Package leaflet: Information for the patient

Briumvi 150 mg concentrate for solution for infusion
Ublituximab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Briumvi is and what it is used for

What Briumvi is

Briumvi contains the active substance ublituximab. It is a type of protein called a monoclonal antibody. Antibodies work by attaching to specific targets in your body.

What Briumvi is used for

Briumvi is used to treat adults with relapsing forms of multiple sclerosis (RMS), where the patient has flare-ups (relapses) followed by periods with milder or no symptoms.

What is Multiple Sclerosis

Multiple Sclerosis (MS) affects the central nervous system, especially the nerves in the brain and spinal cord. In MS, white blood cells called B cells that are part of the immune system (the body's defence system) work incorrectly and attack a protective layer (called myelin sheath) around nerve cells, causing inflammation and damage. Breakdown of the myelin sheath stops the nerves from working properly and causes symptoms of MS. Symptoms of MS depend on which part of the central nervous system is affected and can include problems with walking and balance, muscle weakness, numbness, double vision and blurring, poor coordination and bladder problems.

In relapsing forms of MS, the patient has repeated attacks of symptoms (relapses) that can appear suddenly within a few hours, or slowly over several days. The symptoms disappear or improve between relapses but damage may build up and lead to permanent disability.
How does Briumvi work?

Briumvi works by attaching to a target called CD20 on the surface of B cells. B cells are a type of white blood cell which are part of the immune system. In multiple sclerosis, the immune system attacks the protective layer around nerve cells. B cells are involved in this process. Briumvi targets and removes the B cells and thereby reduces the chance of a relapse, relieves symptoms and slows down the progression of the disease.

2. What you need to know before you are given Briumvi

You must not be given Briumvi:

- if you are **allergic** to ublituximab or any of the other ingredients of this medicine (listed in section 6),
- if you are suffering from a severe infection,
- if you have been told that you have severe problems with your immune system, or
- if you have cancer.

If you are not sure, talk to your doctor before you are given Briumvi.

Warnings and precautions

Talk to your doctor before you are given Briumvi if any of the following apply to you. Your doctor may decide to delay your treatment with Briumvi, or may decide you cannot receive Briumvi if:

- you have an **infection**. Your doctor will wait until the infection is resolved before giving you Briumvi.
- you have ever had **hepatitis B** or are a carrier of the hepatitis B virus. This is because medicines like Briumvi can cause the hepatitis B virus to become active again. Before your Briumvi treatment, your doctor will check if you are at risk of hepatitis B infection. Patients who have had hepatitis B or are carriers of the hepatitis B virus will have a blood test and will be monitored by a doctor for signs of hepatitis B infection.
- you have recently been given any vaccine or might be given a vaccine in the near future.
- you have **cancer** or if you have had cancer in the past. Your doctor may decide to delay your treatment.

Infusion-related reactions

- The most common side effect of Briumvi treatment are infusion-related reactions, types of allergic reactions that develop during or shortly after a medicine is given. These can be serious.
- Symptoms of an infusion-related reaction may include:
  - itchy skin
  - hives
  - redness of the face or skin
  - throat irritation
  - trouble breathing
  - swelling of tongue or throat
  - wheezing
  - chills
  - fever
  - headache
  - dizziness
  - feeling faint
  - nausea
  - abdominal (belly) pain
  - rapid heartbeat.

- **Tell your doctor or nurse straight away if you have or think you may have any infusion-related reaction**. Infusion-related reactions can happen during the infusion or up to 24 hours after the infusion.
- To reduce the risk of infusion-related reaction, your doctor will give you other medicines before each infusion of Briumvi (see section 3) and you will be closely monitored during the infusion.
- If you get an infusion reaction, your doctor may need to stop or slow down the rate of infusion.

Infections

- Talk to your doctor before you are given Briumvi if you have or think you have an infection. Your doctor will wait until the infection is resolved before giving you Briumvi.
- You might get infections more easily with Briumvi. This is because the immune cells that Briumvi targets also help to fight infection.
- **Tell your doctor or nurse straight away if you have an infection or any of the following signs of infection during or after Briumvi treatment:**
  - fever or chills
  - cough that does not go away
  - herpes (such as cold sore, shingles or genital sores)
- **Tell your doctor or nurse straight away if you think your MS is getting worse or if you notice any new symptoms.** This is because of a very rare and life-threatening brain infection, called 'progressive multifocal leukoencephalopathy' (PML), which can cause symptoms similar to those of MS. PML can occur in patients taking medicines like Briumvi, and other medicines used for treating MS.
- **Tell your partner or carer** about your Briumvi treatment. They might notice symptoms of PML that you do not, such as memory lapses, trouble thinking, difficulty walking, sight loss, changes in the way you talk, which your doctor may need to investigate.

