Package leaflet: Information for the user

Refixia 500 IU powder and solvent for solution for injection
Refixia 1 000 IU powder and solvent for solution for injection
Refixia 2 000 IU powder and solvent for solution for injection
Refixia 3 000 IU powder and solvent for solution for injection
nonacog beta pegol

▼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 Refixia is and what it is used for

What Refixia is
Refixia contains the active substance nonacog beta pegol. It is a long-acting version of factor IX. Factor IX is a protein naturally found in the blood that helps to stop bleeding.

What Refixia is used for
Refixia is used to treat and prevent bleeding in all groups of patients with haemophilia B (inborn factor IX deficiency).

In patients with haemophilia B, factor IX is missing or does not work properly. Refixia replaces this faulty or missing factor IX and helps blood to form clots at the site of bleeding.

2. What you need to know before you use Refixia

Do not use Refixia
- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to hamster proteins.

If you are not sure if either of the above applies to you, talk to your doctor before using this medicine.

Warnings and precautions
Traceability

It is important to keep a record of the batch number of your Refixia. So, every time you get a new package of Refixia, note down the date and the batch number (which is on the packaging after Lot) and keep this information in a safe place.

Allergic reactions and development of inhibitors
There is a rare risk that you may experience a sudden and severe allergic reaction (e.g. anaphylactic reaction) to Refixia. Stop the injection and contact your doctor or an emergency unit immediately if you have signs of an allergic reaction such as rash, hives, weals, itching of large areas of skin, redness and/or swelling of lips, tongue, face or hands, difficulty in swallowing or breathing, shortness of breath, wheezing, tightness of the chest, pale and cold skin, fast heartbeat, and/or dizziness.

Your doctor may need to treat you promptly for these reactions. Your doctor may also carry out a blood test to check if you have developed factor IX inhibitors (neutralising antibodies) against your medicine, as inhibitors may develop together with allergic reactions. If you have such inhibitors, you may have a higher risk of sudden and severe allergic reactions (e.g. anaphylactic reaction) during future treatment with factor IX.

Because of the risk of allergic reactions with factor IX, your initial treatment with Refixia should be given in a medical clinic or in the presence of health care professionals where proper medical care for allergic reactions can be provided if needed.

Talk to your doctor immediately if your bleeding does not stop as expected or if you have to significantly increase the amount of Refixia you need to stop a bleed. Your doctor will do a blood test to check if you have developed inhibitors (neutralising antibodies) against Refixia. The risk for developing inhibitors is highest in people who have have not been treated with factor IX medicines before, typically small children.

Blood clots
Tell your doctor, if any of the following apply to you as there is an increased risk of blood clots during treatment with Refixia:
- you have recently had surgery
- you suffer from other serious illness e.g. liver disease, heart disease, or cancer
- you have risk factors for heart disease e.g high blood pressure, obesity, or smoking.

Kidney disorder (nephrotic syndrome)
There is a rare risk of developing a specific kidney disorder called “nephrotic syndrome” following high doses of factor IX in haemophilia B patients with factor IX inhibitors and a history of allergic reactions.

Catheter-related problems
If you have a central venous access device (CVAD), you may develop infections or blood clots at the site of the catheter.

Other medicines and Refixia
Tell your doctor if you are taking, have recently taken or might take any other medicines.

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 Refixia.

Driving and using machines
Refixia has no influence on the ability to drive and use machines.

Refixia contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially “sodium-free”. In case of treatment with multiple vials, the total sodium content should be taken into consideration.

3. How to use Refixia

Treatment with Refixia will be started by a doctor who is experienced in the care of patients with haemophilia B. Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure about how to use Refixia.

Your doctor will calculate the right dose for you. The dose will depend on your weight and what the medicine is being used for.

Prevention of bleeding
The usual dose of Refixia is 40 international units (IU) per kg of body weight. This is given as one injection every week. Your doctor may choose another dose or change how often the injections should be given, based on your need.

