OCREVUS® (ocrelizumab) Subcutaneous injection – Dosing & Administration Guide

This guide presents instructions for healthcare professionals on how to handle, prepare and administer the OCREVUS® Subcutaneous injection

Roche

OCREVUS®
ocrelizumab
Subcutaneous injection

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1. About OCREVUS® Subcutaneous injection[1]

Indications:

OCREVUS® Subcutaneous injection is indicated for the treatment of adult patients with:

- Relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features
- Early primary progressive multiple sclerosis (PPMS) in terms of disease duration and level of disability, and with imaging features characteristic of inflammatory activity
- Refer to the OCREVUS® SmPC and your local guidelines for any additional indications

Formulation:

OCREVUS® Subcutaneous formulation:

- Is provided as a 23 mL solution
- Is contained in a 50 mL glass vial as a sterile, single-dose liquid with a concentration of 40 mg/mL
- Is co-formulated with the rHuPH20 enzyme at a concentration of 1000 U/mL
- Is a ready-to-use solution, and should ***NOT*** be diluted or mixed with other medicinal products
- Is normally a colourless to yellowish solution

About rHuPH20 enzyme[2,3]

- The subcutaneous layer contains a matrix of hyaluronan fibres and collagen fibres, which limit the subcutaneous administration of volumes to <1–2 mL
- The addition of rHuPH20 enzyme temporarily and locally breaks down hyaluronan at the injection site, with no changes in the structure-providing macromolecules, collagen and elastin
- The breakdown of hyaluronan, over time, results in a temporary increase in the local subcutaneous dispersion area, allowing large volumes of fluids to be administered
- After the injection administration, the structure of the skin is re-formed within 1–2 days, due to rapid clearance of rHuPH20, and a fast rate of hyaluronan turnover

2. Dosing of OCREVUS® Subcutaneous injection[1]

Dosing: A single subcutaneous injection into the abdomen, **once every 6 months**

NOTE: Unlike OCREVUS® IV, the initial dose of the Subcutaneous formulation is ***NOT*** administered in two separate injections.

DAY 1

Initial dose: One single subcutaneous injection of 920 mg (23 mL)

Injection time: Administration of the injection itself takes around 10 minutes, and should be done under clinical observation with appropriate instruments

NOTE: See timing for all OCREVUS® administration stages at the end of this page

EVERY 6 MONTHS

Subsequent doses are given as a single injection of 920 mg (23 mL) every 6 months

NOTE: A minimum interval of 5 months should be maintained between each dose of OCREVUS®

PRE-INJECTION MEDICATION

Pre-medication is given orally shortly before each administration. This will include:

- 20 mg oral dexamethasone (or equivalent)
- Oral antihistamine (desloratadine or equivalent)
- Pre-medication with antipyretic (e.g. paracetamol) may also be considered shortly before each administration

Total administration time

Administration time for OCREVUS® Subcutaneous injection takes approximately 10 minutes. **Please factor in enough time for check-In and pre-medication administration.**

OCREVUS® SC: Administration stages & times

Injection time:	approx 10 minutes
Post-injection monitoring time*:	1 hr

*For the initial dose, post-injection monitoring for at least one hour after injection is recommended. For subsequent doses, the need for post injection monitoring is at the treating physician's discretion

3. Equipment needed for administration[1,4]

- OCREVUS® Subcutaneous injection is ready to use, and should ***NOT*** be diluted or mixed with other medical products
- OCREVUS® Subcutaneous injection can be administered manually ***OR*** with the use of a syringe pump
- Please ensure you are familiar with the different equipment needed for each method

Equipment needed for each administration method

Syringe pump-assisted administration	Manual administration
• OCREVUS® Subcutaneous injection vial	• OCREVUS® Subcutaneous injection vial
• Transfer needle (21 G recommended)	• Transfer needle (21 G recommended)
• Syringe (Please ensure that the syringe is compatible with the syringe pump)*	• Syringe
• SC infusion set (e.g. winged/butterfly) containing a 24-26 G needle for injection. • **The residual hold-up volume must NOT exceed 0.8 mL**	• SC infusion set (e.g. winged/butterfly) containing a 24-26 G needle for injection. • **The residual hold-up volume must NOT exceed 0.8 mL**
• Syringe pump (any with occlusion limit >6 psi, compatible with the chosen syringe, and a flow rate capability of 1-5 mL/min)	
• 2 Antiseptic pads • Cotton ball / gauze pad • Plaster / band-aid • Gloves	• 2 Antiseptic pads • Cotton ball / gauze pad • Plaster / band-aid • Gloves

