Package leaflet: Information for the user

Octanate 250 IU, Octanate 500 IU and Octanate 1000 IU
Powder and Solvent for Solution for Injection
Human Coagulation Factor VIII

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 further questions, ask your doctor, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Octanate is and what it is used for

Octanate belongs to a group of medicines called clotting factors and contains human blood coagulation factor VIII. This is a special protein involved in blood clotting.

Octanate is used to treat and prevent bleeding in patients with haemophilia A. This is a condition in which bleeding can go on for longer than expected. It is due to an hereditary lack of coagulation factor VIII in the blood.

2. What do you need to know before you use Octanate

It is strongly recommended that every time you receive a dose of Octanate the name and batch number of the product are recorded in order to maintain a record of the batches used.

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly or repeatedly receive human-derived Factor VIII products.

Do not use Octanate

if you are allergic to human blood coagulation factor VIII or to any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Octanate.

Octanate contains very small amounts of other human proteins. Any medicine which contains proteins and which is injected into a vein (administered intravenously) can cause allergic reactions (See Section 4., "Possible side effects").

The formation of inhibitors (antibodies) is a known complication that can occur during treatment with all Factor VIII medicines. These inhibitors, especially at high levels, stop the treatment working properly and you or your child will be monitored carefully for the development of these inhibitors. If you or your child´s bleeding is not being controlled with Octanate, tell your doctor immediately.

Information about the blood and plasma used for Octanate
When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B (HBV) virus and hepatitis C virus (HCV), and for the non-enveloped hepatitis A virus (HAV). The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

Parvovirus B19 infection may be serious for pregnant women (infection of the baby) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or abnormal breakdown of red blood cells).

Other medicines and Octanate

Tell your doctor or pharmacist if you are taking, have recently taken or might taken any other medicines, including medicines obtained without prescription.

Human blood coagulation factor VIII products are not known to interact with other medicinal products. Nonetheless, do not combine Octanate with other medicines during infusion.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

No effects on ability to drive and use machines have been observed.

Octanate contains
for 250 IU/vial
less than 1 mmol sodium (23 mg) (main component of cooking/table salt) per vial, i.e. essentially `sodium-free`

for 500 and 1000 IU/vial
up to 40 mg sodium (main component of cooking/table salt) per vial. This is equivalent to 2% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Octanate

Octanate should be administered intravenously after reconstitution with the supplied solvent.

Treatment should be started under medical supervision.

Dosage for the prevention of bleeding If you suffer from severe haemophilia A you should inject 20 to 40 IU of factor VIII per kg body weight every two or three days for long-term prevention. Your dosage should be adjusted according to your response. In some cases shorter dosage intervals or higher dosages may be necessary.

Dosage calculation

Always use Octanate exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Factor VIII activity refers to the amount of factor VIII present in the plasma. It is expressed either as a percentage (relative to normal human blood plasma) or in International Units (IU). The dosage of factor VIII is expressed in IU.

One IU of factor VIII activity is equivalent to the amount of factor VIII in one ml of normal human blood plasma. One IU of factor VIII per kg body weight raises the plasma factor VIII activity by 1.5% - 2% of normal activity. To calculate your dosage, the level of factor VIII activity in your blood plasma is measured. This will indicate by how much the activity needs to be increased. Please consult your doctor if you are uncertain how much your factor VIII activity has to be increased or how to calculate your dosage.

The dosage required is calculated using the following formula:

$$\text{Required units} = \text{body weight (kg)} \times \text{desired increase in factor VIII (\%)} \times \text{(IU/dl)} \times 0.5$$

Your dosage and how often it must be administered (frequency) should always be oriented by the clinical efficacy in the individual patient.

In the following bleeding events, factor VIII activity should not fall below the plasma activity level (in % of normal) shown in the following table, for the corresponding period.

