briumvi®
ublituximab-xiiy 150 mg/6 mL injection for IV

Dosing and Administration Guide

BRIUMVI injection is a 150 mg/6 mL (25 mg/mL) clear to opalescent, colorless to slightly yellow solution in a single-dose vial.[1]

BRIUMVI is a 1-hour, 450 mg intravenous (IV) infusion given every 24 weeks following the starting dose.[1*]

Please see accompanying full Prescribing Information for full Dosing and Administration instructions.

*First infusion is a 150 mg infusion over 4 hours, followed 2 weeks later by a second infusion of 450 mg over 1 hour.

INDICATION

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.

IMPORTANT SAFETY INFORMATION

Contraindications: BRIUMVI is contraindicated in patients with:

- Active HBV infection
- A history of life-threatening infusion reaction to BRIUMVI

This Dosing Guide is not a substitute for the full Prescribing Information.

Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

Table of Contents

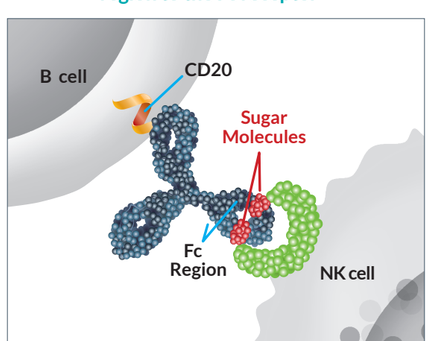
Overview of BRIUMVI

briumvi® ublituximab-xiiy 150 mg/6 mL injection for IV

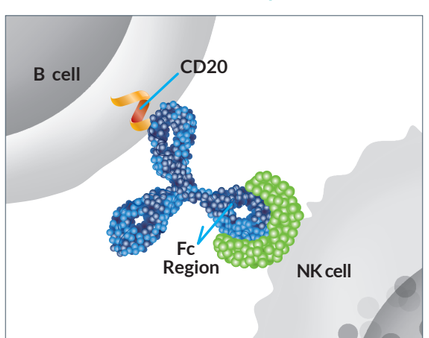
Glycoengineering removes certain sugar molecules in the Fc region, allowing for closer interaction and improved affinity[2-4]

The precise mechanism by which BRIUMVI exerts its therapeutic effects is unknown[1]

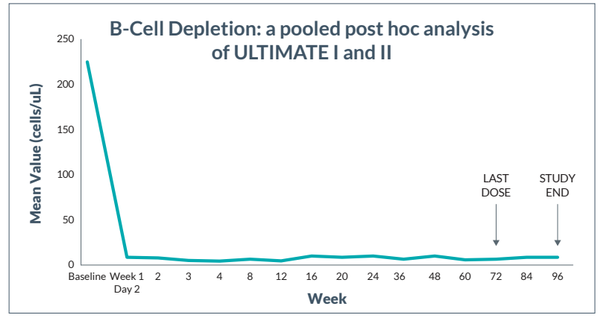
BRIUMVI is glycoengineered, excluding certain sugar molecules that can interfere with the binding of the Fc region to the Fc receptor[1,6]



Removal of these sugar molecules enhances affinity for the natural killer (NK)/effector cells, with the goal of efficient B-cell depletion[5]



B-cell counts were depleted by 96% at 24 hours after a single dose, and were maintained at this level for the remainder of the study[7]



The ARR (the Primary Endpoint for our clinical studies) for BRIUMVI observed in the ULTIMATE I and II identical 2-year Phase 3 trials with 543 patients treated with BRIUMVI and 546 treated with teriflunomide. The ARR for Study 1: 0.076 for BRIUMVI vs. 0.188 for teriflunomide (P<0.001) and for Study 2: 0.091 for BRIUMVI vs. 0.178 for teriflunomide (P=0.002).[1]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Infusion Reactions: BRIUMVI can cause infusion reactions, which can include pyrexia, chills, headache, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and an anaphylactic reaction. In MS clinical trials, the incidence of infusion reactions in BRIUMVI-treated patients who received infusion reaction-limiting premedication prior to each infusion was 48%, with the highest incidence within 24 hours of the first infusion. 0.6% of BRIUMVI-treated patients experienced infusion reactions that were serious, some requiring hospitalization.

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Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

BRIUMVI is the only therapy for RMS administered as a 1-hour infusion, twice per year following the starting dose[1]

Summary of select RMS treatment maintenance dosing

Frequency	Treatment	Administration	Post-infusion Monitoring
Twice a year	**BRIUMVI® (ublituximab-xiiy)**	**1-hour IV infusion**	**Flexible***
	OCREVUS® (ocrelizumab)	2 to 3.5-hour IV infusion†	1 hour
Once a month	TYSABRI® (natalizumab) KESIMPTA® (ofatumumab)	1-hour IV infusion Subcutaneous	1 hour‡ *(Not an infusion)*
Once a day or 3 times per week	COPAXONE® (glatiramer acetate)	Subcutaneous	*(Not an infusion)*
Once a day	AUBAGIO® (teriflunomide)	Pill	*(Not an infusion)*
Twice a day	VUMERITY® (diroximel fumarate)	Pill	*(Not an infusion)*

The comparison pertains only to differences in dosing and administration and should not be considered a comparison of efficacy or safety. Includes BRIUMVI and the top 6 FDA-approved RMS treatments for patients starting or switching to a new MS treatment (Q4 2021 to Q1 2022 Komodo claims), combining both generic and branded formulations. Fumarate class includes Vumerity, Tecfidera, and generic Tecfidera. This is not a complete list of all the available treatments for RMS.

