every 24 weeks thereafter	450 mg (18ml)

Exceptions

- Hepatitis B virus screening and quantitative serum immunoglobulin screening are required before first dose
- 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.

Reference Information

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 21, 2023.
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 20, 2023.
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: August 30, 2023. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: October 19, 2023.
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, 2023.

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.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy Adoption	N/A	6/28/2024

Revised: 01/26/2024