

PACKAGE LEAFLET

Package leaflet: Information for the user

Replenine-VF 50 IU/ml powder and solvent for solution for injection

high purity factor IX

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

1. What Replenine-VF is and what it is used for

Replenine-VF contains a high purity factor IX concentrate, a protein that is used to prevent and treat bleeding in patients with haemophilia B (an inherited shortage of factor IX in the blood). Your doctor will explain further why this medicine has been given to you.

Replenine-VF can be used in patients of all age groups.

2. What you need to know before you use Replenine-VF

Do not use Replenine-VF

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

Talk to your doctor if you think this applies to you.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Replenine-VF if you:

- have heart or liver disease
- have a risk of blood clotting
- have had surgery recently
- have a high level of antibodies to factor IX (Your doctor may give you an alternative treatment).

Your doctor or nurse will check the level of factor IX and antibodies in your blood before and after treatment, especially for your first injections.

The formation of inhibitors (antibodies) is a known complication that can occur during treatment with all factor IX 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 your or your child's bleeding is not being controlled with Replenine-VF, or if you suddenly have unusual bruising and feel very unwell, tell your doctor immediately.**

If you require a central venous access device (CVAD) for the administration of Replenine-VF, you may be at risk of complications including local infections, bacteria in the blood (bacteraemia) and the blood clot at the catheter site.

Virus safety

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
- the testing of each donation and pools of plasma for signs of virus/infections
- the inclusion of 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 virus and hepatitis C virus, and for the non-enveloped hepatitis A and parvovirus B19 viruses.

It is strongly recommended that every time you receive a dose of Replenine-VF, the name and batch number of the product are recorded 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 plasma-derived factor IX products.

Children and adolescents

The listed warnings and precautions apply to both adults and children.

Other medicines and Replenine-VF

Tell your doctor if you are taking, or have recently taken, any other medicines.

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 for advice before using this medicine.

Driving and using machines

Replenine-VF does not affect your ability to drive or operate machines.

Replenine-VF contains sodium

This medicine contains up to 83 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 4% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Replenine-VF

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

Replenine-VF should be injected directly into a vein.

Before injecting this medicine, you should have received training by your healthcare professional on how to do this.

Use only the recommended injection equipment provided with your medicine.

Your doctor will explain how much you should use and when you should use it.

Your doctor will tell you your dose and how many vials you should use to inject the dose you need. If further treatment is needed, doses may be repeated. Your doctor will advise you if this is necessary.

The amount of factor IX you or your child need and the duration of treatment will depend on several factors, such as your body weight, the severity and nature of your condition, the site and intensity of the bleeding or the need to prevent bleeding during an operation or medical procedure.

When to inject Replenine-VF

Replenine-VF can be used to stop bleeding, when it occurs, or to prevent bleeding from happening.

When to inject Replenine-VF to stop bleeding:

- The medicine should be injected when the first sign of bleeding occurs.
- The injection should be repeated as necessary to stop the bleeding.
- Each individual bleed should be judged on its own severity.
- If you are using this product for the first time, your doctor will supervise you.

If you are using Replenine-VF to prevent bleeding from happening, your doctor will tell you when to inject your medicine.

Dissolving your medicine before use

Vial of Replenine-VF	Quantity of Water Supplied	Quantity of water required for Half Volume
500 IU	10 ml	5 ml
1000 IU	20 ml	10 ml

1. Replenine-VF must only be dissolved in the water provided with the product.
2. Before you remove the cap, make sure that the vials of Replenine-VF and the water supplied, are both at room temperature (between 20°C and 25°C).
3. Your doctor will tell you if you can dissolve Replenine-VF in half the normal volume of water.

How to Dissolve Replenine-VF

You can dissolve your product in two ways using a needle and syringe:

- A) Dissolving in Full Volume or
- B) Dissolving with Half Volume

A) Dissolving in Full Volume

1. Remove the cap from the Replenine-VF vial.
2. Clean the top of the medicine stopper with a spirit swab.
3. Sterile water for use with Replenine-VF is provided in a glass vial with a stopper.
 - pierce the stopper with a needle and syringe and draw up the required volume of water, or
 - if the glass vial is labelled with the precise volume of water you require, insert one end of a double-spiked needle (which your doctor will provide) through the stopper into the water then invert the water vial and needle and insert the other end of this double needle into the product container.
4. Once you have pierced the Replenine-VF vial with the needle and syringe filled with water (or the double-ended needle attached to the water vial) water will flow into the container.
5. As the water enters the vial, swirl the vial gently around to wet the powder, but do not shake it.
6. Remove the syringe or empty water container from the needle before removing the needle from the medicine vial.
7. Continue swirling the vial around gently until the powder is completely dissolved. A clear or slightly pearl-like solution should be obtained, usually in about 2 to 2½ minutes (5 minutes maximum).