*Starting with the third infusion, post-infusion monitoring is at physician discretion unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion. †Based on dosing option. ‡For patients who have received 12 infusions without evidence of a hypersensitivity reaction, observe patients post-infusion for the 13th and subsequent infusions according to clinical judgment.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Observe treated patients for infusion reactions during the infusion and for at least one hour after the completion of the first two infusions unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion. Inform patients that infusion reactions can occur up to 24 hours after the infusion. Administer the recommended pre-medication to reduce the frequency and severity of infusion reactions. If life-threatening, stop the infusion immediately, permanently discontinue BRIUMVI, and administer appropriate supportive treatment. Less severe infusion reactions may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

BRIUMVI infusion experience[1,5]

briumvi® ublituximab-xiiy 150 mg/6 mL injection for IV

Pre-appointment overview

Patient and caregiver counseling

Pre-infusion assessments

Supply and storage

Appointment overview

Preparation

Premedication Oral or IV

1-hour infusion*

Administration and infusion rate table

AE expectations

*Following the starting dose.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Infections: Serious, life-threatening or fatal, bacterial and viral infections have been reported in BRIUMVI-treated patients. In MS clinical trials, the overall rate of infections in BRIUMVI-treated patients was 56% compared to 54% in teriflunomide-treated patients. The rate of serious infections was 5% compared to 3% respectively. There were 3 infection-related deaths in BRIUMVI-treated patients. The most common infections in BRIUMVI-treated patients included upper respiratory tract infection (45%) and urinary tract infection (10%). Delay BRIUMVI administration in patients with an active infection until the infection is resolved.

This Dosing Guide is not a substitute for the full Prescribing Information.

Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

Patient counseling at time of prescription and on infusion day[1]

briumvi® ublituximab-xiiy 150 mg/6 mL injection for IV

Be sure to discuss and set expectations with patients and caregivers on the following:

PRE-SCREENINGS

Timing of previous vaccinations

Advise patients to complete any required live or live-attenuated vaccinations at least 4 weeks and, whenever possible, non-live vaccinations at least 2 weeks prior to initiation of BRIUMVI. Administration of live-attenuated or live vaccines is not recommended during BRIUMVI treatment and until B-cell recovery.

Hepatitis B virus (HBV) reactivation

Advise patients that BRIUMVI may cause reactivation of hepatitis B virus infection and that monitoring will be required if they are at risk.

Serum immunoglobulins

Advise patients that they will need to have blood drawn to perform testing for immunoglobulin levels.

Progressive multifocal leukoencephalopathy (PML)

Advise patients that PML is rare and is caused by a virus. It has happened with drugs that are similar to BRIUMVI and may happen with BRIUMVI. Inform the patient that PML is characterized by a progression of deficits and usually leads to death or severe disability over weeks or months. Instruct the patient of the importance of contacting their doctor if they develop any symptoms suggestive of PML. Inform the patient that typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

INFUSION SCREENINGS

Infection assessment

Advise patients to contact their healthcare provider for any signs of infection during treatment or after the last infusion. Signs can include fever, chills, constant cough, or painful urination.

Pregnancy testing/fetal risk

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with BRIUMVI and for 6 months after the last BRIUMVI dose. Advise patients to notify their healthcare provider if they are pregnant during treatment with BRIUMVI.

INFUSION REACTIONS

Inform patients about the signs and symptoms of infusion reactions and that infusion reactions can occur up to 24 hours after infusion. Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion reactions.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Consider the potential for increased immunosuppressive effects when initiating BRIUMVI after immunosuppressive therapy or initiating an immunosuppressive therapy after BRIUMVI.

