WellMed Doctors helping patients for more than 25 years	**Effective Date: 10/27/23**	**Revision Date(s):**
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Policy Number: 068.000

Title: Coverage Determination Policy for Briumvi (Ublituximab-Xiiy)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

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Coverage Policy Number: 068.000

Line of Business: Medicare Part B

Policy Type: Prior Authorization

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Coverage Determination:

Initial/New Requests

Briumvi (ublituximab-xiiy) is proven for the treatment of:

Relapsing Forms of Multiple Sclerosis

Briumvi is medically necessary for the treatment of relapsing forms of **Multiple Sclerosis (MS)** when **ALL** of the following criteria are met:

A. Diagnosis of relapsing forms of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses); and
B. Patient is NOT receiving Briumvi in combination with **ANY** of the following:
    I. Disease modifying therapy (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, cladribine, siponimod, or teriflunomide).
    II. B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab, ocrelizumab).
    III. Lymphocyte trafficking blockers (e.g., alemtuzumab, mitoxantrone).
C. Briumvi dosing is in accordance with the United States Food and Drug Administration approved labeling
D. Initial authorization is for no more than 6 months.

Note: Hepatitis B virus screening and quantitative serum immunoglobulin screening is required before first dose

Renewal/Continuation of Therapy Requests

Briumvi is medically necessary for the treatment of relapsing forms of **Multiple Sclerosis (MS)** when **ALL** of the following criteria are met:

A. Patient has previously received treatment with Briumvi; and
B. Documentation of positive clinical response to Briumvi therapy; and
C. Patient is NOT receiving Briumvi in combination with **ANY** of the following:
    I. Disease modifying therapy (e.g., interferon beta preparations, dimethyl fumarate, glatiramer acetate, natalizumab,fingolimod, cladribine, siponimod, or teriflunomide).
    II. B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab, ocrelizumab).
    III. Lymphocyte trafficking blockers (e.g., alemtuzumab, mitoxantrone).
D. Briumvi dosing is in accordance with the United States Food and Drug Administration approved labeling
E. Authorization is for no more than 12 months.

FDA Approved Dose and Indication

FDA Approved Indication	Approved Dose	
Relapsing Forms of Multiple Sclerosis	Initial Dose	150 mg followed by 450 mg 2 weeks later
	Subsequent Dosing	450 mg every 24 weeks after first followed by 450 mg every 24 weeks

General Background

Multiple Sclerosis (MS) is a disease of the central nervous system that is currently incurable. This disease is characterized with fully or partially reversible periods of neurological disability.

Initial presentation of symptoms include: unilateral optic neuritis, painless binocular diplopia, focal brainstem or cerebellar syndrome, partial transverse myelitis and sensory with or without motor symptoms.

Magnetic Resonance Imagining (MRI) is commonly used to confirm diagnosis of MS. MRI can confirm presence of lesions that are the hallmark of MS. These lesions can be found throughout the central nervous system.

The cause of MS is unknown but can be due to a number of environmental and genetic risk factors including but not limited to: Sex (female), family history, tobacco exposure, obesity and history of mononucleosis.

Lesion development is thought to be immune mediated involving T cells, B cells, antibodies as wells as the glia and neurons. Currently available therapies for treatment of MS target the aforementioned cells of the immune system.

Briumvi a recombinant chimeric monoclonal antibody directed against CD20-expressing B-cells. The precise mechanism by which Briumvi exerts its therapeutic effects in multiple sclerosis is unknown, but is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, Briumvi results in cell lysis through mechanisms including antibody-dependent cellular cytolysis and complement-dependent cytolysis.