***Depending on the syringe pump, please check that the syringe is compatible with the chosen pump and can be selected in the settings of the pump. Syringe pumps might not supporta flow rate of 180 mL/hr for syringes smaller than 50 mL and a lower flow rate and extended administration time might be the consequence**

4. Storage and preparation of the syringe[1,4]

A

Bring the vial to room temperature:

- Store the OCREVUS® vial solution in a refrigerator at 2-8°C (36-46°F)*
- To prepare the injection syringe, remove the vial from the refrigerator
- Wait for the solution to warm to room temperature (<=25°C/77°F) before filling the syringe
- Visually check the solution to see there is no particulate matter or discolouration prior to administration

*** If necessary, the unopened vial may be stored outside the refrigerator at room temperature (<= 25°C/77°F) for up to 12 hours**

B

Prepare the syringe:

- Attach the transfer needle to the syringe

C

Withdraw the solution from the vial:

- Withdraw the entire contents of OCREVUS® Subcutaneous solution from the vial
- This includes the target volume (23 mL) plus priming volume

D

Attach and prime the SC infusion set:

- Remove the transfer needle and attach the SC infusion set
- Prime the SC infusion line with the solution to eliminate the air in the infusion line
- Ensure that the syringe contains exactly 23 mL of OCREVUS® Subcutaneous solution, and expel any excess volume from the syringe

E

Storage of the prepared syringe:

- Do not store the prepared syringe that has been attached to the already-primed SC infusion set
- If the dose is not administered immediately, use aseptic technique to withdraw the entire content of OCREVUS® Subcutaneous solution
- Replace the transfer needle with a syringe closing cap. **DO NOT** attach an SC infusion set for storage
- If the syringe was stored in a refrigerator, allow the syringe to reach room temperature (<=25°C/77°F) prior to administration

5. Preparation of the equipment[1,4]

If the prepared syringe has been refrigerated, place the syringe on a clean flat surface, away from direct sunlight, and allow the syringe to come to room temperature.

Do not warm up the syringe in any other way.

Setting up the syringe pump

Load the syringe pump:

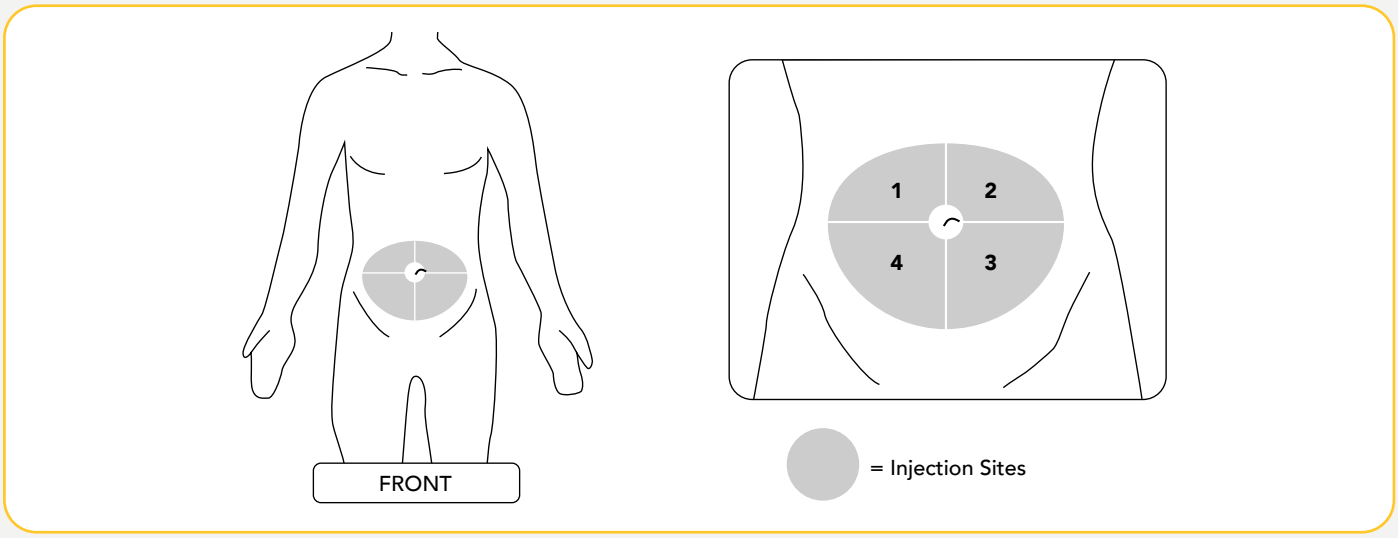
- Before using the syringe pump, refer to the user manual for this pump
- Load the syringe onto the syringe pump