Treatment of bleeding
The usual dose of Refixia is 40 international units (IU) per kg of body weight. Depending on the location and the severity of bleeding you may need a higher dose (80 IU per kg) or extra injections. Discuss with your doctor the dose and number of injections you need.

Use in children and adolescents
Refixia can be used in children and adolescents of all ages. The dose in children and adolescents is also calculated according to body weight and is the same dose as for adults.

How Refixia is given
Refixia is available as powder and solvent that is made up into a solution (reconstitution) and given as an injection into a vein. See "Instructions on how to use Refixia" for more information.

If you use more Refixia than you should
If you use more Refixia than you should, contact your doctor.

If you have to significantly increase the amount of Refixia you need to stop a bleed, talk to your doctor immediately. For further information, see section 2 "Allergic reactions and development of inhibitors".

If you forget to use Refixia
If you forget a dose, inject the missed dose as soon as you remember. Do not inject a double dose to make up for a forgotten dose. If you are in doubt contact your doctor.

If you stop using Refixia
If you stop using Refixia you may no longer be protected against bleeding or a current bleed may not stop. Do not stop using Refixia without talking to 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.

Allergic reactions are possible with this medicine.
If sudden and severe allergic reactions (e.g. anaphylactic reactions) occur, the injection must be stopped immediately. You must contact your doctor or an emergency unit immediately if you have early signs of a severe allergic reaction (anaphylactic reaction) such as:
- difficulty in swallowing or breathing
- shortness of breath or wheezing
- chest tightness

- redness and/or swelling of the lips, tongue, face or hands
- rash, hives, weals or itching
- pale and cold skin, fast heartbeat, and/or dizziness (low blood pressure).

For children not previously treated with factor IX medicines, inhibitors (see section 2) may form commonly (up to 1 in 10 patients). If this happens, the medicine may stop working properly and your child may experience persistent bleeding. If this happens, you should contact your doctor immediately.

The following side effects have been observed with Refixia:

Common side effects (may affect up to 1 in 10 people)
- allergic reactions (hypersensitivity). This may become severe and could be life-threatening (anaphylactic reactions)
- itching (pruritus)
- skin reactions at the site of injection
- feeling sick (nausea)
- feeling very tired.
- rash
- Children not previously treated with factor IX medicines: neutralising antibodies (inhibitors), anaphylactic reactions.

Uncommon side effects (may affect up to 1 in 100 people)
- heart palpitations
- hot flush.

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

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

5. How to store Refixia

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

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

Store in a refrigerator (2 °C – 8 °C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

Refixia may be taken out of the refrigerator for a maximum period of 1 year and stored at room temperature (up to 30 °C). Please record on the carton the date Refixia is removed from the refrigerator and placed at room temperature. This new expiry date should never exceed the one initially mentioned on the outer carton. If the medicine has not been used before the new expiry date, it should be disposed of. After storage at room temperature the medicine must not be put back in the refrigerator.

Use the injection immediately after making up the solution (reconstitution). If it cannot be used immediately, use within 24 hours if stored in a refrigerator at 2 °C – 8 °C or within 4 hours if stored out of the refrigerator at a maximum temperature of 30 °C.

The powder in the vial appears as a white to off-white powder. Do not use the powder if the colour has changed.

The reconstituted solution will be clear and colourless to slightly yellow. Do not use the reconstituted solution if you notice any particles or discolouration.

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 Refixia contains

- The active substance is nonacog beta pegol (pegylated human coagulation factor IX (rDNA)). Each vial of Refixia contains nominally 500 IU, 1 000 IU, 2 000 IU or 3 000 IU nonacog beta pegol corresponding to approximately 125 IU/ml, 250 IU/ml, 500 IU/ml or 750 IU/ml respectively after reconstitution with histidine solvent.
- The other ingredients in the powder are sodium chloride, histidine, sucrose, polysorbate 80, mannitol, sodium hydroxide and hydrochloric acid. See section 2 “Refixia contains sodium”.
- The ingredients in the sterilised solvent are histidine, water for injections, sodium hydroxide and hydrochloric acid.

