These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

**Ublituximab-xiiy (Briumvi) Clinical Guideline for Home Intravenous Therapy**

**Section:** Clinical Guideline
**Policy ID:** CG050
**Effective:** 3/9/2026
**Reviewed:** 3/9/2026
**Revised:** N/A
**Approved by, Title and Date Approved:** David Benedict, President, 3/9/26

## I. BACKGROUND

Ublituximab-xiiy (Briumvi) is a chimeric IgG monoclonal antibody that binds to CD-20 on the surface of pre-B and mature B lymphocytes. After binding to CD-20, ublituximab results in cell lysis with mechanisms including antibody-dependent cellular cytolysis and complement-dependent cytolysis. B-cells are thought to affect the pathophysiology of multiple sclerosis through antigen presentation, pro-inflammatory cytokine production, soluble toxic factor production, and contribution to formation of ectopic lymphoid aggregates in the meninges. Ublituximab received orphan drug status in 2022 for the treatment of multiple sclerosis in adult patients including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease. The following outlines the procedures for servicing patients in need of outpatient ublituximab home infusions.

## II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Age
4. Other relevant social and/or medical history
5. Recent baseline CBC with differential

C. Physician orders for ublituximab must include:

1. Drug and dose
2. Route of administration
3. Frequency of administration
4. Emergency medications per protocol
5. Orders for pre-medications
6. Order for concurrent 250 mL 0.9% sodium chloride IV hydration if approved for first dose at home
7. Line care protocol

8. Routine lab monitoring, if applicable

D. Baseline labs or tests prior to starting therapy:

1. Hepatitis B virus (HBV) screening
2. Recent CBC with differential
3. Serum immunoglobulins: low levels should be reviewed before therapy
4. Liver function tests: baseline serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), alkaline phosphatase, and bilirubin
5. Vaccinations: completion of age-appropriate vaccinations. See *Vaccinations* under *Warnings and Precautions* for more information.
6. Pregnancy testing is recommended for females of reproductive potential prior to each infusion.

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*).

## III. PHARMACOLOGY OVERVIEW

**Refer to manufacturer's full Prescribing Information for most up to date information**

A. Indication: relapsing forms of multiple sclerosis (MS) including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adult patients

B. Dosing:

1. First infusion: 150 mg IV
2. Second infusion: 450 mg IV administered 2 weeks after first infusion
3. Subsequent infusions: 450 mg IV 24 weeks after the first infusion and every 24 weeks thereafter

*Dosing is based off actual body weight. Ublituximab has not been studied in extremes of body weights.

C. Dose Adjustment

1. Delayed or missed doses: If a planned infusion is missed, administer as soon as possible. Do not wait until the next scheduled infusion. Reset the infusion schedule to administer the next sequential infusion 24 weeks after the missed infusion is administered. Infusions must be separated by at least 5 months.
2. No dose adjustments for renal or hepatic impairment.

D. Duration: Duration of therapy is dependent on patient response and adverse reactions.

E. Contraindications:

1. Active HBV infection
2. A history of life-threatening infusion reaction to ublituximab

F. Warnings and Precautions:

1. **Infusion reactions:** infusion-related reactions, including pyrexia, headache, chills, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and anaphylaxis, can occur with ublituximab. 48% (262/545) of patients in the clinical studies experienced infusion reactions with most occurring within 24 hours of the first infusion. None were fatal, but 0.6% (3/545) of patients who received ublituximab experienced serious infusion-related reactions. For life-threatening reactions, discontinue ublituximab and provide supportive treatment. Educate patients that infusion reactions can occur up to 24 hours after the infusion. The following pre-medications are recommended to minimize the risk of infusion-related reactions:

    a. Methylprednisolone 100 mg IV or its equivalent 30 minutes before each ublituximab infusion
    b. Antihistamine (e.g., diphenhydramine) PO/IV 30-60 minutes before each infusion
    c. Consider administering an antipyretic, such as acetaminophen, before the infusion.