INFUSION DAY

Starting dose

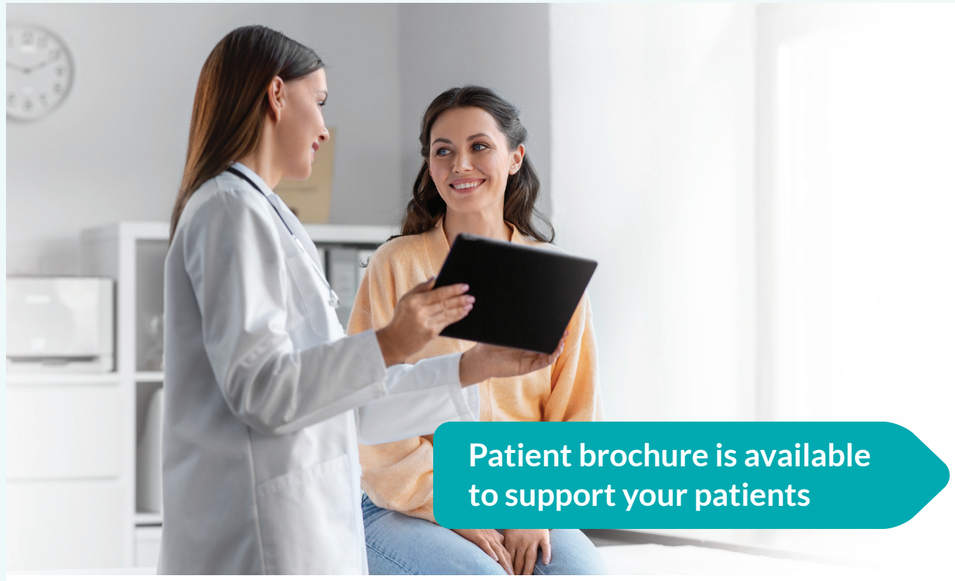
Set expectations on the 4-hour starting dose. Explain that the starting dose duration is important to ensure medication and rate tolerance and introduce the patient to the infusion experience.

Reduce reaction anxiety

Prepare patients for infusion reactions. Emphasize that an infusion reaction *does not mean you won't get your medicine.* Explain that there are ways to manage infusion reactions.

Communication

Stress the importance of alerting your infusion team of any changes, no matter how subtle. Ensure patients know who to call if they experience delayed reactions after they leave the infusion center.



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Hepatitis B Virus (HBV) Reactivation: HBV reactivation occurred in an MS patient treated with BRIUMVI in clinical trials. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with BRIUMVI. Do not start treatment with BRIUMVI in patients with active HBV confirmed by positive results for HBsAg and anti-HB tests. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult a liver disease expert before starting and during treatment.

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Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19

Pre-infusion assessements[1]

PRE-SCREENINGS

Conducted prior to the patient's first infusion; often a component of the PA process.

HBV screening

- Prior to initiating BRIUMVI, perform HBV screening. BRIUMVI is contraindicated in patients with active HBV confirmed by positive results for hepatitis B surface antigen (HBsAg) and anti-HBV tests
- For patients who are negative for HBsAg and positive for hepatitis B core antibody (HBcAb+) or are carriers of HBV (HBsAg+), consult liver disease experts before starting and during treatment with BRIUMVI

Serum immunoglobulins

- Prior to initiating BRIUMVI, perform testing for quantitative serum immunoglobulins. For patients with low serum immunoglobulins, consult immunology experts before initiating treatment with BRIUMVI

Timing of previous vaccinations

- Because vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation until B-cell repletion, administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of BRIUMVI for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of BRIUMVI for non-live vaccines

INFUSION SCREENINGS

Performed on the day of the infusion prior to administration.

Infection assessment

- Prior to every infusion of BRIUMVI, determine whether there is an active infection. In case of an active infection, delay infusion of BRIUMVI until the infection resolves

Pregnancy testing (recommended)

- Pregnancy testing is recommended for females of reproductive potential prior to each infusion with BRIUMVI

Supply and storage[1]

briumvi® ublituximab-xiiy 150 mg/6 mL injection for IV

How BRIUMVI is supplied

BRIUMVI injection is a sterile, clear to opalescent, colorless to slightly yellow, preservative-free solution for IV use

Supplied as a carton containing one 150 mg/6 mL (25 mg/mL) **single-dose vial** (NDC 73150-150-06)

How BRIUMVI is stored

Store BRIUMVI in the **refrigerator** at **2°C to 8°C** (36°F to 46°F)

Store BRIUMVI in the outer carton to **protect from light**

Do not freeze

Do not shake

Progressive Multifocal Leukoencephalopathy (PML): Although no cases of PML have occurred in BRIUMVI-treated MS patients, JCV infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies.

If PML is suspected, withhold BRIUMVI and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

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Preparation[1]

Only use 0.9% NaCl injection, USP to dilute BRIUMVI. BRIUMVI must be prepared by a healthcare professional using aseptic technique

BRIUMVI 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, whenever solution and container permit. **Do not use the solution if discolored or if the solution contains discrete foreign particulate matter**

PREPARATION OF SOLUTION FOR THE **FIRST INFUSION**

1. **Prepare** infusion bags for the **first infusion** (150 mg) using 1 vial (150 mg/6 mL) of BRIUMVI
2. **Withdraw** 6 mL 0.9% NaCl injection, USP from the 250 mL infusion bag and **discard**
3. **Withdraw** 6 mL BRIUMVI solution from the vial
4. **Add** 6 mL (150 mg) BRIUMVI into the infusion bag containing 0.9% NaCl injection, USP

PREPARATION OF SOLUTION FOR THE **SECOND** AND **SUBSEQUENT INFUSIONS**

1. Prepare infusion bag for second infusion (450 mg) and **subsequent** infusions (450 mg) using 3 vials (150 mg/6 mL) of BRIUMVI
2. **Withdraw** 18 mL 0.9% NaCl injection, USP from the 250 mL infusion bag and **discard**
3. **Withdraw** 18 mL BRIUMVI solution from the vials (6 mL/vial)
4. **Add** 18 mL (450 mg) BRIUMVI into the infusion bag containing 0.9% NaCl injection, USP

Mix diluted solution by gentle inversion. Do not shake.

