Package leaflet: Information for the user

OBIZUR 500 U powder and solvent for solution for injection
Susoctocog alfa

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 start using 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What OBIZUR is and what it is used for
2. What you need to know before you use OBIZUR
3. How to use OBIZUR
4. Possible side effects
5. How to store OBIZUR
6. Contents of the pack and other information

1. What OBIZUR is and what it is used for

OBIZUR contains the active substance susoctocog alfa, antihaemophilic Factor VIII, porcine sequence. Factor VIII is necessary for the blood to form clots and stop bleedings. In patients with acquired haemophilia, FVIII is not working properly because the patient has developed antibodies to his own Factor VIII which neutralize this blood clotting factor.

OBIZUR is used for the treatment of bleeding episodes in adults with acquired haemophilia (a bleeding disorder caused by lack of Factor VIII activity due to antibody development). These antibodies have less neutralizing effect against OBIZUR than against human Factor VIII.

OBIZUR restores this missing Factor VIII activity and helps blood to form clots at the site of bleeding.

2. What you need to know before you use OBIZUR

The product is for in-patient administration only. It requires clinical supervision of the bleeding status of the patient.

Do not use OBIZUR:
- if you are allergic to susoctocog alfa or any of the other ingredients of this medicine (listed in section 6)
- if you are allergic to hamster proteins (trace amounts may be present in Obizur arising from the manufacturing process)

If you are not sure, talk to your doctor before using this medicine.

Warnings and precautions
Talk to your doctor before using OBIZUR.
There is a rare chance that you may experience an allergic reaction to OBIZUR. You should be aware of the early signs of allergic reactions (see section 4 for signs and symptoms). If any of these symptoms occur, the injection should be stopped. Severe symptoms, including difficulty in breathing and (near) fainting, require emergency treatment.

Patients developing inhibitory antibodies to OBIZUR
Your doctor may check if you have inhibitory antibodies to porcine Factor VIII. Your doctor will check your blood Factor VIII to confirm that enough Factor VIII is being given to you. Your doctor will also check if the bleeding is adequately controlled.

Talk to your doctor if you have had a cardiovascular disease in the past or if you have a known risk of thrombosis (diseases from blood clots in normal vasculature), because the possibility of developing thromboembolic diseases at high and sustained blood Factor VIII levels cannot be excluded.

Name and batch number
It is strongly recommended that every time OBIZUR is used, the name and batch number of the medicine are recorded by the medical professional to maintain a link between your treatment and the batch of the medicine.

Use in children and adolescents
OBIZUR is not currently approved for treatment of patients under 18 years of age, in whom acquired haemophilia is rare.

Other medicines and OBIZUR
Tell your doctor if you are using, have recently used or might use any other medicines. No interactions of OBIZUR with other medicines are known.

Pregnancy and breast-feeding
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 using this medicine.

Driving and using machines
OBIZUR has no influence on your ability to drive and use machines.

OBIZUR contains sodium
This medicine contains 4.4 mg sodium per milliliter once it is made up.

Talk to your doctor if you are on a controlled sodium diet.

3. How to use OBIZUR

Treatment with OBIZUR will be conducted by a doctor who is experienced in the care of patients with haemophilia (bleeding disorders).

Your doctor will calculate your dose of OBIZUR (in units or U) depending on your condition and body weight. The frequency and duration of administration will depend on how well OBIZUR is working for you. Usually, the replacement therapy with OBIZUR is a temporary treatment until bleeding is resolved or the antibodies against your own Factor VIII are eradicated.

The recommended first dose is 200 U per kilogram bodyweight given by intravenous injection.

Your doctor will measure your Factor VIII activity regularly to decide the subsequent dose and frequency of OBIZUR.

The bleeding will usually respond within the first 24 hours, your doctor will adjust the dose and duration of OBIZUR until the bleeding stopped.
The total volume of reconstituted OBIZUR should be administered at a rate of 1 to 2 mL per minute.

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

If you use more OBIZUR than you should
Always use OBIZUR exactly as your doctor has told you. If you use more OBIZUR than recommended, tell your doctor as soon as possible.

If you forget to use OBIZUR
Do not use a double dose to make up for a forgotten dose. You should contact your doctor if you missed a dose and do not know how to compensate for this.

If you stop using OBIZUR
Do not stop using OBIZUR without consulting your doctor.

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.

If severe and sudden allergic reactions occur, the injection must be stopped immediately. You must contact your doctor immediately if you have any of the following early symptoms:

- Swelling of lips and tongue
- Burning and stinging at the injection site
- Chills, flushing
- Hives, generalised itching
- Headache, low blood pressure
- Lethargy, sickness, restlessness
- Rapid beating of the heart, tightness of the chest
- Tingling, vomiting
- Wheezing

Common side effects (may affect up to 1 in 10 people)
Development of antibodies against the medicine

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via listed below.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard.

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpра.ie

By reporting side effects, you can help provide more information on the safety of this medicine.
5. **How to store OBIZUR**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton, on the vial and on the pre-filled syringe after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).
Do not freeze.

Use the reconstituted solution immediately but no longer than 3 hours once the powder is completely dissolved.

After reconstitution the solution should be clear and colourless.
Do not administer if particulate matter or discoloration is found.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. **Contents of the pack and other information**

**What OBIZUR contains**
- The active substance is susoctocog alfa (antihaemophilic Factor VIII, porcine sequence produced by recombinant DNA technology). Each powder vial contains 500 U susoctocog alfa.
- The other ingredients in the powder are polysorbate 80, sodium chloride (see also section 2), calcium chloride dihydrate, sucrose, Tris base, Tris HCl, Tri-sodium citrate dihydrate.
- The solvent is 1 ml sterilised water for injections.

