Medical Policy Bulletin

Title:
Ublituximab-xiiy (Briumvi®) for intravenous use
Policy #:
MA08.160b

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

Ublituximab-xiiy (Briumvi®) is considered medically necessary and, therefore, covered for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), and active secondary progressive multiple sclerosis (SPMS) in adults when **all** of the following are met:

- The individual has a confirmed diagnosis of relapsing MS (RMS)
- The individual has active disease
- The individual does not have a diagnosis of primary progressive MS (PPMS)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for ublituximab-xiiy (Briumvi) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on Off-label Coverage for Prescription Drugs and Biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of

the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Guidelines

There is no Medicare coverage determination addressing ublituximab-xiiy (Briumvi); therefore, the Company policy is applicable.

BENEFIT APPLICATION

Subject to the applicable Evidence of Coverage, ublituximab-xiiy (Briumvi) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

For Medicare Advantage members, certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when ublituximab-xiiy (Briumvi) is covered under a member's medical benefit (Part B benefit). It does not address instances when ublituximab-xiiy (Briumvi) is covered under a member's pharmacy benefit (Part D benefit).

DOSING

The dosing of ublituximab-xiiy (Briumvi) is as follows:

- Initial dose: 150 mg intravenous (IV) infusion
- Second dose: 450 mg IV infusion administered 2 weeks after the first infusion
- Subsequent doses: 450 mg IV infusion administered 24 weeks after the first infusion and every 24 weeks thereafter
- Observe the individual for at least 1 hour after completion of the first two infusions. Post-infusion monitoring of subsequent infusions is at the provider's discretion unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion.

US FOOD AND DRUG ADMINISTRATION STATUS

Ublituximab-xiiy (Briumvi) was approved by the US Food and Drug Administration (FDA) on December 28, 2022, for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), and active secondary progressive disease, in adults.

PEDIATRIC USE
The safety and effectiveness of ublituximab-xiiy (Briumvi) have not been established in pediatric individuals.

Description

Multiple sclerosis (MS) is a disease that disrupts the flow of information in the central nervous system (CNS), which affects the brain, spinal cord, and optic nerves in individuals with MS. A triggering event causes the individual's immune system to attack the CNS, resulting in damage to the outer protective layer, called myelin, of the CNS system. This results in unpredictable disruptions in the flow of signals from the brain to the body along the CNS pathways. Some common symptoms are fatigue, numbness/tingling, pain, paralysis, mood changes, and memory problems. A 2019 study found that nearly 1 million people in the United States are living with MS. The exact cause of MS is not known. Most individuals who are diagnosed with MS are between 20 and 50 years old, and most are female. Each individual with MS experiences the disease differently, but there are four basic types of MS: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).

CIS is the first episode of neurological symptoms that lasts for at least 24 hours in an individual. The episode does

not meet the diagnosis of MS because the individual who experiences CIS may not go on to develop MS. If CIS is accompanied with identifiable CNS lesions on a magnetic resonance imaging (MRI) scan, it is more likely that the individual will later be diagnosed with MS. There are some therapies approved for CIS that can delay the onset of MS.

RRMS is the most common course of the disease in individuals diagnosed with MS. This disease course type is characterized by clearly defined exacerbations (relapses) of new or increasing neurological symptoms that are followed by periods of complete or partial recovery (remissions). The disease may be active (with or without MRI activity) or not active, and the symptoms may worsen or not worsen during each episode.

PPMS is the course of MS characterized by the lack of early relapses or remissions as the neurological functioning worsens. PPMS can be further classified as active (with or without MRI activity) or not active, as well as with progression or without progression. The individual may have brief periods of stable disease as well as periods of increasing disability with or without new relapses or MRI activity.

SPMS is the progression of MS after a time of RRMS. Some individuals with RRMS will transition to SPMS. This course of the disease is characterized by a progressive worsening of CMS function, with the accumulation of disability, over time. This course of the disease can also be further classified as active (with or without MRI activity) or not active, as well as with progression or without progression. During this course of the disease, the individual may still occasionally experience relapses as well as times of stable disease.