USP, United States Pharmacopeia.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

MRI findings may be apparent before clinical signs or symptoms; monitoring for signs consistent with PML may be useful. Further investigate suspicious findings to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis.

Storage[1]

Storage of infusion solution and contingency plan for delayed infusion

Prior to the start of the IV infusion, the contents of the infusion bag should be at **room temperature**. It takes ~2 hours for the refrigerated solution to equilibrate to room temperature

Use the prepared infusion solution **immediately**. If the diluted solution is not administered immediately, store for up to:

- **24 hours** in the **refrigerator** at 2°C to 8°C (36°F to 46°F)
- An additional **8 hours** at **room temperature** up to 25°C (77°F)*

No incompatibilities between BRIUMVI and PVC or PO bags and IV administration sets **have been observed**

*Includes the equilibration time and infusion time.
PO, polyolefin; PVC, polyvinyl chloride.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

If PML is confirmed, treatment with BRIUMVI should be discontinued.

Vaccinations: Administer all immunizations according to immunization guidelines: for live or live-attenuated vaccines at least 4 weeks and, whenever possible at least 2 weeks prior to initiation of BRIUMVI for non-live vaccines. BRIUMVI may interfere with the effectiveness of non-live vaccines. The safety of immunization with live or live-attenuated vaccines during or following administration of BRIUMVI has not been studied. Vaccination with live virus vaccines is not recommended during treatment and until B-cell repletion.

Vaccination of Infants Born to Mothers Treated with BRIUMVI During Pregnancy: In infants of mothers exposed to BRIUMVI during pregnancy, assess B-cell counts prior to administration of live or live-attenuated vaccines as measured by CD19+ B-cells. Depletion of B-cells in these infants may increase the risks from live or live-attenuated vaccines. Inactivated or non-live vaccines may be administered prior to B-cell recovery. Assessment of vaccine immune responses, including consultation with a qualified specialist, should be considered to determine whether a protective immune response was mounted.

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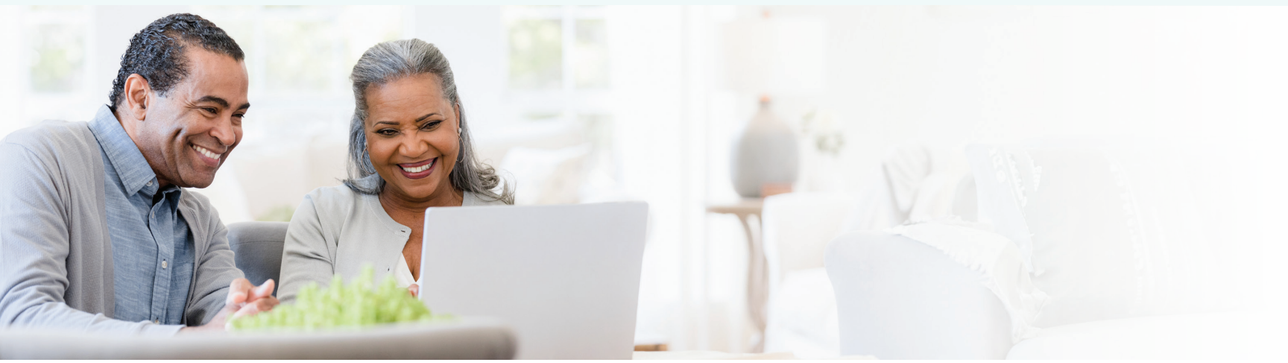
Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

BRIUMVI offers flexibility in premedication route of administration

- Premedicate with 100 mg of methylprednisolone **administered intravenously (or an equivalent oral dosage or equivalent corticosteroid)** approximately 30 minutes prior to each BRIUMVI infusion to reduce the frequency and severity of infusion reactions.
- Premedicate with an antihistamine (eg, diphenhydramine) administered orally or intravenously approximately 30-60 minutes prior to each BRIUMVI infusion to further reduce the frequency and severity of infusion reactions.
- The addition of an antipyretic (eg, acetaminophen) may also be considered.