Vaccinations

- Tell your doctor if you have recently been given any vaccine or might be given a vaccine in the near future.
- Your doctor will check if you need any vaccinations before you start your treatment with Briumvi. You should receive a type of vaccine called a live or live attenuated vaccines at least 4 weeks before you start treatment with Briumvi. While you are being treated with Briumvi, you should not be given live or live attenuated vaccines until your doctor tells you that your immune system is no longer weakened.
- When possible, you should receive other types of vaccine called inactivated vaccines at least 2 weeks before you start treatment with Briumvi. If you would like to receive any inactivated vaccines while you are being treated with Briumvi, talk to your doctor.

Children and adolescents

Briumvi is not intended to be used in children and adolescents under 18 years old. This is because it has not yet been studied in this age group.

Other medicines and Briumvi

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. In particular tell your doctor:

- if you are taking, have recently taken or might take medicines that affect your immune system, such as chemotherapy, immunosuppressants (except corticosteroids) or other medicines used to treat MS. This is because these may have an added effect on the immune system.
- if you plan to have any vaccinations (see "Warnings and Precautions" above).

If any of the above apply to you (or you are not sure), talk to your doctor before you are given Briumvi.

Pregnancy and breast-feeding

- Tell your doctor before being given Briumvi if you are pregnant, think that you might be pregnant or are planning to have a baby. This is because Briumvi may cross the placenta and affect your baby.
- Do not use Briumvi if you are pregnant unless you have discussed this with your doctor. Your doctor will consider the benefit of you taking Briumvi against the risk to your baby.
- If you have a baby and you received Briumvi during your pregnancy, it is important to tell your baby's doctor about receiving Briumvi so they can recommend when your baby should get vaccinated.
- It is not known whether Briumvi passes into your breast milk. Talk to your doctor about the best way to feed your baby if you take Briumvi.

Contraception for women

If you are able to become pregnant (conceive), you must use contraception:
- during treatment with Briumvi and
- for at least 4 months after your last infusion of Briumvi.

Driving and using machines

Briumvi is unlikely to affect your ability to drive and use machines.

Briumvi contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free.'

3. How Briumvi is given

Briumvi will be given to you by a doctor or nurse who is experienced in the use of this treatment. They will watch you closely while you are being given this medicine. This is in case you get any side effects. You will always be given Briumvi as a drip (intravenous infusion).

Medicines you will have before you are given Briumvi

Before you are given Briumvi, you will receive other medicines to prevent or reduce possible side effects such as infusion-related reactions (see sections 2 and 4 for information about infusion-related reactions).

You will receive a corticosteroid and an antihistamine before each infusion and you may also receive other medicines to reduce fever.

How much and how often you will be given Briumvi

- The first dose of Briumvi will be 150 mg. This infusion will last 4 hours.
- The second dose of Briumvi will be 450 mg given 2 weeks after the first dose. This infusion will last 1 hour.
- Subsequent dosing of Briumvi will be 450 mg given 24 weeks after the first dose and every 24 weeks thereafter. These infusions will last 1 hour.

How Briumvi is given

- Briumvi will be given to you by a doctor or a nurse. Briumvi must be diluted before it is given to you. Dilution will be done by a healthcare professional. It will be given as an infusion into a vein (intravenous infusion).
- You will be closely monitored while you are being given Briumvi and for at least 1 hour after the first two infusions have been given. This is in case you have any side effects such as infusion-related reactions. The infusion may be slowed, temporarily stopped, or permanently stopped if you have an infusion-related reaction, depending on how serious it is (see sections 2 and 4 for information about infusion-related reactions).

If you miss an infusion of Briumvi

- If you miss an infusion of Briumvi, talk to your doctor to arrange to have it as soon as possible. Do not wait until your next planned infusion.
- To get the full benefit of Briumvi, it is important that you receive each infusion when it is due.

If you stop Briumvi treatment

- It is important to continue your treatment for as long as you and your doctor decide that it is helping you.
- Some side effects can be related to having low levels of B cells. After you stop Briumvi treatment, you may still experience such side effects until your B cells return to normal levels.
- Before your start any other medicines, tell your doctor when you had your last Briumvi infusion.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been reported with Briumvi:

Serious side effects

Infusion-related reactions

- Infusion-related reactions are the most common side effect of Briumvi treatment (very common: may affect more than 1 in 10 people). In most cases these are mild reactions, but some serious reactions can happen.
- **Tell your doctor or nurse straight away if you experience any signs or symptoms of an infusion-related reaction during the infusion or up to 24 hours after the infusion.**
  Symptoms can include, but are not limited to:
  - itchy skin
  - hives
  - redness of the face or skin
  - throat irritation
  - trouble breathing
  - swelling of tongue or throat
  - wheezing
  - chills
  - fever
  - headache
  - dizziness
  - feeling faint
  - nausea
  - abdominal (belly) pain

- rapid heartbeat.