**What OBIZUR looks like and contents of the pack**
One pack contains 1, 5 or 10 of the following:
- glass vial of OBIZUR 500 U white, friable powder with a rubber stopper and a flip-off seal
- pre-filled glass syringe of 1 ml sterilised water for injections with a rubber tip cap and a Luer Lock adapter
- fluid transfer device with an integral plastic spike

**Marketing Authorisation Holder and Manufacturer**

**Marketing authorisation holder**
Baxalta Innovations GmbH
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**Manufacturer**
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A-1221 Vienna
Austria

This leaflet was last revised in June 2017.

This medicine has been authorised under ‘exceptional circumstances’. This means that because of the rarity of this disease it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: [http://www.ema.europa.eu](http://www.ema.europa.eu), and on the website of [name of MS Agency (link)]. There are also links to other websites about rare diseases and treatments.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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The following information is intended for healthcare professionals only:

**INSTRUCTIONS FOR PREPARATION AND ADMINISTRATION**

**Preparation**

Before starting reconstitution you will need the following:

- Calculated number of powder vials
- Same number of 1 mL solvent syringes and sterile vial adapters
- Alcohol swabs
- Large sterile syringe to contain the final volume of reconstituted product

The procedures below are provided as general guidelines for the preparation and reconstitution of OBIZUR. Repeat following reconstitution instructions for each powder vial to be reconstituted.

**Reconstitution**

Use aseptic technique during the reconstitution procedure.

1. Bring the OBIZUR powder vial and pre-filled diluent solvent syringe to room temperature.
2. Remove the plastic cap from the OBIZUR powder vial ([Figure A](#)).
3. Wipe the rubber stopper with an alcohol swab (not supplied) and allow it to dry prior to use.
4. Peel back the cover of the vial adapter package ([Figure B](#)). Do not touch the luer lock (tip) in the centre of the vial adapter. Do not remove the vial adapter from the package.
5. Place the vial adapter package on a clean surface with the luer lock pointing up.
6. Snap off the tamper resistant cap of the pre-filled solvent syringe ([Figure C](#)).
7. While firmly holding the vial adapter package connect the pre-filled solvent syringe to the vial adapter by pushing the syringe tip down onto the luer lock in the centre of the vial adapter, and turning it clockwise until the syringe is secured. Do not over tighten ([Figure D](#)).
8. Remove the plastic package ([Figure E](#)).
9. Place the OBIZUR powder vial on a clean, flat, hard surface. Place the vial adapter over the OBIZUR powder vial and firmly push the filter spike of the vial adapter through the centre of the OBIZUR powder vial’s rubber circle until the clear plastic cap snaps onto the vial ([Figure F](#)).
10. Push the plunger down to slowly inject all of the diluent from the syringe into the OBIZUR powder vial.
11. Gently swirl (in a circular motion) the OBIZUR powder vial without removing the syringe until all of the powder is fully dissolved/reconstituted ([Figure G](#)). The reconstituted solution should be inspected visually for particulate matter before administration. Do not use if particulate matter or discoloration is observed.
12. With one hand hold the powder vial and vial adapter, and with the other hand firmly grasp the barrel of the pre-filled solvent syringe and in a counterclockwise motion unscrew the syringe from the vial adapter ([Figure H](#)).
13. Use OBIZUR immediately and within 3 hours after reconstitution when stored at room temperature.

**Administration**

**For intravenous injection only!**

- Inspect the reconstituted OBIZUR solution for particulate matter and discoloration prior to administration. The solution should be clear and colorless in appearance. Do not administer if particulate matter or discoloration is observed.
- Do not administer OBIZUR in the same tubing or container with other medicinal products for injection.

Using aseptic technique, administer using the following procedure:
1. Once all vials have been reconstituted, connect a large syringe to the vial adapter by gently pushing the syringe tip down onto the luer lock in the centre of the vial adapter, and turning clockwise until the syringe is secured.
2. Invert the vial; push the air in the syringe into the vial and withdraw the reconstituted OBIZUR into the syringe (Figure I).

![Figure I](image)

3. Unscrew the large syringe counterclockwise from the vial adapter, and repeat this process for all reconstituted vials of OBIZUR until the total volume to be administered is reached.
4. Administer the reconstituted OBIZUR intravenously at a rate of 1 to 2 mL per minute.

The required initial dose of Obizur for a patient is calculated using the following formula:

\[ \text{Initial dose (U/kg)} \div \text{Product strength (U/vial)} \times \text{Body weight (kg)} = \text{Number of vials} \]

e.g. for a 70 kg subject the number of vials for an initial dose will be calculated as follows:

\[ 200 \text{ U/kg} \div 500 \text{ U/vial} \times 70 \text{ kg} = 28 \text{ vials} \]
**Dosing**

The recommended initial dose is 200 U per kilogram bodyweight, given by injection.

<table>
<thead>
<tr>
<th>Type of Bleeding</th>
<th>Target Factor VIII Trough Activity (Units per dL or % of normal)</th>
<th>Initial Dose (Units per kg)</th>
<th>Subsequent Dose</th>
<th>Frequency and Duration of Subsequent Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild and moderate superficial muscle/no neurovascular compromise and joint bleeding</td>
<td>&gt;50%</td>
<td>200</td>
<td>Titrate subsequent doses based on clinical response and to maintain target Factor VIII trough activity</td>
<td>Dose every 4 to 12 hours, frequency may be adjusted based on clinical response and measured Factor VIII activity</td>
</tr>
<tr>
<td>Major moderate to severe intramuscular, retroperitoneal, gastrointestinal, intracranial bleeding</td>
<td>&gt;80%</td>
<td></td>
<td></td>
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