IMPORTANT SAFETY INFORMATION (continued)

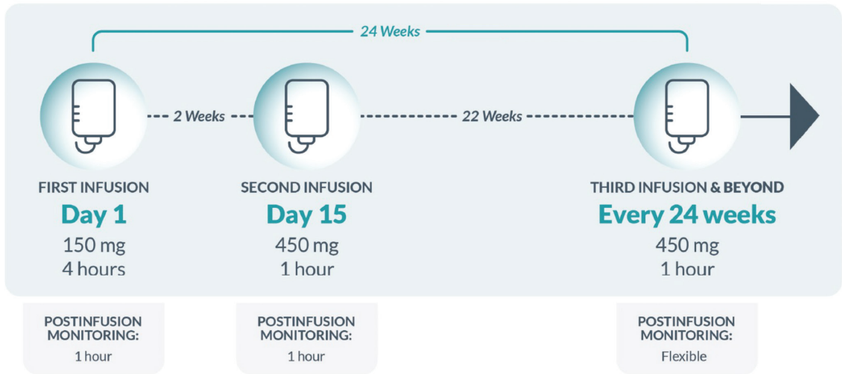
WARNINGS AND PRECAUTIONS (continued)

Fetal Risk: Based on data from animal studies, BRIUMVI may cause fetal harm when administered to a pregnant woman. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 B-cell depleting antibodies during pregnancy. A pregnancy test is recommended in females of reproductive potential prior to each infusion. Advise females of reproductive potential to use effective contraception during BRIUMVI treatment and for 6 months after the last dose.

Reduction in Immunoglobulins: As expected with any B-cell depleting therapy, decreased immunoglobulin levels were observed. Decrease in immunoglobulin M (IgM) was reported in 0.6% of BRIUMVI-treated patients compared to none of the patients treated with teriflunomide in RMS clinical trials. Monitor the levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections, and after discontinuation of therapy until B-cell repletion. Consider discontinuing BRIUMVI therapy if a patient with low immunoglobulins develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

BRIUMVI is the first and only anti-CD20 therapy that is administered as a twice-yearly 1-hour infusion[1,9,10*]

- Administer BRIUMVI under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion reactions
- The first IV infusion is 150 mg over 4 hours
- Followed by a second IV infusion of 450 mg administered 2 weeks after the first infusion
- Subsequent infusions of 450 mg IV over 1 hour are given every 24 weeks after the **FIRST** 150 mg IV infusion and every 24 weeks thereafter
- Observe the patient during and for at least 1 hour after the completion of the first 2 infusions. **Post-infusion monitoring of subsequent infusions is at physician discretion unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion**



95%

of all BRIUMVI 1-hour infusions were completed in 1 hour without interruption in the clinical trials[8,a]

BRIUMVI is the only anti-CD20 with discretionary post-infusion monitoring for the 3rd infusion and beyond[9,10,b]

Delayed or missed doses[1]

- If a planned infusion of BRIUMVI is missed, administer BRIUMVI 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 of BRIUMVI must be separated by at least 5 months

*Following the starting dose. Day 1 infusion is 150 mg over 4 hours, day 15 infusion is 450 mg over 1 hour, and subsequent infusions are 450 mg over 1 hour every 24 weeks.

[a]±5 minutes.

[b]Post-infusion monitoring on 3rd infusion and beyond is at physician discretion unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion.

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Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

Administration and infusion rate table[1]

Recommended dose, infusion rate, and infusion duration for relapsing forms of MS

FIRST INFUSION

BRIUMVI dose	150 mg
Total volume	250 mL
Infusion Rate	
0-30 min	10 mL/hr
30 min-hour 1	20 mL/hr
Hours 1-2	35 mL/hr
Hours 2-4	100 mL/hr
Total infusion time*	4 hours

SECOND INFUSION

2 weeks after the first infusion

BRIUMVI dose	450 mg
Total volume	250 mL
Infusion Rate	
0-30 min	100 mL/hr
30 min-hour 1	400 mL/hr
Total infusion time*	1 hour

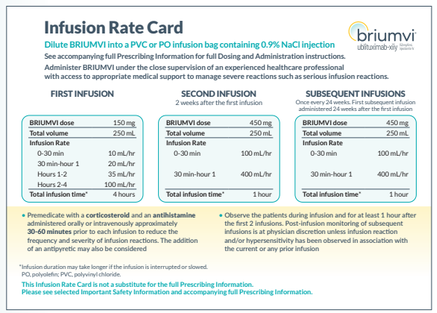
SUBSEQUENT INFUSIONS

Once every 24 weeks. First subsequent infusion administered 24 weeks after the first infusion

BRIUMVI dose	450 mg
Total volume	250 mL
Infusion Rate	
0-30 min	100 mL/hr
30 min-hour 1	400 mL/hr
Total infusion time*	1 hour

REMINDER:

Administer the diluted infusion solution through a dedicated line. A filter is not required.



Infusion Rate Card

briumvi ublituximab-xiiy

Dilute BRIUMVI into a PVC or PO infusion bag containing 0.9% NaCl injection

See accompanying full Prescribing Information for full Dosing and Administration instructions.

Administer BRIUMVI under the close supervision of an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion reactions.