- If you have an infusion-related reaction, you will be given medicines to treat it and the infusion may need to be slowed down or stopped. When the reaction has stopped, the infusion may be continued. If the infusion-related reaction is life-threatening, your doctor will permanently stop your treatment with Briumvi.

Infections

- You might get infections more easily with Briumvi. Some of them might be serious. The following infections have been seen in patients treated with Briumvi in MS:
  - **Very common** (may affect more than 1 in 10 people)
    - upper respiratory tract infections (nose and throat infections)
    - respiratory tract infections (infection of the airways)
  - **Common** (may affect up to 1 in 10 people)
    - lower respiratory tract infections (infection of the lungs such as bronchitis or pneumonia)
    - herpes infections (cold sore or shingles)

- Tell your doctor or nurse straight away if you notice any of these signs of infection:
  - fever or chills
  - cough which does not go away
  - herpes (such as cold sore, shingles or genital sores)

  Your doctor will wait until the infection is resolved before giving you Briumvi.

Other side effects

Common (may affect up to 1 in 10 people)
- neutropenia (low levels of neutrophils, a type of white blood cell)
- pain in extremity (arms or legs)

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the **Google Play** or **Apple App Store**. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Briumvi

Store in a refrigerator (2°C – 8°C).

Briumvi will be stored by the healthcare professionals at the hospital or clinic under the following conditions:
- This medicine is not to be used after the expiry date which is stated on the outer carton and the vial label after 'EXP'. The expiry date refers to the last day of that month.
- This medicine is to be stored in a refrigerator (2-8 °C). It is not to be frozen. The vial is to be kept in the outer carton in order to protect from light.

It is recommended that the product is used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the healthcare professional and would normally not be longer than 24 hours at 2-8 °C and subsequently 8 hours at room temperature.

Do not throw away any medicines via wastewater. These measures will help to protect the environment.

6. Contents of the pack and other information

What Briumvi contains

- The active substance is ublituximab. Each vial contains 150 mg of ublituximab in 6 mL at a concentration of 25 mg/mL.
- The other ingredients are sodium chloride, trisodium citrate dihydrate, polysorbate 80, hydrochloric acid and water for injections.

What Briumvi looks like and contents of the pack

- Briumvi is a clear to opalescent, and colourless to slightly yellow solution.
- It is supplied as a concentrate for solution for infusion.
- This medicine is available in packs containing 1 vial (glass vial of 6 mL concentrate).

Marketing Authorisation Holder

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Manufacturer

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The following information is intended for healthcare professionals only:

Read the SmPC for additional information.

<u>Posology</u>

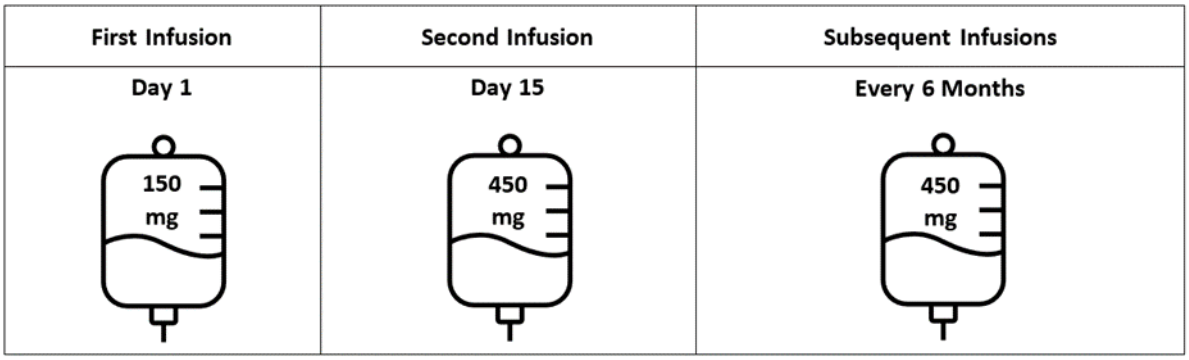
- <u>First and second doses</u>

The first dose is administered as a 150 mg intravenous infusion (first infusion), followed by a 450 mg intravenous infusion 2 weeks later (second infusion).