Note: If you have to use more than one vial to make up your dose, you need to draw up the solution in each vial into one syringe for your injection, but you must use a new sterile filter needle to draw the contents of each vial up into the plastic syringe.

B) Dissolving with Half Volume

When dissolving Replenine-VF in half volume, it is first necessary to remove and discard half the volume of water from the vial of sterile water. See the table above, under “Dissolving your medicine before use”, for the quantity of water needed.

- Remove the cap from the vial of water and clean the top of the stopper with spirit swab.
- Pierce the stopper of the vial of water with a needle and syringe and draw up half the volume of sterile water.
- Check that the correct amount is withdrawn. The needle and syringe can now be safely disposed of.
- The remaining water in the vial will be used for dissolving (half the original volume).

To complete the dissolving process follow steps 1-7 in Section A above. The product is then ready for administration.

Do not use this medicine if:

- the water is not pulled into the product vial with either method of reconstitution (this indicates a loss of vacuum in the vial, so the product must not be used).
- the dissolved product and water form a gel or a clot or if the solution is cloudy
- there are any particles in the syringe

If any of these happen, tell your doctor or pharmacist, reporting the batch number printed on the vials.

If you use more Replenine-VF than you should

If you think you may be using too much, stop the injection and tell your doctor.

If you know you have used too much, tell your doctor as soon as possible.

If you forget to use Replenine-VF

Do not use a double dose to make up for a forgotten dose. Inject your normal dose as soon as you remember and then continue to use as told by your doctor.

If you stop using Replenine-VF

Always talk to your doctor before deciding to stop your treatment.

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

4. Possible side effects

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

Stop the injection and tell your doctor immediately or go to the emergency department of your nearest hospital, if you get any of the following symptoms:

- swelling around the face and throat
- nettle-rash (urticaria)
- restlessness
- burning and stinging at the infusion site
- hives
- rapid heart beat
- chills
- low blood pressure
- tightness of the chest or wheezing
- flushing

- lethargy
- tingling
- nausea or vomiting

These symptoms may worsen into severe shock. The above allergic-type reactions are rare (may affect up to 1 in 1,000 people).

Kidney problems (such as nephrotic syndrome) have been reported in some haemophilia B patients who have inhibitors (antibodies) to factor IX and a history of allergic reaction to factor IX containing products. This may cause fluid retention (swelling or weight gain) or changes in your urine.

The use of low purity factor IX products has been associated with **heart attack, blood clots and abnormal blood coagulation**. The use of high purity factor IX, such as Replenine-VF, is rarely associated with such side effects.

Other possible side effects

Common (may affect up to 1 in 10 people)

- Reaction at the injection site, e.g. irritation, inflammation, suddenly have unusual bruising and feeling very unwell.
- Headache.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

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

5. How to store Replenine-VF

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 containers after “EXP”. The expiry date refers to the last day of that month.

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

Can be stored up to 3 months at 25°C. Record date of removal from refrigerator on carton.

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

Do not use this medicine if you notice small bits in the dissolved product. Once reconstituted, Replenine-VF must be used immediately or within 1 hour.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist or doctor 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 Replenine-VF contains

- The active substance is human coagulation factor IX.

- The other ingredients are: lysine hydrochloride, glycine, sodium citrate, citric acid monohydrate, disodium phosphate dihydrate, sodium chloride and sodium hydroxide (for pH adjustment).

What Replenine-VF looks like and contents of the pack

Replenine-VF is a white or pale yellow coloured powder in quantities of 500 International Units (IU) or 1000 IU in glass vials. These vials are closed with a rubber stopper under vacuum, held with a tamper-evident cap.

Replenine-VF should only be reconstituted with water for injections which is supplied with Replenine-VF in vials.

An administration user kit for administrative components can be provided separately upon request.

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