FIRST INFUSION	
BRIUMVI dose	150 mg
Total volume	250 mL
Infusion Rate	
0-30 min	10 mL/hr
30 min-hour 1	20 mL/hr
Hours 1-2	35 mL/hr
Hours 2-4	100 mL/hr
Total infusion time*	4 hours

SECOND INFUSION (2 weeks after the first infusion)	
BRIUMVI dose	450 mg
Total volume	250 mL
Infusion Rate	
0-30 min	100 mL/hr
30 min-hour 1	400 mL/hr
Total infusion time*	1 hour

SUBSEQUENT INFUSIONS (Once every 24 weeks. First subsequent infusion administered 24 weeks after the first infusion)	
BRIUMVI dose	450 mg
Total volume	250 mL
Infusion Rate	
0-30 min	100 mL/hr
30 min-hour 1	400 mL/hr
Total infusion time*	1 hour

- Premedicate with a **corticosteroid** and an **antihistamine** administered orally or intravenously approximately **30-60 minutes** prior to each infusion to reduce the frequency and severity of infusion reactions. The addition of an antipyretic may also be considered
- Observe the patients during infusion and for at least 1 hour after the first 2 infusions. Post-infusion monitoring of subsequent infusions is at physician discretion unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion

*Infusion duration may take longer if the infusion is interrupted or slowed.
PO, polyolefin; PVC, polyvinyl chloride.

This Infusion Rate Card is not a substitute for the full Prescribing Information.
Please see selected Important Safety Information and accompanying full Prescribing Information.

*Infusion duration may take longer if the infusion is interrupted or slowed.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Most Common Adverse Reactions: The most common adverse reactions in RMS trials (incidence of at least 10%) were infusion reactions and upper respiratory tract infections.

Infusion Reactions: BRIUMVI can cause infusion reactions, which can include pyrexia, chills, headache, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and an anaphylactic reaction. In MS clinical trials, the incidence of infusion reactions in BRIUMVI-treated patients who received infusion reaction-limiting premedication prior to each infusion was 48%, with the highest incidence within 24 hours of the first infusion. 0.6% of BRIUMVI-treated patients experienced infusion reactions that were serious, some requiring hospitalization.

In clinical trials, most common adverse reactions for BRIUMVI were infusion reactions[1,5]

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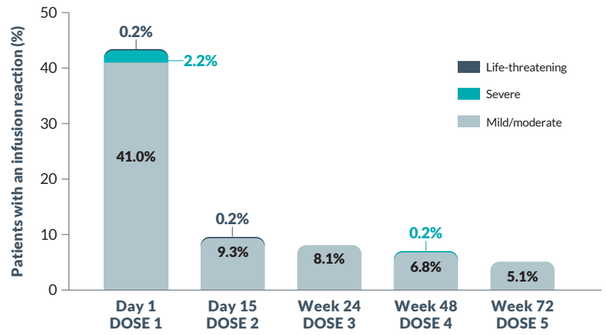
Infusion reactions were highest at the first dose and decreased with subsequent doses.[11] The incidence of infusion reactions was 43.4% for the first 4-hour infusion but decreased over time. **Infusion reactions were primarily mild to moderate in severity, and <10% of patients experienced infusion reactions after the day 1 infusion.**

- In the trials, oral acetaminophen (650 mg or equivalent) was only used as an intervention for subjects who experienced pyrexia after their day 1 dose, or as was clinically warranted at the discretion of the physician[5,11]
- 48% of patients in the clinical trials experienced an infusion reaction on BRIUMVI vs 12% on the comparator[1]

The infusion reaction rate decreased with each infusion[11]



Infusion reactions can occur in patients treated with BRIUMVI and may include:[1,8]

- Pyrexia (9.5%)
- Chills (7.9%)
- Headache (7.5%)
- Influenza-like illness (5.9%)
- Nausea (3.3%)
- Throat irritation (2.6%)
- Tachycardia (2.4%)
- Erythema (1.3%)
- Anaphylactic reaction (0.2%)

There were **no fatal infusion reactions**, and 0.6% of BRIUMVI-treated patients experienced infusion reactions that were serious, with some requiring hospitalization.[1]

1 hr

Observe patients treated with BRIUMVI for infusion reactions during infusion and for at least 1 hour after the completion of the first 2 infusions.[1]

Post-infusion monitoring of subsequent infusions is at physician discretion unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion.[1]

Inform patients that infusion reactions can occur for up to 24 hours after the infusion.

REMINDER:

Premedication (eg, methylprednisolone or an equivalent corticosteroid, and an antihistamine) may reduce the frequency and severity of infusion reactions.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Observe treated patients for infusion reactions during the infusion and for at least one hour after the completion of the first two infusions unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion.

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Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

Rate modifications due to infusion reactions[1]

Rate modifications in response to infusion reactions depend on the severity

MILD TO MODERATE

Reduce the infusion rate to half the rate at the onset of the infusion reaction and maintain the reduced rate for at least 30 minutes. If the reduced rate is tolerated, increase the rate as described in the Administration and Infusion Rate Table. This change in rate will increase the total duration of the infusion but not the total dose.