2. **Infections**: serious, including fatal or life threatening, bacterial and viral infections have been reported in ublituximab patients. Patients receiving other anti-CD20 B-cell depleting therapies have suffered a higher risk of infections, including serious and fatal bacterial, fungal, and new or reactivated viral infections during and post-treatment. Upper respiratory infection and urinary tract infection were the most common infections. Administration should be delayed in currently infected patients until infection resolution.

    a. Possible increased risk of immunosuppressant effect with other immunosuppressants. The potential for increased immunosuppressive effects should be considered when initiating ublituximab after immunosuppressive therapy or vice versa.
    b. HBV Reactivation: HBV reactivation occurred in clinical trials. Fulminant hepatitis, liver failure, and death caused by HBV reactivation has occurred in patients receiving anti-CD20 antibodies. All patients should be screened for HBV before ublituximab therapy.
    c. Progressive Multifocal Leukoencephalopathy (PML): No cases have occurred in MS patients receiving ublituximab. However, JC viral infection causing PML has been documented in patients treated with other anti-CD20 antibodies. At the first sign of PML, hold ublituximab and perform further workup. Symptoms of PML are gradual and typically include progressive weakness on one side of the body, limb clumsiness, visual disturbances, changes in alertness and memory resulting in confusion and personality changes. Magnetic resonance imaging (MRI) findings in conjunction with positive JC Virus may appear before clinical status changes. Discontinue ublituximab if PML confirmed.
    d. Vaccinations: Follow immunization guidelines. Live vaccines should be given at least 4 weeks before ublitixumab is started and inactivated vaccines should be administered at least 2 weeks before therapy because ublituximab could result in reduced efficacy of non-live vaccines. Live vaccines are not recommended during treatment and until B-cell repletion.

3. **Fetal Risk**: ublituximab may cause harm to unborn fetus when used in pregnant women. Transient lymphocytopenia and peripheral B-cell depletion have been reported in infants born to mothers who received other anti-CD20 B-cell depleting antibodies while pregnant. Females of childbearing potential should be advised to use effective contraception during ublituximab therapy and 6 months after the final infusion.

4. **Reduction in Immunoglobulins**: ublituximab therapy can decrease immunoglobulin levels as expected with B-cell depleting therapies. Serum immunoglobulins levels should be monitored during treatment, especially in patients with recurrent infections or opportunistic infections, and after completing therapy until B-cell repletion. Consideration for discontinuing ublitixumab should be made if a patient with low immunoglobulins develops serious opportunistic or recurrent infections, or if a patient with prolonged hypogammaglobinemia needs treatment with immunoglobulins.

5. **Liver Injury**: clinically significant drug-induced hepatic injury has occurred with ublituximab use within weeks to months after administration. Patients with ALT or AST levels over three times the upper limit of normal (ULN) and serum total bilirubin over twice the ULN are potentially at risk for severe drug-induced hepatic injury. Baseline liver function tests should be obtained in patients receiving ublituximab, and patients should be monitored for signs and symptoms of liver impairment including new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. In patients who report symptoms of liver injury, monitor AST, ALT, alkaline phosphatase, and bilirubin levels, ublituximab should be discontinued if an alternative cause for liver injury cannot be identified.

G. Pregnancy and lactation: fetal risk may occur when used during pregnancy. See *Fetal Risk* under *Warnings and Precautions* for more information. Women who become pregnant while on ublituximab or within 6 months of their last dose are encouraged to join the pregnancy registry via calling 1-877-411-4546 or visiting www.briumvipregnancyregistry.com. The risk of fetal harm cannot be ruled out in breastfeeding mothers receiving ublituximab therapy and the benefits of treatment must be weighed against the potential risk to the breastfeeding infant.

