**Package leaflet: Information for the patient**

**Ocrevus 300 mg concentrate for solution for infusion**
ocrelizumab

**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 Ocrevus is and what it is used for

**What Ocrevus is**

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

**What Ocrevus is used for**

Ocrevus is used to treat adults with:
- Relapsing forms of multiple sclerosis (RMS)
- Early primary progressive multiple sclerosis (PPMS)

**What is Multiple Sclerosis**

Multiple Sclerosis (MS) affects the central nervous system, especially the nerves in the brain and spinal cord. In MS, the immune system (the body's defence system) works incorrectly and attacks a protective layer (called myelin sheath) around nerve cells and causes inflammation. Breakdown of the myelin sheath stops the nerves working properly.

Symptoms of MS depend on which part of the central nervous system is affected and can include problems with walking and balance, weakness, numbness, double vision and blurring, poor coordination and bladder problems.

- **In relapsing forms of MS,** the patient has repeated attacks of symptoms (relapses). The symptoms 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.

- **In primary progressive MS,** the symptoms generally continue to worsen from the start of the disease.

**How does Ocrevus work?**

Ocrevus attaches to specific B cells, which are a type of white blood cells that are part of the immune system and play a role in MS. Ocrevus targets and removes those specific B cells. This reduces inflammation and attacks on the myelin sheath, reduces the chance of having a relapse and slows the progression of your disease.

- **In Relapsing forms of MS (RMS)**, Ocrevus helps to significantly reduce the number of attacks (relapses) and significantly slow down the progression of the disease. Ocrevus also significantly increases the chance of a patient having no evidence of disease activity (brain lesions, relapses and worsening of disability).

- **In Primary Progressive MS (PPMS)**, Ocrevus helps to slow down the progression of the disease and reduce deterioration in walking speed.

## 2. What you need to know before you are given Ocrevus

**You must not be given Ocrevus:**

- if you are allergic to ocrelizumab or any of the other ingredients of this medicine (listed in section 6).
- if you currently have an infection.
- if you have been told that you have severe problems with your immune system.
- if you have cancer.

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

**Warnings and precautions**

**Talk to your doctor before you are given Ocrevus** if any of the following apply to you. Your doctor may decide to delay your treatment with Ocrevus, or may decide you cannot receive Ocrevus if:
- you have an **infection**. Your doctor will wait until the infection is resolved before giving you Ocrevus.
- you have ever had **hepatitis B** or are a carrier of the hepatitis B virus. This is because medicines like Ocrevus can cause the hepatitis B virus to become active again. Before your Ocrevus 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 **cancer** or if you have had cancer in the past. Your doctor may decide to delay your treatment with Ocrevus.

**Effect on the immune system:**

- **Diseases that affect your immune system**: if you have another disease which affects the immune system. You may not be able to receive Ocrevus.
- **Medicines that affect your immune system**: if you have ever taken, are taking or are planning to take medicines that affect the immune system – such as chemotherapy, immunosuppressants or other medicines used to treat MS. Your doctor may decide to delay your treatment with Ocrevus or may ask you to stop such medicines before starting treatment with Ocrevus. See under ‘Other medicines and Ocrevus’, below for more information.

***Infusion-related reactions***

- Infusion-related reactions are the most common side effect of Ocrevus treatment.
- **Tell your doctor or nurse straight away if you have any infusion-related reaction** (see section 4 for a list of infusion-related reactions). 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 Ocrevus (see section 3) and you will be closely monitored during the infusion and for at least one hour after the infusion has been given.

***Infections***

- Talk to your doctor before you are given Ocrevus if you think you have an infection. Your doctor will wait until the infection is resolved before giving you Ocrevus.
- You might get infections more easily with Ocrevus. This is because the immune cells that Ocrevus targets also help to fight infection.
- Before you start treatment with Ocrevus and before subsequent infusions, your doctor may ask you to have a blood test to verify your immune system because infections may occur more frequently in case of severe problems with your immune system.
- If you are treated with Ocrevus for primary progressive multiple sclerosis, and you have swallowing difficulties, Ocrevus may increase the risk of severe pneumonia.
- **Tell your doctor or nurse straight away if you have any of these signs of infection during or after Ocrevus 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 Ocrevus.
  **Tell your partner or carer** about your Ocrevus 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.
- While you are being treated with Ocrevus, you should not be given live or live attenuated vaccines (for example BCG for tuberculosis or vaccines against yellow fever).
- Your doctor may recommend that you are given a seasonal influenza vaccine.
- Your doctor will check if you need any vaccinations before you start treatment with Ocrevus. Any vaccinations should be given at least 6 weeks before you start treatment with Ocrevus.