What Refixia looks like and contents of the pack

- Refixia is provided as a powder and solvent for solution for injection (500 IU, 1 000 IU, 2 000 IU or 3 000 IU powder in a vial and 4 ml solvent in a pre-filled syringe, a plunger rod with a vial adapter – pack size of 1). Not all strengths may be marketed.
- The powder is white to off-white and the solvent is clear and colourless.

Marketing Authorisation Holder and Manufacturer

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd, Denmark

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Instructions on how to use Refixia

Read these instructions carefully before using Refixia.

Refixia is supplied as a powder. Before injection a solution must be made up (reconstituted) with the solvent supplied in the syringe. The solvent is a histidine solution. The reconstituted solution must be injected into a vein (intravenous (IV) injection). The equipment in this package is designed to reconstitute and inject Refixia.

You will also need an infusion set (tubing and butterfly needle), sterile alcohol swabs, gauze pads and plasters. These items are not included in the Refixia package.

Do not use the equipment without proper training from your doctor or nurse.

Always wash your hands and ensure that the area around you is clean.

When you prepare and inject medicine directly into the veins, it is important to **use a clean and germ- free (aseptic) technique.** Incorrect technique can introduce germs that can infect the blood.

Do not open the equipment until you are ready to use it.

Do not use the equipment if it has been dropped, or if it is damaged. Use a new package instead.

Do not use the equipment if it has expired. Use a new package instead. The expiry date is printed on the outer carton, on the vial, on the vial adapter, and on the pre-filled syringe.

Do not use the equipment if you suspect it is contaminated. Use a new package instead.

Do not dispose of any of the items until after you have injected the reconstituted solution.

The equipment is for single use only.

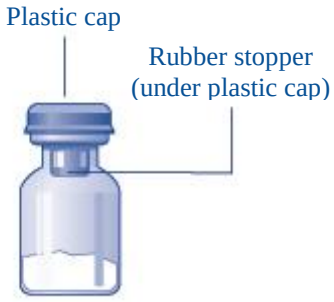
Contents

The package contains:

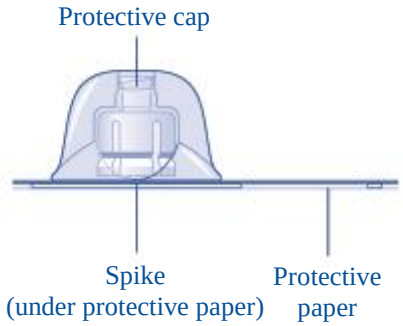
- 1 vial with Refixia powder
- 1 vial adapter
- 1 pre-filled syringe with solvent
- 1 plunger rod (placed under the syringe)