This table can be used to guide dosing in bleeding episodes and for surgery:

Degree of bleeding/ **Type of surgical procedure**	**Factor VIII level required (%) (IU/dl)**	**Frequency of dosage (hours between dosages) /** **Duration of therapy (in days)**
Bleeding		
Bleeding into a joint (early haemarthrosis), muscle bleeding or oral bleeding	20 - 40	Repeat every 12 to 24 hours for at least 1 day, until the pain decreases or healing is achieved.
More extensive bleeding into a joint (haemarthrosis), muscle bleeding or effusion of blood (haematoma)	30 - 60	Repeat infusion every 12 to 24 hours for 3-4 days or more until pain and disability have resolved.
Life-threatening bleeding such as in head surgery, bleeding in the throat, major abdominal bleeding	60 - 100	Repeat the infusion every 8 to 24 hours until the threat is resolved.
Surgery		
Minor including tooth extraction	30 - 60	Every 24 hours for at least 1 day, until healing is achieved.
Major	80 - 100 (before and after an operation)	Repeat infusion every 8 to 24 hours until adequate wound healing, then therapy for at least another 7 days to maintain factor VIII activity at 30% to 60%.

Your doctor will advise you about the dosage and the frequency with which you should use Octanate.

Your response to factor VIII products may vary. The factor VIII level in your blood should therefore be measured during the treatment to calculate the correct dosage and frequency of infusion.

Use in children

Clinical studies did not identify any special dosage requirements for children. For both treatment and prophylaxis, the dosage is the same in adults and children.

Instructions for Home Treatment

- **Please read all the instructions and follow them carefully!**
- **Do not use Octanate after expiry date given on the label.**
- **During the procedure described below, sterility must be maintained!**
- **Reconstituted medicinal product should be inspected visually for particulate matter and discoloration prior to administration.**
- **The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits.**
- **Use the prepared solution immediately, to prevent microbial contamination.**
- **Only use the infusion set provided. The use of other injection/infusion equipment can cause additional risks and treatment failure.**

Instructions for preparing the solution:

1. Do not use the product directly from the refrigerator. Allow the solvent and the powder in the closed vials to reach room temperature.

2. Remove the flip off caps from both vials and clean the rubber stoppers with one of the provided alcohol swabs.

3. The transfer set is depicted in Fig. 1. Place the solvent vial on an even surface and hold it firmly. Take the transfer set and turn it upside down. Place the blue part of the transfer set on top of the solvent vial and press firmly down until it snaps (Fig. 2+3). Do not twist while attaching.

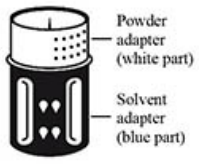

Fig. 1

Fig. 2

Fig. 3

4. Place the powder vial on an even surface and hold it firmly. Take the solvent vial with the attached transfer set and turn it upside down. Place the white part on top of the powder vial and press firmly down until it snaps (Fig. 4). Do not twist while attaching. The solvent flows automatically into the powder vial.

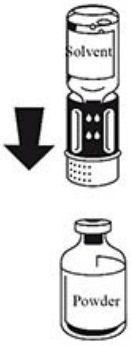

Fig. 4

5. With both vials still attached, gently swirl the powder vial until the product is dissolved.
The dissolving is completed in less than 10 minutes at room temperature. Slight foaming might occur during preparation. Unscrew the transfer set into two parts (Fig. 5). Foaming will disappear.

Dispose the empty solvent vial with the blue part of the transfer set.

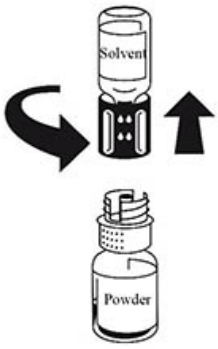

Fig. 5

Instructions for injection:
As a precaution, your pulse rate should be taken before and during the injection. If a marked increase in your pulse rate occurs, reduce the injection speed or interrupt the administration for a short time.

1. Attach the syringe to the white part of the transfer set. Turn the vial upside down and draw the solution into the syringe (Fig. 6).
The solution should be clear or slightly opalescent.
Once the solution has been transferred, firmly hold the plunger of the syringe (keeping it facing down) and remove the syringe from the transfer set (Fig. 7).

   Dispose the empty vial together with the white part of the transfer set.