Ublituximab-xiiy (Briumvi) is a recombinant chimeric monoclonal immunoglobulin (Ig) G1 antibody directed against cluster of differentiation (CD)20-expressing B cells. The precise mechanism by which ublituximab-xiiy (Briumvi) exerts its therapeutic effects in MS 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, ublituximab-xiiy (Briumvi) results in cell lysis through mechanisms including antibody-dependent cellular cytolysis and complement-dependent cytolysis.

The safety and efficacy of ublituximab-xiiy (Briumvi) was evaluated in two identical, simultaneously run clinical trials: NCT03277261 (ULTIMATE 1) and NCT03277248 (ULTIMATE 2). The clinical trials were phase III randomized, multicenter, double-blinded, active-controlled studies comparing individuals who received intravenous (IV) ublituximab-xiiy (Briumvi) and oral placebo versus individuals who received IV placebo and oral teriflunomide (Aubagio). The primary endpoint was the annualized relapse rate (ARR). Some secondary endpoints included total number of gadolinium (Gd)-enhancing T1 lesions per MRI scan, total number of new and enlarging T2 hyperintense lesions per MRI scan, and time to confirmed disability progression (CDP) for at least 12 weeks.

In ULTIMATE 1, 271 individuals were randomly assigned to receive ublituximab-xiiy (Briumvi) and 274 individuals received teriflunomide (Aubagio). The ARR for the ublituximab-xiiy (Briumvi) cohort was 0.076 versus 0.188 for the teriflunomide (Aubagio) cohort, which represented a 59 percent relative reduction rate (P<0.001). The mean number of T1 Gd-enhancing lesions in the ublituximab-xiiy (Briumvi) cohort was 0.016 versus 0.491 for the teriflunomide (Aubagio) cohort, which represented a 97 percent relative reduction rate (P<0.001). The mean number of new or enlarging T2 hyperintense lesions for the ublituximab-xiiy (Briumvi) cohort was 0.213 versus 2.789 for the teriflunomide (Aubagio) cohort, which represented a 92 percent relative reduction rate (P<0.001).

In ULTIMATE 2, 272 individuals were randomly assigned to receive ublituximab-xiiy (Briumvi) and 272 individuals received teriflunomide (Aubagio). The ARR for the ublituximab-xiiy (Briumvi) cohort was 0.091 versus 0.178 for the teriflunomide (Aubagio) cohort, which represented a 49 percent relative reduction rate (P=0.002). The mean number of T1 Gd-enhancing lesions in the ublituximab-xiiy (Briumvi) cohort was 0.009 versus 0.250 for the teriflunomide (Aubagio) cohort, which represented a 97 percent relative reduction rate (P<0.001). The mean number of new or enlarging T2 hyperintense lesions for the ublituximab-xiiy (Briumvi) cohort was 0.282 versus 2.831 for the teriflunomide (Aubagio) cohort, which represented a 90 percent relative reduction rate (P<0.001). The proportion of individuals with 12-week CDP risk reduction (pooled analysis between ULTIMATE 1 and ULTIMATE 2) was 5.2 percent for the ublituximab-xiiy (Briumvi) cohort versus 5.9 percent for the teriflunomide (Aubagio) cohort, which was an insignificant change (16 percent; P=0.510).

OFF-LABEL INDICATION

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

G35.A Relapsing-remitting multiple sclerosis

G35.C1 Active secondary progressive multiple sclerosis

G35.D Multiple sclerosis, unspecified

HCPCS Level II Code Number(s)

J2329 Injection, ublituximab-xiiy, 1mg

Policy History

Revisions From MA08.160b:

12/15/2025	This version of the policy will become effective 12/15/2025. Inclusion of a policy in a Code Update memo does not imply that a full review of the policy was completed at this time. The following ICD-10 codes have been **added** to this policy: G35.A Relapsing-remitting multiple sclerosis G35.C1 Active secondary progressive multiple sclerosis G35.D Multiple sclerosis, unspecified The following ICD-10 code has been **removed** from this policy: G35 Multiple sclerosis

New policy MA08.160:

03/28/2025	This policy has been reissued in accordance with the Company's annual review process.
05/07/2024	The following new policy has been developed to communicate the Company's coverage criteria for ublituximab-xiiy (Briumvi™) for intravenous use. The policy will become effective 05/07/2024.

Version Effective Date:
12/15/2025
Version Issued Date:
12/15/2025
Version Reissued Date:
N/A