- **Ensure that the occlusion alarm is set to >6 psi, high or the least-sensitive equivalent.** This will ensure the patient's tissue pressure does not inadvertently trigger an alarm and halt the infusion
- **Select the specific syringe** in the syringe pump menu settings
- Program the syringe pump for an injection of **23 mL aiming at a rate of 180 mL per hour (3.0 mL/minute)**
- The injection rate may be increased or decreased depending on the patient's feedback and administrator's judgment
- Enter the target injection volume (23 mL)

6. Preparing the injection site and starting administration[1,4]

Choose an injection site on the abdomen:

The injection site should be on the abdomen, except for 2 inches (5 cm) around the navel:



a. Injections should never be given into areas where the skin is red, bruised, tender or hard, or areas where there are moles or scars

b. Disinfect the injection site

c. Allow the injection site to air dry. Do not fan or blow on the cleaned area. Do not touch the cleaned area prior to the injection

Insert the injection needle:

Make sure the patient is position comfortably and that the injection site can be accessed easily. Any position between sitting or supine position is appropriate for administration.

d. Pinch a wide area of skin surrounding the injection site

e. Maintaining the wide pinch with one hand, use the other hand to gently push the injection needle straight into the skin

f. To secure the injection line, apply an adhesive covering over the injection site

Start the injection:

g. For the syringe pump-assisted administration: check the pump program is correct

h. Start the injection / the syringe pump

i. Injection takes less than 10 minutes

j. If administration is interrupted, continue administering at the same site, or at a different site, but restrict this to the abdomen

Complete the administration:

1. When the target injection volume (23 mL) is administered, remove the adhesive covering and remove the needle from the skin
2. Push the infusion set wings closed, by applying even pressure on the safety closure circles located at the tip of the wings
3. After the wings are securely closed, dispose of the infusion set and syringe properly
4. If there is any blood, you may press a cotton ball or gauze on the injection site and cover it with a small plaster / band aid

Optional: *apply a cold compress and/or topical antihistamine to help mitigate or alleviate injection reactions*

7. Management and monitoring of injection reactions[1]

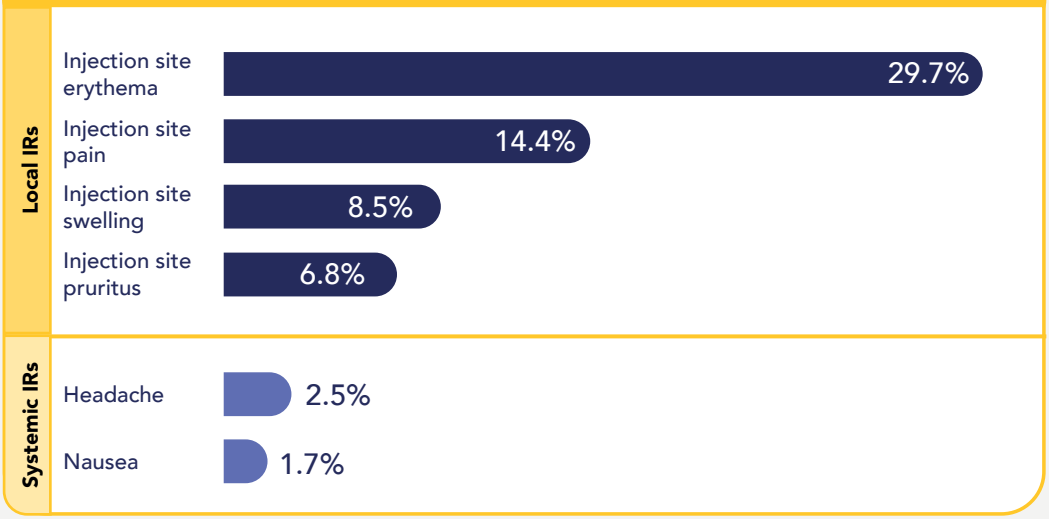
Treatment with OCREVUS® Subcutaneous injection is associated with injection reactions (IRs) which:

- Have been more frequently reported with the first injections
- Can occur during, or within 24 hours of administration

Appropriate management resources for severe IRs (hypersensitivity reactions and/or anaphylactic reactions):

