Package leaflet: Information for the user

NovoEight 250 IU powder and solvent for solution for injection
NovoEight 500 IU powder and solvent for solution for injection
NovoEight 1000 IU powder and solvent for solution for injection
NovoEight 1500 IU powder and solvent for solution for injection
NovoEight 2000 IU powder and solvent for solution for injection
NovoEight 3000 IU powder and solvent for solution for injection

turoctocog alfa (human coagulation factor VIII (rDNA))

▼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 NovoEight is and what it is used for

NovoEight contains the active substance turoctocog alfa, human coagulation factor VIII. Factor VIII is a protein naturally found in the blood that helps it to clot.

NovoEight is used to treat and prevent bleeding episodes in patients with haemophilia A (inborn factor VIII deficiency) and can be used for all age groups.

In patients with haemophilia A, factor VIII is missing or not working properly. NovoEight replaces this faulty or missing 'factor VIII' and helps blood to form clots at the site of bleeding.

2. What you need to know before you use NovoEight

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

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

Warnings and precautions

Talk to your doctor before using NovoEight.

There is a rare chance that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to NovoEight. Early signs of allergic reactions are rash, hives, weals, generalised itching, swelling of lips and tongue, difficulty in breathing, wheezing, tightness of the chest, general feeling of being unwell, and dizziness.

If any of these symptoms occur, stop the injection immediately and contact your doctor.

Talk to your doctor if you think that your bleed is not being controlled with the dose you receive, as there can be several reasons for this. Some people using this medicine can develop antibodies to factor VIII (also known as factor VIII inhibitors). Factor VIII inhibitors make NovoEight less effective in preventing or controlling bleeding. If this happens you may need a higher dose of NovoEight or a different medicine to control your bleed. Do not increase the total dose of NovoEight to control your bleed without talking to your doctor. You should tell your doctor if you have been previously treated with factor VIII products, especially if you developed inhibitors, since there might be a higher risk that it happens again.

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 NovoEight, tell your doctor immediately.

Other medicines and NovoEight
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 that you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

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

NovoEight contains sodium
This medicine contains 28 mg sodium (7 mg/ml) after it has been reconstituted.
Talk to your doctor if you are on a controlled sodium diet.

3. How to use NovoEight

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

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

Prevention of bleeding
The usual dose of NovoEight is 20 to 50 international units (IU) per kg of body weight. The injection is given every 2 to 3 days. In some cases, especially in younger patients, more frequent injections or higher doses may be needed.

Treatment of bleeding
The dose of NovoEight is calculated depending on your body weight and the factor VIII levels to be achieved. The target factor VIII levels will depend on the severity and location of the bleeding.

Use in children and adolescents
NovoEight can be used in children of all ages. In children (below the age of 12) higher doses or more frequent injections may be needed. Children (above the age of 12) and adolescents can use the same dose as adults.

How NovoEight is given
NovoEight is given as an injection into a vein. See 'Instructions on how to use NovoEight' for more information.

If you use more NovoEight than you should
If you use more NovoEight than you should, tell your doctor or go to a hospital straight away.

If you forget to use NovoEight
You should contact your doctor if you have missed a dose and do not know how to compensate for this.

If you stop using NovoEight
If you stop using NovoEight you may no longer be protected against bleeding or a current bleed may not stop. Do not stop using NovoEight 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. The following side effects may occur with this medicine.

If severe, sudden allergic reactions (anaphylactic reactions) occur (very rare), the injection must be stopped immediately. You must contact your doctor immediately if you have one of the following early symptoms:

- difficulty in breathing, shortness of breath or wheezing
- chest tightness
- swelling of the lips and tongue
- rash, hives, weals or generalised itching
- feeling dizzy or loss of consciousness
- low blood pressure (having pale and cold skin, fast heartbeat).

Severe symptoms, including difficulty in swallowing or breathing and red or swollen face or hands, require prompt emergency treatment.

If you have a severe allergic reaction, your doctor may change your medicine.

For patients who have received previous treatment with Factor VIII (more than 150 days of treatment) inhibitor antibodies (see section 2) may form uncommonly (less than 1 in 100 patients). If this happens your medicine may stop working properly and you may experience persistent bleeding. If this happens, you should contact your doctor immediately.

Common side effects (may affect up to 1 in 10 people)
- blood tests showing changes in the way the liver functions
- reactions (redness and itching) around the site where you injected the medicine

Uncommon side effects (may affect up to 1 in 100 people)
- feeling tired
- headache

- feeling dizzy
- difficulty sleeping (insomnia)
- fast heartbeat
- increased blood pressure
- rash
- fever
- feeling hot
- stiffness of muscles
- pain in muscles
- pain in legs and arms
- swelling of legs and feet
- joint disease
- bruising.