Fig. 6

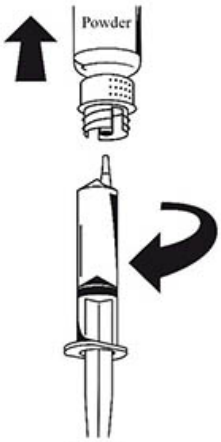

Fig. 7

2. Clean the chosen injection site with one of the provided alcohol swabs.

3. Attach the provided infusion set to the syringe

4. Insert the injection needle into the chosen vein. If you have used a tourniquet to make the vein easier to see, this tourniquet should be released before you start injecting Octanate.
5. No blood must flow into the syringe due to the risk of formation of fibrin clots.

6. Inject the solution into the vein at a slow speed, not faster than 2-3 ml per minute.

If you use more than one vial of Octanate powder for one treatment, you may use the same infusion set and syringe again. The transfer set is for single use only.

Any unused product or waste material should be disposed of in accordance with local requirements.

If you use more Octanate than you should

No symptoms of overdose with human coagulation factor VIII have been reported. However, the recommend dosage should not be exceeded.

If you forget to use Octanate
Do not take a double dose to make up for a forgotten dose. Proceed with the next dose immediately and continue as advised by your doctor or pharmacist

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

4. Possible side effects

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

Even though **rare** (may affect up to 1 in 1,000 people), hypersensitivity or allergic reactions have been observed in patients treated with factor VIII containing products.

Contact your doctor if you suffer from the symptoms:
being sick (vomiting), burning and stinging at the infusion site, chest tightness, chills, faster heart beat (tachycardia), feeling sick (nausea), feeling of pins and needles (tingling), flushing, headache, hives (urticaria), low blood pressure (hypotension), rash, restlessness, swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema), tiredness (lethargy), wheezing.

In **very rare** (may affect up to 1 in 10,000 people)) cases, this hypersensitivity may lead to a severe life-threatening allergic reaction called anaphylaxis, which may include shock, as well as some or all of the symptoms described above. In this case please contact your doctor immediately or call for an ambulance.

Other rare side effects (may affect up to 1 in 1,000 people)
Fever may occur in **rare** cases.

For children not previously treated with Factor VIII medicines, inhibitor antibodies (see section 2) may form very commonly (more than 1 in 10 patients); however patients who have received previous treatment with Factor VIII (more than 150 days of treatment) the risk is uncommon (less than 1 in 100 patients). If this happens you or your child´s medicines may stop working properly and you or your child may experience persistent bleeding. If this happens, you should contact your doctor immediately.

For information on viral safety see section 2. (Take special care with Octanate - Information about the blood and plasma used for Octanate).

Reporting of suspected adverse reactions
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Octanate

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 label. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Keep the vials in the outer carton in order to protect from light.

Use the reconstituted solution immediately and for single use only.

Do not use this medicine if you notice cloudy or incompletely dissolved solutions.

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 to protect the environment.

6. Contents of the pack and other information

What Octanate contains

The **active substance** is the human blood coagulation factor VIII.

Volume and concentrations

Octanate® powder vial size (IU FVIII)	Solvent vial size (to be added to Octanate® powder vial) (ml)	Nominal concentration of reconstituted solution (IU FVIII/ml)
250 IU	5	50
500 IU	5	100
1000 IU	5	200

The **other ingredients** are:

For the powder: sodium citrate, sodium chloride, calcium chloride, glycine

For the solvent: water for injections.

What Octanate looks like and contents of the pack

Octanate is presented as a powder and solvent for solution for injection.

The powder is white or pale yellow, also appearing as a friable solid.

The solvent is a clear, colourless liquid.

The three available pack sizes differ in the amount of human blood coagulation factor VIII and solvent:

- 250 IU/vial: reconstitution with 5 ml leads to 50 IU/ml
- 500 IU/vial: reconstitution with 5 ml leads to 100 IU/ml
- 1000 IU/vial: reconstitution with 5 ml leads to 200 IU/ml

All pack sizes include:

- 1 equipment pack for intravenous injection (1 transfer set, 1 infusion set, 1 disposable syringe)
- 2 alcohol swabs

Not all pack sizes may be marketed.

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