**Children and adolescents**

Ocrevus 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 Ocrevus**

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

- you have ever taken, are taking or are planning to take **medicines that affect the immune system** – such as chemotherapy, immunosuppressants or other medicines used to treat MS. The effect on the immune system of these medicines with Ocrevus could be too strong. Your doctor may decide to delay your treatment with Ocrevus or may ask you to stop such medicines before starting treatment with Ocrevus.
- you are taking **medicines for high blood pressure**. This is because Ocrevus may lower blood pressure. Your doctor may ask you to stop taking your blood pressure medicines for 12 hours before each Ocrevus infusion.

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

**Pregnancy**

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. This is because Ocrevus may cross the placenta and affect your baby.
- Do not use Ocrevus if you are pregnant unless you have discussed this with your doctor. Your doctor will consider the benefit of you taking Ocrevus against the risk to your baby.
- Talk to your doctor before vaccinating your baby.

**Contraception for women**

Women who could become pregnant must use contraception:

- during treatment with Ocrevus and
- for 12 months after your last infusion of Ocrevus.

**Breast-feeding**

Do not breast-feed while you are being treated with Ocrevus. This is because Ocrevus may pass into breast milk.

**Driving and using machines**

It is not known whether Ocrevus can affect your ability to drive or use tools or machines.
Your doctor will tell you whether your MS may affect your ability to drive or use tools and machines safely.

**Ocrevus contains sodium**

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

## 3. How Ocrevus is given

Ocrevus 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 Ocrevus as a drip (intravenous infusion).

**Medicines you will have before you are given Ocrevus**

Before you are given Ocrevus, 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 anti-histamine before each infusion and you may also receive medicines to reduce fever.

**How much and how often you will be given Ocrevus**

You will be given a total dose of 600 mg of Ocrevus every 6 months.
- The first 600 mg dose of Ocrevus will be given as 2 separate infusions (300 mg each), given 2 weeks apart. Each infusion will last about 2 hours 30 minutes.
- The next 600 mg doses of Ocrevus will be given as a single infusion. Depending on the rate of the subsequent infusion, each infusion will either last about 3 hours 30 minutes or 2 hours.

**How Ocrevus is given**

- Ocrevus will be given to you by a doctor or a nurse. It will be given as an infusion into a vein (intravenous infusion or IV infusion).
- You will be closely monitored while you are being given Ocrevus and for at least 1 hour after the infusion has 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 Ocrevus**

- If you miss an infusion of Ocrevus, 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 Ocrevus, it is important that you receive each infusion when it is due.

**If you stop Ocrevus 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 B cells. After you stop Ocrevus treatment, you may still experience side effects until your B-cells return to normal. Your blood B-cells will gradually increase to normal levels. This can take from six months to two and a half years, or up to several years in rare cases.
- Before you start any other medicines, tell your doctor when you had your last Ocrevus 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 Ocrevus:

**Serious side effects:**

**Infusion-related reactions**

- Infusion-related reactions are the most common side effect of Ocrevus 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
  - rash
  - hives
  - redness of the skin
  - throat irritation or pain
  - shortness of breath
  - swelling of the throat
  - flushing
  - low blood pressure
  - fever
  - feeling tired
  - headache
  - feeling dizzy
  - feeling sick (nausea)
  - fast heart beat.
- 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 Ocrevus.

**Infections**

- You might get infections more easily with Ocrevus. The following infections have been seen in patients treated with Ocrevus in MS:
  - **Very common** (may affect more than 1 in 10 people)
    - sore throat and runny nose (upper respiratory tract infection)
    - flu
  - **Common** (may affect up to 1 in 10 people)
    - sinus infection
    - bronchitis (bronchial tube inflammation)
    - herpes infection (cold sore or shingles)
    - infection of the stomach and bowel (gastroenteritis)
    - respiratory tract infection
    - viral infection
    - skin infection (cellulitis)

  Some of them might be serious.