SEVERE

Immediately interrupt the infusion and administer appropriate supportive treatment, as necessary. Restart the infusion only after all symptoms have resolved.

When restarting, begin at **half of the infusion rate at the time of onset of the infusion reaction**. If this rate is tolerated, increase the rate as described in the Administration and Infusion Rate Table. This change in rate will increase the total duration of the infusion but not the total dose.

LIFE-THREATENING

Immediately stop infusion and permanently discontinue BRIUMVI if there are signs of a life-threatening or disabling infusion reaction. Provide appropriate supportive treatment.

In clinical trials, 97% of all infusions were delivered without interruption, and 95% of all BRIUMVI 1-hour infusions were completed in 1 hour +/- 5 minutes without interruption.[8]

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Inform patients that infusion reactions can occur up to 24 hours after the infusion. Administer the recommended pre-medication to reduce the frequency and severity of infusion reactions. If life-threatening, stop the infusion immediately, permanently discontinue BRIUMVI, and administer appropriate supportive treatment. Less severe infusion reactions may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

Infections: Serious, life-threatening or fatal, bacterial and viral infections have been reported in BRIUMVI-treated patients. In MS clinical trials, the overall rate of infections in BRIUMVI-treated patients was 56% compared to 54% in teriflunomide-treated patients. The rate of serious infections was 5% compared to 3% respectively. There were 3 infection-related deaths in BRIUMVI-treated patients. The most common infections in BRIUMVI-treated patients included upper respiratory tract infection (45%) and urinary tract infection (10%). Delay BRIUMVI administration in patients with an active infection until the infection is resolved.

Simplified scheduling may help the patient and staff experience

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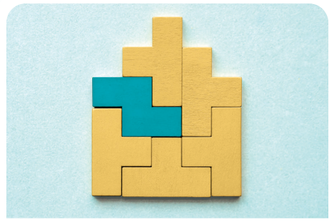
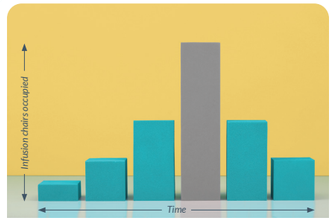


Shorter infusions may enable scheduling flexibility to help you solve the **scheduling puzzle**



Shorter infusions may allow for scheduling flexibility between appointments and during **non-peak hours**

Shorter infusions may allow patients to be seen faster and help to **reduce wait times**

This Dosing Guide is not a substitute for the full Prescribing Information.

Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

Important Safety Information

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INDICATION

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.

IMPORTANT SAFETY INFORMATION

Contraindications: BRIUMVI is contraindicated in patients with:

- Active HBV infection
- A history of life-threatening infusion reaction to BRIUMVI

WARNINGS AND PRECAUTIONS

Infusion Reactions: BRIUMVI can cause infusion reactions, which can include pyrexia, chills, headache, influenza-like illness, tachycardia, nausea, throat irritation, erythema, and an anaphylactic reaction. In MS clinical trials, the incidence of infusion reactions in BRIUMVI-treated patients who received infusion reaction-limiting premedication prior to each infusion was 48%, with the highest incidence within 24 hours of the first infusion. 0.6% of BRIUMVI-treated patients experienced infusion reactions that were serious, some requiring hospitalization.

Observe treated patients for infusion reactions during the infusion and for at least one hour after the completion of the first two infusions unless infusion reaction and/or hypersensitivity has been observed in association with the current or any prior infusion. Inform patients that infusion reactions can occur up to 24 hours after the infusion. Administer the recommended pre-medication to reduce the frequency and severity of infusion reactions. If life-threatening, stop the infusion immediately, permanently discontinue BRIUMVI, and administer appropriate supportive treatment. Less severe infusion reactions may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

Infections: Serious, life-threatening or fatal, bacterial and viral infections have been reported in BRIUMVI-treated patients. In MS clinical trials, the overall rate of infections in BRIUMVI-treated patients was 56% compared to 54% in teriflunomide-treated patients. The rate of serious infections was 5% compared to 3% respectively. There were 3 infection-related deaths in BRIUMVI-treated patients. The most common infections in BRIUMVI-treated patients included upper respiratory tract infection (45%) and urinary tract infection (10%). Delay BRIUMVI administration in patients with an active infection until the infection is resolved.

Consider the potential for increased immunosuppressive effects when initiating BRIUMVI after immunosuppressive therapy or initiating an immunosuppressive therapy after BRIUMVI.

Hepatitis B Virus (HBV) Reactivation: HBV reactivation occurred in an MS patient treated with BRIUMVI in clinical trials. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with BRIUMVI. Do not start treatment with BRIUMVI in patients with active HBV confirmed by positive results for HBsAg and anti-HB tests. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult a liver disease expert before starting and during treatment.

Progressive Multifocal Leukoencephalopathy (PML): Although no cases of PML have occurred in BRIUMVI-treated MS patients, JCV infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies.