- Should be available for the initial dose of OCREVUS® Subcutaneous injection
- IRs can be managed with symptomatic treatment, should they occur

Most common IRs with OCREVUS® Subcutaneous injection:



Management of injection reactions (IRs) during OCREVUS® administration:

- **Life-threatening IRs:** if there are any signs of life-threatening IRs, the administration should be stopped immediately, and the patient should receive appropriate treatment. OCREVUS® treatment must be permanently discontinued in these patients
- **Severe IRs:** if a patient experiences a severe IR, the injection should be interrupted immediately, and the patient should receive symptomatic treatment. The injection should be completed only after all symptoms have been resolved

Post-treatment monitoring:

- For the initial dose, post-injection monitoring for at least one hour after the injection is recommended
- For subsequent doses, the need for post-injection monitoring is at the treating physician's discretion
- Warn your patients that an IR can occur within 24 hours of the injection, so they should watch out for any signs of IRs

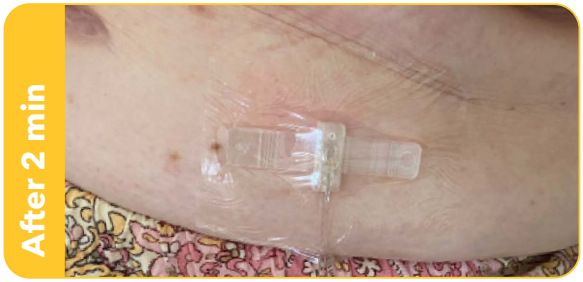
8. Examples of what to expect after the administration in patients

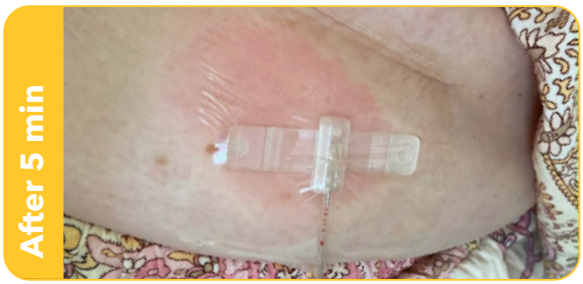
The images below illustrate examples of local injection reactions after the administration of Ocrevus SC; however, they are merely indicative and do not ensure that all patients will have the same experience. Individual responses to treatment can differ, and the outcomes shown may not represent the norm.

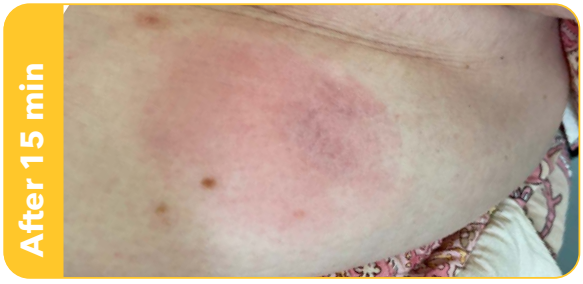
Please adhere to the recommended post-monitoring guidelines and familiarize yourself with possible injection reactions (IRs) and their management strategies.