Overview

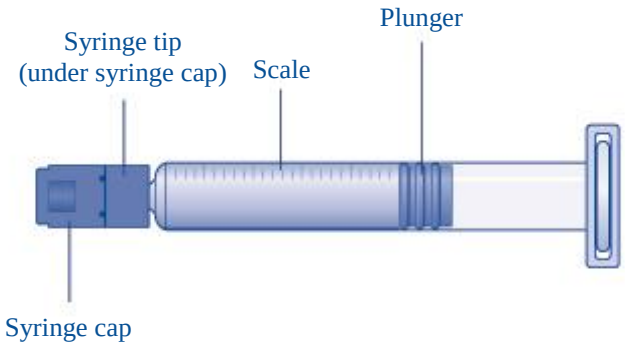
Vial with Refixia powder

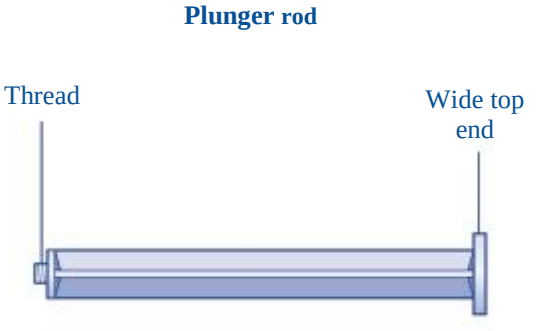


Vial adapter

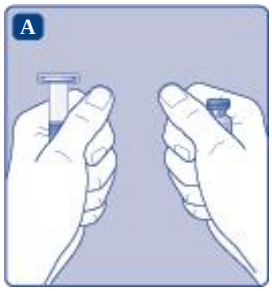


Pre-filled syringe with solvent



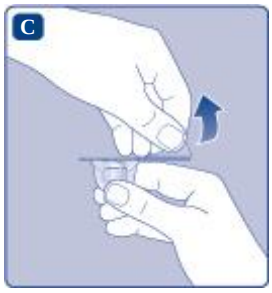
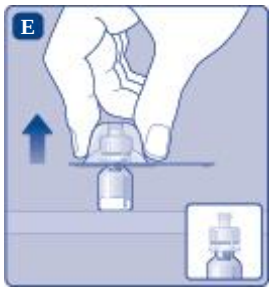
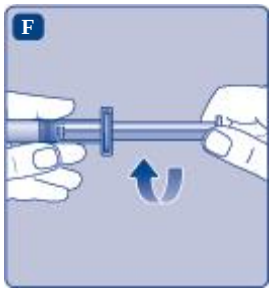


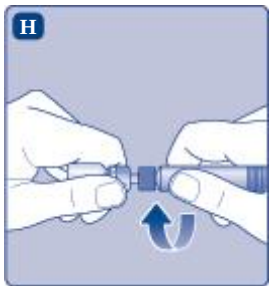
1. Prepare the vial and the syringe



- **Take out the number of Refixia packages you need.**
- **Check the expiry date.**
- **Check the name, strength and colour** of the package, to make sure it contains the correct product.
- **Wash your hands** and dry them properly using a clean towel or air dry.
- Take the vial, the vial adapter and the pre-filled syringe out of the carton. **Leave the plunger rod untouched in the carton.**
- **Bring the vial and the pre-filled syringe to room temperature.** You can do this by holding them in your hands until they feel as warm as your hands.
- **Do not use any other way to warm** the vial and pre-filled syringe.

- **Remove the plastic cap** from the vial**. If the plastic cap is loose or missing, do not use the vial.**
- **Wipe the rubber stopper with a sterile alcohol swab** and allow it to air dry for a few seconds before use to ensure that it is as germ free as possible.
- **Do not touch the rubber stopper with your fingers as this can transfer germs.**

2. Attach the vial adapter • **Remove the protective paper from the vial adapter.** **If the protective paper is not fully sealed or if it is broken, do not use the vial adapter.** **Do not take the vial adapter out of the protective cap with your fingers.** If you touch the spike on the vial adapter, germs from your fingers can be transferred.	
• **Place the vial on a flat and solid surface.** • **Turn over the protective cap,** and snap the vial adapter onto the vial. **Once attached, do not remove the vial adapter from the vial.**	
• Lightly **squeeze the protective cap** with your thumb and index finger as shown. **Remove the protective cap** from the vial adapter. **Do not lift the vial adapter from the vial** when removing the protective cap.	
3. Attach the plunger rod and the syringe • Grasp the plunger rod by the wide top end and take it out of the carton. **Do not touch the sides or the thread of the plunger rod.** If you touch the sides or the thread, germs from your fingers can be transferred. • **Immediately** connect the plunger rod to the syringe by turning it clockwise into the plunger inside the pre-filled syringe until resistance is felt.	