H. Pharmacokinetics:

1. Volume of distribution: 3.18 L
2. Metabolism: enzymatic degradation.
3. Elimination half-life: 22 days

I. Adverse Reactions:

1. >10%:

    a. Infection (56%; serious infection 5%)
    b. Infusion-related reaction (48% but less than <1% severe)
    c. Upper respiratory tract infection (45%)
    d. Decreased serum immunoglobulins (IgM: 21%, IgA and IgG 2-6%)
    e. Decreased neutrophils (15%)

2. 1-10%:

    a. Urinary tract infection (10%)
    b. Lower respiratory infection (9%)
    c. Limb pain (6%)
    d. Insomnia (6%), fatigue (5%),
    e. Herpes virus infection (4%)

3. Frequency undefined: reactivation of HBV, hepatic injury

J. Drug Interactions: Drug-drug interactions may exist. Consult interaction database for patient specific assessment. The concomitant usage of ublituximab with other immune-modulating or immunosuppressant drugs, including immunosuppressant doses of corticosteroids, may increase the risk of infection.

## IV. ADMINISTRATIVE GUIDELINES

A. Administration: IV infusions should be given immediately after reconstitution and dilution. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.

B. Do not co-administer with other products in the same IV line

## V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. IV access supplies as applicable
    a. Peripheral IV access supplies for patients requiring peripheral IV access
        1) IV start Kit
        2) Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
        3) Extension set 8" with needless connector
    b. Port access supplies for patients with a port
        1) Port needle (ex. 22 Gauge x ¾ to 1" safe step)
        2) Needless connector
        3) Central line dressing change kit
5. IV Pole
6. Syringes (20-35 mL) with needles (20 G x 1")
7. Sharps container
8. Pole mounted ambulatory infusion pump
9. Ambulatory pump tubing
10. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
11. Battery change procedure teaching sheet
12. Continuous delivery mode teaching sheet
13. Pump return box
14. For normal saline hydration with any first doses:
    a. IV administration set (flow regulator or gravity tubing)
    b. Y-site IV connector

B. Prescription items:

1. Ublituximab vials
2. 250 mL 0.9% sodium chloride bag
3. Standard flushes per protocol

4. Anaphylaxis kit
5. Pre-medications (IV methylprednisolone, diphenhydramine, and acetaminophen)
6. 250 mL 0.9% sodium chloride bag (for first dose at home)

C. How Supplied: single-dose vial 150 mg/6 mL (25 mg/mL) containing a clear to opalescent, colorless to slightly yellow, preservative-free solution

D. Storage and Handling: refrigerate vials at 2°C to 8°C (36°F to 46°F) in original container to protect from light. Do not freeze or shake.

E. Compatibility: Compatible with 0.9% sodium chloride. No observed incompatibilities with polyvinyl chloride (PVC) or polyolefin (PO) bags and IV administration sets.

F. Procedures:

1. Explain the reasoning for visit and use of ublituximab.
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication. Notify ordering physician and pharmacist if signs or symptoms are present.
4. Establish venous access prior to preparation of drug.
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to: infusion-related reactions, risk of infections, and fatigue.
6. Administer pre-medications 30 minutes prior to ublituximab infusion.
7. Prepare Product

    a. Prior to preparation, inspect ublituximab vial. The product should be a clear to opalescent, colorless to slightly yellow solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not use the solution if discolored or if the solution contains discrete foreign particulate matter.
    b. For 150 mg dose, withdraw 6 mL of 0.9% sodium chloride from 250 mL stock bag and discard. Withdraw 150 mg/6mL of ublituximab from vial and add to the normal saline bag for a total volume of 250 mL.
    c. For 450 mg dose, withdraw 18 mL of 0.9% sodium chloride from the 250 mL stock bag and discard. Withdraw 450mg/18mL from the ublituximab vials and add to the normal saline bag for a total volume of 250 mL.
    d. Mix solution by gentle inversion of the bag. Do not shake.