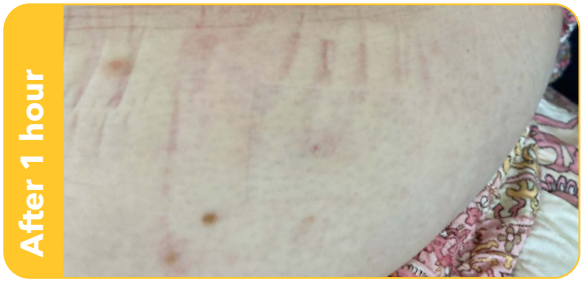
Patient A

Your results may vary



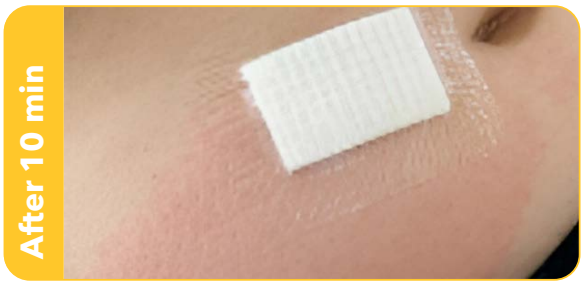


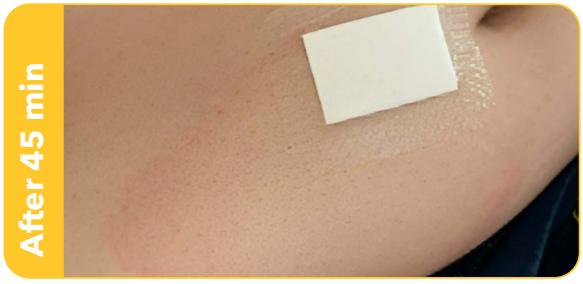


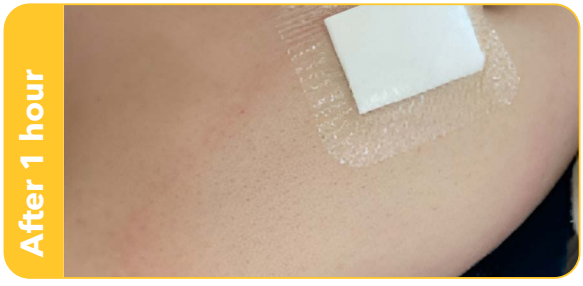


Patient B

Your results may vary







References

1. OCREVUS® Summary of Product Characteristics (SmPC)
2. Locke, KW, et al. Drug Deliv. 2019 Dec;26(1):98-106.
3. Knowles, SP, et al. Expert Opin Drug Deliv. 2021 Nov;18(11):1673-85.
4. Data on file, CN42097/OCARINA II PHARMACY MANUAL.

Ocrevus® (ocrelizumab)

ABBREVIATED PRESCRIBING INFORMATION
Important note: Before prescribing, consult full prescribing information*.