• **Remove the syringe cap** from the pre-filled syringe by bending it down until the perforation breaks. • **Do not touch the syringe tip under the syringe cap.** If you touch the syringe tip, germs from your fingers can be transferred. **If the syringe cap is loose or missing, do not use the pre-filled syringe.**	
• **Screw the pre-filled syringe securely** onto the vial adapter until resistance is felt.	
4. Reconstitute the powder with the solvent • **Hold the pre-filled syringe slightly tilted** with the vial pointing downwards. • **Push the plunger rod** to inject all the solvent into the vial.	
• **Keep the plunger rod pressed down and swirl** the vial gently until all the powder is dissolved. **Do not shake the vial as this will cause foaming.** • **Check the reconstituted solution.** It must be clear and colourless to slightly yellow and no particles should be visible. **If you notice particles or discolouration, do not use it.** Use a new package instead.	

Refixia is recommended to be used immediately after it has been reconstituted. This is because if left, the medicine may no longer be sterile and could cause infections.

If you cannot use the reconstituted Refixia solution immediately, it should be used within 4 hours when stored at room temperature (up to 30 °C) and within 24 hours when stored in a refrigerator (2 °C – 8 °C). Store the reconstituted product in the vial.

Do not freeze reconstituted Refixia solution or store it in syringes.

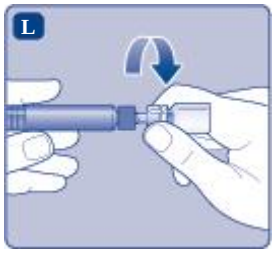
Keep reconstituted Refixia solution out of direct light.

If your dose requires more than one vial, repeat steps **A** to **J** with additional vials, vial adapters and pre-filled syringes until you have reached your required dose.

- **Keep the plunger rod pushed completely in**.
- **Turn the syringe** with the vial upside down.
- **Stop pushing the plunger rod and let it move back** on its own while the reconstituted solution fills the syringe.
- **Pull the plunger rod slightly downwards** to draw the reconstituted solution into the syringe.
- **In case you only need part of the entire vial, use the scale on the syringe to see how much reconstituted solution you withdraw, as instructed by your doctor or nurse.**

  If, at any point, there is air in the syringe, inject the air back into the vial.
- While holding the vial upside down, **tap the syringe gently** to let any air bubbles rise to the top.
- **Push the plunger rod** slowly until all air bubbles are gone.

- **Unscrew the vial adapter** with the vial.
- **Do not touch the syringe tip.** If you touch the syringe tip, germs from your fingers can be transferred.



5. Inject the reconstituted solution

Refixia is now ready to inject into your vein.
- Inject the reconstituted solution as instructed by your doctor or nurse.
- Inject slowly over 1 to 3 minutes.
- Do not mix Refixia with any other intravenous infusions or medicines.

Injecting Refixia via needleless connectors for intravenous (IV) catheters

Caution: The pre-filled syringe is made of glass and is designed to be compatible with standard luer-lock connections. Some needleless connectors with an internal spike are incompatible with the pre-filled syringe. This incompatibility may prevent administration of the medicine and/or result in damage to the needleless connector.

Injecting the solution via a central venous access device (CVAD) such as a central venous catheter or a subcutaneous port:

- Use a clean and germ-free (aseptic) technique. Follow the instructions for proper use for your connector and CVAD in consultation with your doctor or nurse.
- Injecting into a CVAD may require using a sterile 10 ml plastic syringe for withdrawal of the reconstituted solution. This should be done right after step J.
- If the CVAD line needs to be flushed before or after Refixia injection, use sodium chloride 9 mg/ml solution for injection.

Disposal

- **After injection, safely dispose** of all unused Refixia solution, the syringe with the infusion set, the vial with the vial adapter and other waste materials as instructed by your pharmacist.

  Do not throw it out with the ordinary household waste.

Do not disassemble the equipment before disposal.

Do not reuse the equipment.