Briumvi® (Ublituximab-Xiiy) (for Ohio Only)

Policy Number: CSOH2024D0122.B
Effective Date: May 1, 2024

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Related Policies

None

Application

This Medical Benefit Drug Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Briumvi® is medically necessary for the treatment of relapsing forms of multiple sclerosis (MS) when all of the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of relapsing forms of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses); **and**
  - Patient is **not** receiving Briumvi® in combination with **any** of the following:
    - Disease modifying therapy (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, cladribine, siponimod, or teriflunomide); **or**
    - B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab, ocrelizumab); **or**
    - Lymphocyte trafficking blockers (e.g., alemtuzumab, mitoxantrone)

    and
  - Briumvi® dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization is for no more than 12 months
- For **continuation of therapy**, **all** of the following:
  - Patient has previously received treatment with Briumvi®; **and**
  - Documentation of positive clinical response to Briumvi® therapy; **and**
  - Patient is **not** receiving Briumvi® in combination with **any** of the following:
    - Disease modifying therapy (e.g., interferon beta preparations, dimethyl fumarate, glatiramer acetate, natalizumab, fingolimod, cladribine, siponimod, or teriflunomide); **or**
    - B cell targeted therapy (e.g., rituximab, belimumab, ofatumumab, ocrelizumab); **or**
    - Lymphocyte trafficking blockers (e.g., alemtuzumab, mitoxantrone)

    and
  - Briumvi® dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Authorization is for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements 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 Code	Description
J2329	Injection, ublituximab-xiiy, 1mg

Diagnosis Code	Description
G35	Multiple sclerosis

Background

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

Proven

Relapsing Forms of Multiple Sclerosis (RMS)

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 (ULTIMATE I and II). 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 ULTIMATE I and II 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 ULTIMATE I and II. 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.

A total of 549 participants were enrolled in the ULTIMATE I trial, and 545 were enrolled in the ULTIMATE II trial; the median follow-up was 95 weeks. In the ULTIMATE I trial, the annualized relapse rate was 0.08 with ublituximab and 0.19 with teriflunomide (rate ratio, 0.41; 95% confidence interval [CI], 0.27 to 0.62; P < 0.001); in the ULTIMATE II trial, the annualized relapse rate was 0.09 and 0.18, respectively (rate ratio, 0.51; 95% CI, 0.33 to 0.78; P = 0.002). The mean number of gadolinium-enhancing lesions was 0.02 in the ublituximab group and 0.49 in the teriflunomide group (rate ratio, 0.03; 95% CI, 0.02 to 0.06; P < 0.001) in the ULTIMATE I trial and 0.01 and 0.25, respectively (rate ratio, 0.04; 95% CI, 0.02 to 0.06; P < 0.001), in the ULTIMATE II trial. In the pooled analysis of the two trials, 5.2% of the participants in the ublituximab group and 5.9% in the teriflunomide group had worsening of disability at 12 weeks (hazard ratio, 0.84; 95% CI, 0.50 to 1.41; P = 0.51). Infusion-related reactions occurred in 47.7% of the participants in the ublituximab group. Serious infections occurred in 5.0% in the ublituximab group and in 2.9% in the teriflunomide group.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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.

References

1. Briumvi® [package insert]. Morrisville, NC: TG Therapeutics, Inc.; December 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.

Policy History/Revision Information

Date	Summary of Changes
12/01/2024	**Template Update** • Modified font style; no change to policy content
05/01/2024	**Coverage Rationale** • Changed duration for initial authorization from "no more than ***6*** months" to "no more than ***12*** months" **Supporting Information** • Archived previous policy version CSOH2024D0122.A

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.