OCREVUS® (Ocrelizumab) Intravenous (IV) and OCREVUS ® (ocrelizumab) Subcutaneous (SC): Ocrevus IV vial contains 300 mg of ocrelizumab in 10 ml. Ocrevus SC vial contains 920 mg of ocrelizumab in 23 ml. Refer to Ocrevus Summary of Product Characteri stics (SmPC) for full prescribing information. **Indications:** Ocrevus is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features, as well as for the treatment of adult patients with early primary progressive multiple sclerosis (PPMS) defined by disease duration, level of disability and imaging features characteristic of inflammatory activity.
Posology and Administration: Treatment should be initiated and supervised by specialised doctors who are experienced in the diagnosis and treatment of neurological diseases and who have access to appropriate medical supportive treatment to manage severe reactions. Premedication: *Ocrevus IV:* Premedication prior to each ocrelizumab infusion to reduce the frequency and severity of infusion-related reactions: 100 mg intravenous methylprednisolone (or equivalent) approximately 30 minutes prior to each infusion; antihistamine approximately 30-60 minutes prior to each infusion. If appropriate, premedication with an antipyretic agent (e.g. paracetamol) approximately 30-60 minutes prior to each infusion. *Ocrevus SC:* Premedication prior to each ocrelizumab injection to reduce the risk of local and systemic injection reactions: 20 mg oral dexamethasone (or equivalent) and oral antihistamine (e.g. desloratadine or equivalent). In addition, premedication with an antipyretic agent (e.g. paracetamol) may be considered immediately prior to each administration. Administration: It is important to check the product's labelling to ensure that the correct formulation (intravenous or subcutaneous) is being administered to the patient as prescribed.*Ocrevus IV: Initial dose:* 600 mg administered as two separate intravenous infusions; first as a 300 mg infusion, followed two weeks later by another 300 mg infusion. *Subsequent doses:* Administered as a single 600 mg intravenous infusion every 6 months (3.5 hours). If a patient did not experience a serious infusion-related reaction (IRR) with any previous Ocrevus infusion, a shorter (2-hour)infusion can be administered for subsequent doses. Patients should be monitored during the infusion and for at least one hour after the infusion. *Ocrevus SC:* 920 mg administered every 6 months with no division of the initial or subsequent doses into separate administration. Administered as a subcutaneous injection in the abdomen over approximately 10 minutes, under supervision of a healthcare professional (HCP) recommended for the first injection. For the initial dose, post-injection monitoring for at least one hour is recommended. For subsequent doses, post injection monitoring is at the treating physician's discretion).
Delayed or missed doses: If an infusion/injection has not been given, it should be administered as soon as possible. Do not wait until the next planned dose. *Ocrevus SC 920 mg:* **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Current active infection. Severely immunocompromised patients. Known active malignancies. **Special Warning and Precautions for Use:** The name and the batch number of the administered product should be recorded to improve traceability of biological products. *Ocrevus IV* is associated with infusion related reactions IRRs, which may be related to cytokine release and/or other chemical mediators. IRRs may occur within 24 hours following administration and have been more frequently reported during the first infusion. IRR may present as pruritus, rash, urticaria, erythema, throat irritation, oropharyngeal pain, dyspnoea, pharyngeal or laryngeal oedema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, nausea, tachycardia, and anaphylaxis. Interrupt the infusion immediately and permanently if the patient experiences severe pulmonary symptoms, and administer symptomatic treatment. Monitor the patient until symptoms have resolved. Hypersensitivity Reactions: these may be clinically indistinguishable from IRR symptoms. Stop infusion immediately and permanently if a hypersensitivity reaction is suspected. *Ocrevus SC:* Treatment with subcutaneous ocrelizumab is associated with Injection Reactions (IRs), which may be related to cytokine release and/or other chemical mediators. Physicians should alert patients that IRs can occur during or within 24 hours of administration. Symptoms of IRs have been more frequently reported with the first injection. IRs can be local IRs or systemic IRs. Common symptoms of local IRs at the injection site include erythema, pain, swelling, and pruritus. Common symptoms of systemic IRs include headache and nausea. If there are signs of severe or life-threatening IR, the injection should be stopped immediately, and the patient should receive appropriate treatment. Infection: Administration of ocrelizumab should be delayed in patients with active infection until the infection has resolved. The patient's immune status should be verified before dosing because severely immunocompromised patients must not be treated. In PPMS, patients with swallowing difficulties are at a higher risk of aspiration pneumonia. Treatment with ocrelizumab may further increase the risk of severe pneumonia in these patients. *Progressive multifocal leukoencephalopathy (PML):* In very rare cases, PML has been observed in patients with JC virus treated with anti-CD20 antibodies, including ocrelizumab. If PML is suspected, treatment should be withheld. If PML is confirmed, treatment must be discontinued permanently. *Hepatitis B reactivation:* All patients should be screened for hepatitis B virus prior to initiation of treatment. Hepatitis B virus reactivation, in some cases accompanied by fulminant hepatitis, hepatic failure and death, has been reported in patients treated with anti-CD20 antibodies. Patients with active hepatitis B virus must not be treated with ocrelizumab. *Late neutropenia:* Cases of late onset of neutropenia have been reported at least 4 weeks after the last administration of ocrelizumab. Malignancies: An increased number of malignancies (including breast cancer) has been observed in clinical studies of patients treated with ocrelizumab. The incidence was within that expected for a multiple sclerosis population. Patients with a known active malignancy must not be treated with ocrelizumab. A benefit-risk assessment should be considered in patients with known risk factors for malignancies and in patients who are being actively monitored for recurrence of malignancy. Severely immunocompromised patients: Patients in a severely immunocompromised state must not be treated until the condition has resolved. In other auto-immune diseases, it is advised not to use other immunosuppressants concomitantly with ocrelizumab, except for corticosteroids. Vaccinations: The safety of immunisation with live or live-attenuated vaccines following treatment with ocrelizumab has not been studied and is not advised during treatment and not until B-cell levels have recovered. It is recommended to vaccinate patients being treated with ocrelizumab with inactivated seasonal influenza vaccine. Patients who require vaccination should complete their immunisation at least 6 weeks prior to initiation of treatment. **Interactions:** No interaction studies have been performed, as no drug interactions are expected via cytochrome P450 enzymes, other metabolising enzymes or transporters. **Undesirable effects:** Adverse reactions: Most common: infections (upper respiratory tract infection, nasopharyngitis, influenza), IRRs and decrease in blood IgM. **Fertility, pregnancy and lactation:** Women of childbearing potential: Women of childbearing potential should use contraception during treatment with ocrelizumab and for 12 months after the last administered dose. Pregnancy: Ocrelizumab should be avoided during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. Postponing vaccination with live or live-attenuated vaccines should be considered for neonates and infants if their mothers received ocrelizumab during pregnancy. Lactation: Women should be advised not to breastfeed during treatment. **Packs:** Ocrevus 300 mg concentrate for solution for infusion, 1 vial. Ocrevus SC 920 mg solution for injection. Any unused medicinal product or waste material should be disposed of per local requirements.
* The complete EU SmPC for Ocrevus IV and SC can be found at:
https://www.ema.europa.eu/en/documents/product-information/ocrevus-epar-productinformation_en.pdf

Marketing authorisation holder: Roche Registration GmbH

Full prescribing information should be consulted prior to prescribing.

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OCREVUS®
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