- **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 and genital sores)

**Other side effects:**

**Very common** (may affect more than 1 in 10 people)

- decrease in specific proteins in the blood (immunoglobulins) which help protect against infection

**Common** (may affect up to 1 in 10 people)
- discharge from the eye with itching, redness and swelling (conjunctivitis)
- cough
- a build-up of thick mucus in the nose, throat or chest
- low levels of a type of white blood cell (neutropenia)

**Not known** (it is not known how often these side effects happen)
- a reduction in white blood cells which can be delayed

**Reporting of side effects**

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

**United Kingdom**
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

## 5. How to store Ocrevus

Ocrevus will be stored by the healthcare professionals at the hospital or clinic under the following conditions:
- This medicine is to be kept out of the sight and reach of children.
- 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 (2ºC - 8ºC). It is not to be frozen. The vials are to be kept in the outer carton to protect them from light.

Ocrevus must be diluted before it is given to you. Dilution will be done by a healthcare professional. 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°C - 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 Ocrevus contains**

- The active substance is ocrelizumab. Each vial contains 300 mg of ocrelizumab in 10 mL at a concentration of 30mg/mL.
- The other ingredients are sodium acetate trihydrate (see Section 2 'Ocrevus contains sodium'), glacial acetic acid, trehalose dihydrate, polysorbate 20 and water for injections.

**What Ocrevus looks like and contents of the pack**

- Ocrevus is a clear to slightly opalescent, and colourless to pale brown solution.
- It is supplied as a concentrate for solution for infusion.

- This medicine is available in packs containing 1 or 2 vials (vials of 10 mL concentrate). Not all pack sizes may be marketed.

**Marketing Authorisation Holder and Manufacturer**

Roche Products Limited
6 Falcon Way, Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**United Kingdom**
Roche Products Ltd.
Tel: +44 (0) 1707 366000

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**The following information is intended for healthcare professionals only:**

Read the SmPC for additional information.

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

**Posology**

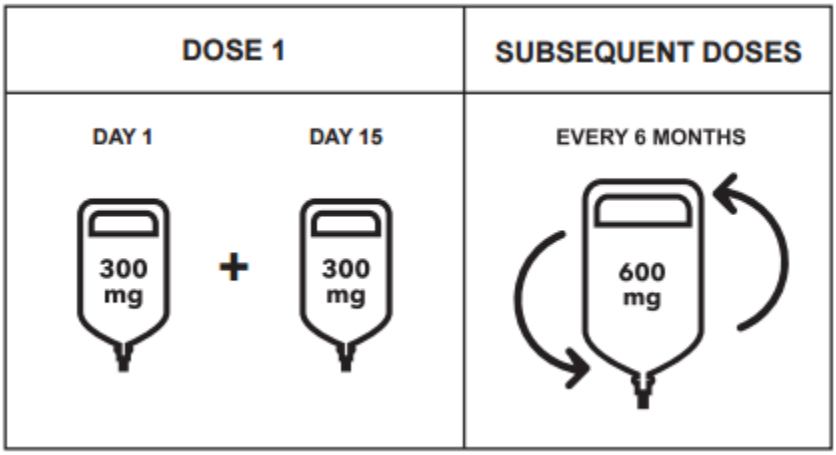
- Initial dose

The initial 600 mg dose is administered as two separate intravenous infusions; first as a 300 mg infusion, followed 2 weeks later by a second 300 mg infusion.

- Subsequent doses

Subsequent doses of ocrelizumab thereafter are administered as a single 600 mg intravenous infusion every 6 months (see Table 1). The first subsequent dose of 600 mg should be administered six months after the first infusion of the initial dose. A minimum interval of 5 months should be maintained between each dose of ocrelizumab.

**Figure 1: Dose and Schedule of Ocrevus**




**Management of IRRs before the infusion**

- 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), hypersensitivity reactions and/or anaphylactic reactions.

- Premedication for IRRs

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

  In addition, premedication with an antipyretic (e.g., paracetamol) may also be considered approximately 30-60 minutes prior to each infusion.

- Hypotension, as a symptom of IRR, may occur during infusions. Therefore, withholding of antihypertensive treatments should be considered for 12 hours prior to and throughout each

Ocrevus infusion. Patients with a history of congestive heart failure (New York Heart Association III & IV) were not studied.