Clinical Evidence

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 RMS treated for 96 weeks [Study 1 (NCT03277261) and Study 2 (NCT03277248)]. 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/second dose, and 450 mg every 24 weeks after the first infusion for subsequent doses (third infusion and beyond) 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 (Gd)-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 Study 1 and Study 2 was the annualized relapse rate (ARR) over the treatment period. Additional outcome measures included: the total number of MRI T1 Gdenhancing lesions by Week 96, the total number of new or enlarging MRI T2 hyperintense lesions by Week 96, and time to confirmed disability progression for at least 12 weeks. Disability progression was defined as an increase of greater than or equal to 1.0 point from the baseline EDSS score that was attributable to MS when the baseline score was 5.5 or less, and greater than or equal to 0.5 points when the baseline score was above 5.5. Confirmed disability progression was evaluated in a pooled analysis of Studies 1 and 2. Disability progression was considered confirmed when the increase in the EDSS was confirmed at a regularly scheduled visit 12 weeks after the initial documentation of neurological worsening. 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 baseline demographic and disease characteristics were balanced between the two treatment groups. At baseline, the mean age was 37 years, 97% were White, and 63% were female. 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 baseline demographic and disease characteristics were balanced between the two treatment groups. At baseline, the mean age was 35 years, 99% were White, and 65% were female. In Study 1 and Study 2, BRIUMVI significantly lowered the ARR compared to teriflunomide. BRIUMVI statistically significantly reduced the number of T1 Gd-enhancing lesions and the number of new or enlarging T2 lesions in both studies compared to teriflunomide. There was no statistically significant difference in disability progression confirmed at 12 weeks between BRIUMVI-treated and teriflunomide-treated patients.

	Study 1		Study 2	
Endpoints	**BRIUMVI 450 mg[7]**	**Teriflunomide 14 mg[7]**	**BRIUMVI 450 mg[7]**	**Teriflunomide 14 mg[7]**
Clinical Endpoints[1]				
Annualized Relapse Rate (Primary Endpoint)	0.076	0.188	0.091	0.178
Relative Reduction	59% (p<0.001)		49% (p = 0.002)	
Proportion of Patients with 12-week Confirmed Disability Progression[2,3]	5.2% BRIUMVI vs. 5.9% teriflunomide			
Risk Reduction (Pooled Analysis)[4]	16% (p = 0.510)			
MRI Endpoints[5]				
Mean number of T1 Gd-enhancing lesions per MRI[6]	0.016	0.491	0.009	0.250
Relative Reduction	97% (p<0.001)		97% (p<0.001)	
Mean number of new or enlarging T2 hyperintense lesions per MRI[6]	0.213	2.789	0.282	2.831
Relative Reduction	92% (p<0.001)		90% (p<0.001)	

[1] Based on Modified Intent-to-Treat (mITT) Population, defined as all randomized patients who received at least one infusion of study medication and had one baseline and post-baseline efficacy assessment. Study 1: BRIUMVI (N=271), teriflunomide (N=274). Study 2: BRIUMVI (N=272), teriflunomide (N=272).
[2] Data prospectively pooled from Study 1 and Study 2: BRIUMVI (N=543), teriflunomide (N=546).
[3] Defined as an increase of 1.0 point or more from the baseline EDSS score for patients with baseline score of 5.5 or less, or 0.5 point or more when the baseline score is greater than 5.5, Kaplan-Meier estimates at Week 96.
[4] Based on Hazard Ratio.
[5] Based on MRI-mITT population (mITT patients who have baseline and post-baseline MRI). Study 1: BRIUMVI (N=265), teriflunomide (N=270). Study 2: BRIUMVI (N=272), teriflunomide (N=267).
[6] At Week 96.
[7] BRIUMVI dosing by intravenous infusion: first dose of 150 mg, second dose 450 mg two weeks after the first; subsequent doses 450 mg every 24 weeks; teriflunomide dosing: 14 mg by mouth once daily.

In exploratory analyses of Study 1 and Study 2, a similar effect of BRIUMVI on the ARR was observed in subgroups defined by gender, prior non-steroid MS therapy, baseline disability (EDSS 3.5 or lower versus greater than 3.5), the number of relapses in the 2 years prior to study enrollment, and number of Gd-enhancing lesions at baseline.

Note: Clinical studies of BRIUMVI did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

HCPCS Code

HCPCS Code	J2329
Dosage Form	150 mg/6 mL single dose vial
Route of Administration	Intravenous

Acronyms

Multiple Sclerosis = MS

Magnetic Resonance Imagining = MRI

References

1. PRESCRIBING INFORMATION FOR BRIUMVITM (ublituximab-xiiy) injection, for intravenous use. Published online 2022.
2. Steinman L, Fox E, Hartung HP, et al. Ublituximab versus Teriflunomide in Relapsing Multiple Sclerosis. N Engl J Med. 2022;387(8):704-714.
3. Reich DS, Lucchinetti CF, Calabresi PA. Multiple Sclerosis. N Engl J Med. 2018 Jan 11;378(2):169-180. doi: 10.1056/NEJMra1401483. PMID: 29320652; PMCID: PMC6942519.