- <u>Subsequent doses</u>

Subsequent doses of Briumvi are administered as a single 450 mg intravenous infusion every 24 weeks (Table 1). The first subsequent dose of 450 mg should be administered 24 weeks after the First Infusion. A minimum interval of 5 months should be maintained between each dose of Briumvi.

Figure 1: Dose and Schedule of Briumvi



Management of IRRs before the infusion

- Briumvi treatment should be initiated and supervised by an experienced healthcare professional with access to appropriate medical support to manage severe reactions such as serious infusion-related reactions (IRRs).

- Premedication for IRRs

  The following two premedications must be administered prior to each Briumvi infusion to reduce the frequency and severity of IRRs:
  - 100 mg methylprednisolone or 10-20 mg dexamethasone (or an equivalent) approximately 30-60 minutes prior to each Briumvi infusion;
  - diphenhydramine approximately 30-60 minutes prior to each Briumvi infusion;

  In addition, premedication with an antipyretic (e.g. paracetamol) may also be considered.

Instructions for dilution

- Briumvi should be prepared by a healthcare professional using aseptic technique. Do not shake the vial.
- The product is intended for single use only.
- Do not use the solution if discoloured or if the solution contains foreign particulate matter.
- Briumvi medicinal product must be diluted before administration. Solutions of Briumvi for intravenous administration are prepared by dilution of the product into an infusion bag containing isotonic 0.9% sodium chloride. For the first infusion, dilute one vial of product into the infusion bag (150 mg/250 mL) to a final concentration of approximately 0.6 mg/mL. For subsequent infusions, dilute three vials of product into the infusion bag (450 mg/250 mL) to a final concentration of approximately 1.8 mg/mL.
- Prior to the start of the intravenous infusion, the content of the infusion bag should be at room temperature.

Method of administration

- After dilution, Briumvi is administered as an intravenous infusion through a dedicated line.
- Briumvi infusions should not be administered as an intravenous push or bolus.

Table 1: Dose and Schedule of Briumvi

	Amount and Volume	Infusion Rate	Duration
First Infusion	150 mg in 250 mL	• Start at 10 mL per hour for the first 30 minutes • Increase to 20 mL per hour for the next 30 minutes • Increase to 35 mL per hour for the next hour • Increase to 100 mL per hour for the remaining 2 hours	4 hours
Second Infusion (2 weeks later)	450 mg in 250 mL	• Start at 100 mL per hour for the first 30 minutes • Increase to 400 mL per hour for the remaining 30 minutes	1 hour
Subsequent Infusions (once every 24 weeks)[2]	450 mg in 250 mL	• Start at 100 mL per hour for the first 30 minutes • Increase to 400 mL per hour for the remaining 30 minutes	1 hour

[1]Infusion duration may take longer if the infusion is interrupted or slowed.
[2]The first subsequent infusion should be administered 24 weeks after the first infusion.

Management of IRRs during and after the infusion

Patients should be monitored during the infusion and for at least one hour after the completion of the first two infusions.

During the infusion

- Infusion Adjustments in case of IRRs

  In case of IRRs during any infusion, see the following adjustments.

Life-threatening IRRs

If there are signs of a life threatening or disabling IRR during an infusion, the infusion must be stopped immediately and the patient should receive appropriate treatment. Briumvi must be permanently discontinued in these patients (see section 4.3).

Severe IRRs

If a patient experiences a severe IRR, the infusion should be interrupted immediately and the patient should receive symptomatic treatment. The infusion should be restarted only after all symptoms have resolved. When restarting, begin at half of the infusion rate at the time of onset of the IRR. If the rate is tolerated, increase the rate as described in Table 1.

Mild to Moderate IRRs

If a patient experiences a mild to moderate IRR, the infusion rate should be reduced to half the rate at the onset of the event. This reduced rate should be maintained for at least 30 minutes. If the reduced rate is tolerated, the infusion rate may then be increased as described in Table 1.

After the infusion

- Patients treated with Briumvi should be observed for at least one hour after the completion of the first two infusions for any symptom of an IRR.

- Physicians should alert patients that an IRR can occur within 24 hours of infusion.

Shelf life

Unopened vial

3 years

Diluted solution for intravenous infusion

- Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C – 8 °C and subsequently for 8 hours at room temperature.
- From a microbiological point of view, the prepared infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8 °C and subsequently for 8 hours at room temperature, unless dilution has taken place in controlled and validated aseptic conditions.
- In the event an intravenous infusion cannot be completed the same day, the remaining solution should be discarded.