**Instructions for dilution**

- The product should be prepared by a healthcare professional using aseptic technique. Do not shake the vial. A sterile needle and syringe should be used to prepare the diluted infusion solution.
- The product is intended for single use only.
- Concentrate may contain fine translucent and/or reflective particles associated with enhanced opalescence. Do not use the concentrate if discoloured or if the concentrate contains foreign particulate matter.
- Medicinal product must be diluted before administration. Solutions for intravenous administration are prepared by dilution of the concentrate into an infusion bag containing isotonic sodium chloride 9 mg/mL (0.9%) solution for injection (300mg/250mL or 600mg/500mL), to a final ocrelizumab concentration of approximately 1.2 mg/mL.
- The diluted infusion solution must be administered using an infusion set with a 0.2 or 0.22 micron in-line filter.
- Prior to the start of the intravenous infusion, the content of the infusion bag should be at room temperature to avoid an infusion reaction due to the administration of the solution at low temperatures.

**Method of administration**

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

**Table 1: Dose and schedule**

<table>
<tr><th colspan="2"></th><th>Amount of ocrelizumab to be administered</th><th>Infusion instruction</th></tr>
<tr><td rowspan="2">Initial dose (600 mg)<br>divided into 2 infusions</td><td>Infusion 1</td><td>300 mg in 250 mL</td><td rowspan="2">• Initiate the infusion at a rate of 30 mL/hour for 30 minutes<br>• The rate can be increased in 30 mL/hour increments every 30 minutes to a maximum of 180 mL/hour.<br>• Each infusion should be given over approximately 2.5 hours.</td></tr>
<tr><td>Infusion 2<br>(2 weeks later)</td><td>300 mg in 250 mL</td></tr>
<tr><td rowspan="4">Subsequent doses (600 mg)<br>single infusion once every 6 months</td><td>Option 1<br><br>Infusion of approx. 3.5 hours duration</td><td>600 mg in 500 mL</td><td>• Initiate the infusion at a rate of 40 mL/hour for 30 minutes<br>• The rate can be increased in 40 mL/hour increments every 30 minutes to a maximum of 200 mL/hour<br>• Each infusion should be given over approximately 3.5 hours.</td></tr>
<tr><td colspan="3">OR</td></tr>
<tr><td>Option 2<br><br>Infusion of approx. 2 hours duration</td><td>600 mg in 500 mL</td><td>• Initiate the infusion at a rate of 100 mL/hour for the first 15 minutes<br>• Increase the infusion rate to 200 mL/hour for the next 15 minutes<br>• Increase the infusion rate to 250 mL/hour for the next 30 minutes<br>• Increase the infusion rate to 300 mL/hour for the remaining 60 minutes<br>• Each infusion should be given over approximately 2 hours.</td></tr>
</table>

**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 infusion.

**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, such as acute hypersensitivity or acute respiratory distress syndrome the infusion must be stopped immediately and the patient should receive appropriate treatment. The infusion must be permanently discontinued in these patients (see section 4.3).

*Severe IRRs*

If a patient experiences a severe IRR (such as dyspnea) or a complex of flushing, fever, and throat pain symptoms, the infusion should be interrupted immediately and the patient should receive symptomatic treatment. The infusion should be restarted only after all symptoms have resolved. The initial infusion rate at restart should be half of the infusion rate at the time of onset of the reaction. No infusion adjustment is necessary for subsequent new infusions, unless the patient experiences an IRR.

*Mild to moderate IRRs*

If a patient experiences a mild to moderate IRR (e.g., headache), 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 tolerated, the infusion rate may then be increased according to the patient's initial infusion rate. No infusion adjustment is necessary for subsequent new infusions, unless the patient experiences an IRR.

- Patients who experience severe pulmonary symptoms, such as bronchospasm or asthma exacerbation, must have their infusion interrupted immediately and permanently. After administering symptomatic treatment, monitor the patient until the pulmonary symptoms have resolved because initial improvement of clinical symptoms could be followed by deterioration.

- Hypersensitivity may be difficult to distinguish from an IRR in terms of symptoms. If a hypersensitivity reaction is suspected during infusion, the infusion must be stopped immediately and permanently.

**After the infusion**

- Patients should be observed for at least one hour after the completion of the infusion for any symptom of an IRR.
- Physicians should alert patients that an IRR can occur within 24 hours of infusion.

**Shelf life**

Unopened vial

2 years

Diluted solution for intravenous infusion

- Chemical and physical in-use stability has been demonstrated for 24 hours at 2-8°C and subsequently 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 8 hours at room temperature, unless dilution undertaken in controlled and validated aseptic conditions.
- In the event an intravenous infusion cannot be completed the same day, the remaining solution should be discarded.