Additional side effects in children and adolescents
The side effects observed in children and adolescents are the same as observed in adults.

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

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

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

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

5. How to store NovoEight

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

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

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

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

Before the NovoEight powder is reconstituted it may be kept at:

- room temperature (≤ 30°C) for a single period no longer than 9 months
  or
- above room temperature (30°C up to 40°C) for a single period no longer than 3 months.

Once the product has been taken out of the refrigerator, the product must not be returned to the refrigerator.

Please record the beginning of storage and the storage temperature on the product carton.

Once you have reconstituted NovoEight it should be used right away. If you cannot use the reconstituted NovoEight solution immediately, it should be used within:
- 24 hours stored at 2°C – 8°C
- 4 hours stored at ≤ 30°C, for product which has been kept for a single period no longer than 9 months at room temperature (≤30°C)
- 4 hours stored up to 40°C, for product which has been kept for a single period no longer than 3 months at above room temperature (30°C up to 40°C).

Store the reconstituted product in the vial. If not used straight away the medicine may no longer be sterile and could cause infection. Do not store the solution without your doctor's advice.

The powder in the vial appears as a white or slightly yellow powder. Do not use the powder if the colour has changed.

The reconstituted solution will be clear to slightly opalescent. Do not use this medicine if you notice that it is cloudy or contains visible particles.

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 NovoEight contains
- The active substance is turoctocog alfa (human coagulation factor VIII (rDNA)). Each vial of NovoEight contains nominally 250, 500, 1000, 1500, 2000 or 3000 IU turoctocog alfa.
- The other ingredients are L-histidine, sucrose, polysorbate 80, sodium chloride, L-methionine, calcium chloride dihydrate, sodium hydroxide and hydrochloric acid.
- The ingredient in the solvent is sodium chloride 9 mg/ml.

After reconstitution with the supplied solvent (sodium chloride 9 mg/ml (0.9%) solution for injection), the prepared solution for injection contains 62.5, 125, 250, 375, 500 or 750 IU turoctocog alfa per ml, respectively, (based on the strength of turoctocog alfa, i.e. 250, 500, 1000, 1500, 2000 or 3000 IU).

What NovoEight looks like and contents of the pack
NovoEight is available in packs containing 250, 500, 1000, 1500, 2000 or 3000 IU.
Each pack of NovoEight contains a vial with white or slightly yellow powder, a 4 ml prefilled syringe with a clear colourless solution, a plunger rod and a vial adapter.

Marketing Authorisation Holder and Manufacturer
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd, Denmark

This leaflet was last revised in 04/2018

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Instructions on how to use NovoEight

READ THESE INSTRUCTIONS CAREFULLY BEFORE USING NOVOEIGHT.

NovoEight is supplied as a powder. Before injection (administration) it must be reconstituted with the solvent supplied in the syringe. The solvent is a sodium chloride 9 mg/ml (0.9%) solution. The reconstituted NovoEight must be injected into your vein (intravenous injection). The equipment in this package is designed to reconstitute and inject NovoEight.

You will also need an infusion set (tubing and butterfly needle), sterile alcohol swabs, gauze pads and plasters. These devices are not included in the NovoEight 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 medication directly into the veins, it is important to **use a clean and germ free (aseptic) technique.** Improper 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 is expired. Use a new package instead. The expiry date is printed after 'EXP' on the outer carton, on the vial, on the vial adapter, and on the prefilled 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.

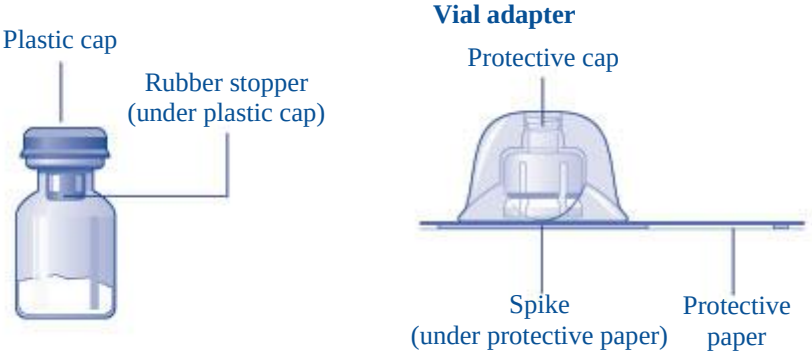
Contents

The package contains:

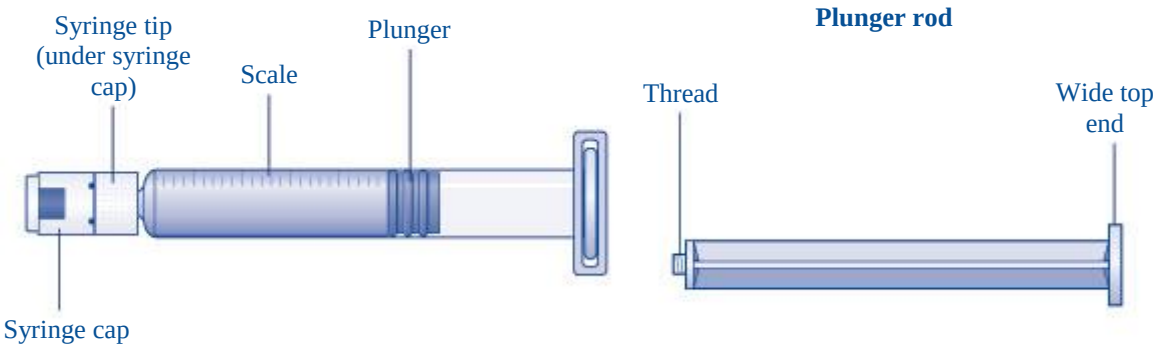
- 1 vial with NovoEight powder
- 1 vial adapter
- 1 prefilled syringe with solvent
- 1 plunger rod (placed under the syringe)

Overview

Vial with NovoEight powder

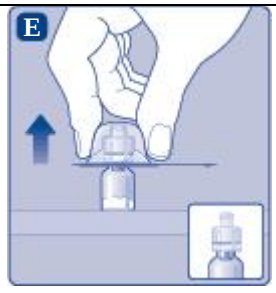
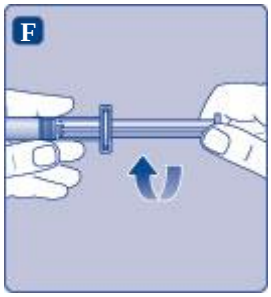


Prefilled syringe with solvent



1. Prepare the vial and the syringe

- **Take out the number of NovoEight 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 prefilled syringe out of the carton. **Leave the plunger rod untouched in the carton.**
- **Bring the vial and the prefilled 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 heat** the

vial and prefilled 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 prefilled syringe until resistance is felt.	
• **Remove the syringe cap** from the prefilled 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 prefilled syringe.**	
• **Screw the prefilled syringe securely** onto the vial adapter until resistance is felt.	
4. Reconstitute the powder with the solvent • **Hold the prefilled 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 to slightly opalescent (slightly unclear). **If you notice visible particles or discolouration, do not use it.** Use a new package instead.	

NovoEight 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 NovoEight solution immediately, it should be used within 4 hours when stored at room temperature or up to 40°C and within 24 hours when stored at 2°C – 8°C. Store the reconstituted product in the vial.

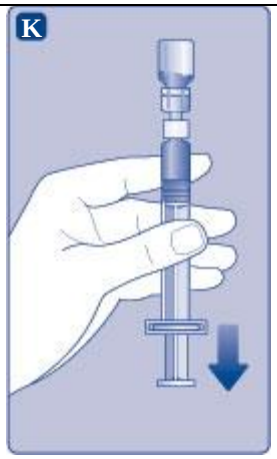
Do not freeze reconstituted NovoEight solution or store it in syringes.
Do not store the solution without your doctor's advice.

Keep reconstituted NovoEight solution out of direct light.

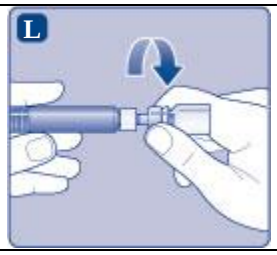
If your dose requires more than one vial, repeat steps **A** to **J** with additional vials, vial adapters and prefilled syringes until you have reached your required dose.

- **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 too much 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

NovoEight is now ready to be injected into your vein.

- Inject the reconstituted solution as instructed by your doctor or nurse.
- Inject slowly over 2 to 5 minutes.
- Do not mix NovoEight with any other intravenous infusions or medications.

Injecting NovoEight via needleless connectors for intravenous (IV) catheters

Caution: The prefilled 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 prefilled syringe. This incompatibility may prevent administration of the drug 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 NovoEight injection, use sodium chloride 9 mg/ml solution for injection.

Disposal

- **After injection, safely dispose** of all unused NovoEight 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.