If PML is suspected, withhold BRIUMVI and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

MRI findings may be apparent before clinical signs or symptoms; monitoring for signs consistent with PML may be useful. Further investigate suspicious findings to allow for an early diagnosis of PML, if present. Following discontinuation of another MS medication associated with PML, lower PML-related mortality and morbidity have been reported in patients who were initially asymptomatic at diagnosis compared to patients who had characteristic clinical signs and symptoms at diagnosis.

If PML is confirmed, treatment with BRIUMVI should be discontinued.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Vaccinations: Administer all immunizations according to immunization guidelines: for live or live-attenuated vaccines at least 4 weeks and, whenever possible at least 2 weeks prior to initiation of BRIUMVI for non-live vaccines. BRIUMVI may interfere with the effectiveness of non-live vaccines. The safety of immunization with live or live-attenuated vaccines during or following administration of BRIUMVI has not been studied. Vaccination with live virus vaccines is not recommended during treatment and until B-cell repletion.

Vaccination of Infants Born to Mothers Treated with BRIUMVI During Pregnancy: In infants of mothers exposed to BRIUMVI during pregnancy, assess B-cell counts prior to administration of live or live-attenuated vaccines as measured by CD19+ B-cells. Depletion of B-cells in these infants may increase the risks from live or live-attenuated vaccines. Inactivated or non-live vaccines may be administered prior to B-cell recovery. Assessment of vaccine immune responses, including consultation with a qualified specialist, should be considered to determine whether a protective immune response was mounted.

Fetal Risk: Based on data from animal studies, BRIUMVI may cause fetal harm when administered to a pregnant woman. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 B-cell depleting antibodies during pregnancy. A pregnancy test is recommended in females of reproductive potential prior to each infusion. Advise females of reproductive potential to use effective contraception during BRIUMVI treatment and for 6 months after the last dose.

Reduction in Immunoglobulins: As expected with any B-cell depleting therapy, decreased immunoglobulin levels were observed. Decrease in immunoglobulin M (IgM) was reported in 0.6% of BRIUMVI-treated patients compared to none of the patients treated with teriflunomide in RMS clinical trials. Monitor the levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections, and after discontinuation of therapy until B-cell repletion. Consider discontinuing BRIUMVI therapy if a patient with low immunoglobulins develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

Most Common Adverse Reactions: The most common adverse reactions in RMS trials (incidence of at least 10%) were infusion reactions and upper respiratory tract infections.

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Please see accompanying full Prescribing Information. For additional Important Safety Information, please see pages 18-19.

References: 1. BRIUMVI (ublituximab-xiiy) Prescribing information. TG Therapeutics, Inc.; 2022. **2.** Sun Y, Izadi S, Callahan M, et al. Antibody-receptor interactions mediate antibody-dependent cellular cytotoxicity. *J Biol Chem.* 2021;297(1):100826. **3.** de Romeuf C, Dutertre C-A, Le Garff-Tavernier M, et al. Chronic lymphocytic leukemia cells are efficiently killed by an anti-CD20 monoclonal antibody selected for improved engagement of FcāRIIIA/CD16. *Br J Haematol.* 2008;140(6):635-643. **4.** Fox E, Lovett-Racke AE, Gormley M, et al. A phase 2 multicenter study of ublituximab, a novel glycoengineered anti-CD20 monoclonal antibody, in patients with relapsing forms of multiple sclerosis. *Mult Scler.* 2021;27(3):420-429. **5.** Steinman L, Fox E, Hartung HP, et al. Ublituximab versus Teriflunomide in Relapsing Multiple Sclerosis. NEJM 2022;387(8):704–714. **6.** Whittam DH, Tallantyre EC, Jolles S, et al. Rituximab in neurological disease: principles, evidence and practice. *Pract Neurol.* 2019:19(1):5-20. **7.** Fox EJ, Steinman L, Hartung H-P, et al. Pharmacodynamics of B-cell depletion and pharmacokinetics of the novel anti-CD20 monoclonal antibody ublituximab in patients with relapsing multiple sclerosis. Poster presented at: 2022 Americas Committee for Treatment and Research in Multiple Sclerosis; February 24-26, 2022; West Palm Beach, FL. **8.** Fox E, Steinman L, Hartung HP, et al. Infusion related reactions (IRRs) with ublituximab in patients with relapsing multiple sclerosis (RMS): post hoc analyses from the phase 3 ULTIMATE I and II studies. Poster presented at: *2022 American Academy of Neurology (AAN) Annual Meeting.* April 2-7, 2022; Seattle, WA. **9.** KESIMPTA (ofatumumab)Prescribing information. Novartis Pharmaceuticals AG; 2022. **10.** OCREVUS (ocrelizumab) Prescribing information. Genentech, Inc.; 2022. **11.** Steinman L, Fox E, Hartung H-P, et al; for ULTIMATE I and ULTIMATE II Investigators. Ublituximab versus teriflunomide in relapsing multiple sclerosis. Supplementary appendix. *N Engl J Med.* 2022;387(8):704-714.

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