8. Infusion Rates:

| | Infusion Rate (mL/hr) | Duration |
|---|---|---|
| First Infusion | 1. Start at 10 mL per hour for the first 30 minutes<br>2. Increase to 20 mL per hour for the next 30 minutes<br>3. Increase to 35 mL per hour for the next hour<br>4. Increase to 100 mL per hour for the remaining 2 hours | 4 hours |

| | | |
|---|---|---|
| Second Infusion (two weeks later) | 1. Start at 100 mL per hour for the first 30 minutes<br>2. Increase to 400 mL per hour for the remaining 30 minutes | 1 hour |
| Subsequent Infusions (once every 24 weeks) | 1. Start at 100 mL per hour for the first 30 minutes<br>2. Increase to 400 mL per hour for the remaining 30 minutes | 1 hour |

9. For first dose ublituximab at home, administer 250 mL 0.9% sodium chloride hydration concurrently with ublituximab with Y-site connector via flow regulator or gravity tubing during the entire duration of the infusion. Fluid administration may be discontinued when ublituximab infusion is complete.
10. Infusions should be started immediately after reconstitution and dilution. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.
11. Infusion Reactions:
    a. Life-threatening infusion reactions: stop infusion immediately if signs of life-threatening or disabling reaction, administer proper supportive therapy, and permanently discontinue ublituximab.
    b. Severe infusion reaction: pause infusion immediately and provide supportive treatment as necessary. After symptom resolution, restart the infusion at half the rate of the infusion when the reaction began. Increase the rate as tolerated.
    c. Mild to moderate reactions: reduce the infusion rate by 50% of the infusion rate when symptoms began. If tolerated for at least 30 minutes, increase the rate.
12. Post infusion monitoring: monitor patient and vital signs periodically during the infusion (including during titration step) and 60 minutes after the infusion ends for the first two infusions. For subsequent infusions, refer to the 30 minutes post infusion monitoring per CarePathRx Nursing Best Practice Administration Guidelines.

## II. CLINICAL MONITORING

A. Prior to therapy:

1. Patients must have a HBV screening. Ublituximab is contraindicated in patients with active HBV.
2. Baseline CBC with differential
3. Patients should have serum immunoglobulins drawn prior to therapy. Low levels should be reviewed before therapy
4. Liver function tests: baseline serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), alkaline phosphatase, and bilirubin
5. Pregnancy testing is recommended for females of reproductive potential prior to each infusion
6. Ensure patients are up to date on vaccinations
7. Ensure patients do not have an active infection
8. Review if patient is currently on or just recently stopped other immunosuppressant medications

B. During therapy:

1. Monitor for infusion related reactions even up to 24 hours after the infusion
2. Monitor for signs or symptoms of infection including upper respiratory infections. Monitor immunoglobulins. Ublituximab may need discontinued in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins
3. Although no cases of PML have occurred in MS patients treated with ublituximab, JCV infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies. Monitor for signs or symptoms of PML including neurological effects such as weakness on one side of the body or clumsiness of limbs, disturbance of vision, changes in thinking, memory, and orientation leading to confusion, and personality changes.
4. For females of child-bearing age, monitor pregnancy status, contraception, and menstrual cycles.
5. Monitor liver function tests during therapy. Ublituximab may need discontinued in patients with evidence of liver injury in the absence of an alternative etiology.

**Please refer to the package insert for the most up to date guidance on this medication.**

**REFERENCES:**

Briumvi [package insert]. Morrisville, NC, TG Therapeutics Inc, 2025.

Briumvi. Micromedex. Merative. Ann Arbor, MI: Micromedex; September 2025. Accessed December 18, 2025.

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## APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

### Emergency Medication After Your Infusion

**Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.**

**Your nurse will tell you when you need to use Emergency Medications.**
**The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.**

Start with a clean work surface and clean hands.

**Open the supply bag labeled Anaphylaxis Kit Contents.**

**You will need:**

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

**All other contents will not be needed.**

**Open the IM Epinephrine Bag**

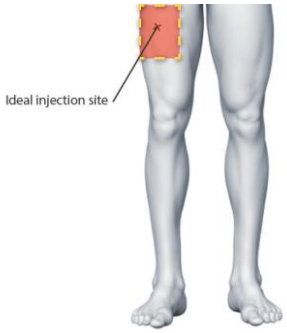
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

**Prepare IM (intramuscular) injection of Epinephrine:**

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampule.**
3. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampule.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection




1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

**Take the pills by mouth.**

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

**Place all trash in the bag the pills came in** and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
**Call 911** or have someone drive you to the emergency department.