PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

This medicine is dispensed with a doctor's prescription only

NovoEight® 500 IU
NovoEight® 1000 IU
NovoEight® 2000 IU

Powder and solvent for solution for injection

Active ingredient: turoctocog alfa

Inactive ingredients and allergens in this medicine: See section 2 under "Important information about some of this medicine's ingredients" and section 6 "Additional information".

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

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.
Therapeutic group: antihaemorrhagics, blood coagulation factor VIII.

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.
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. Before using the medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active substance or to any of the other ingredients this medicine contains (listed in section 6 "Additional information").
- you are allergic to hamster proteins.

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

Special warnings about using this medicine

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.

Tell 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 is 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. Tell your doctor immediately if you or your child's bleeding is not being controlled with NovoEight.

Drug interactions

If you are taking or if you have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think that you may be pregnant or are planning to have a baby, consult your doctor before using this medicine.

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

Important information about some of this medicine's ingredients
After reconstitution, a vial of this medicine contains 30.5 mg sodium (main component of table/cooking salt). This amount is equivalent to 1.5% of the recommended maximum dietrary intake of sodium for an adult.

Consult your doctor if you are on a controlled sodium diet.

3. How to use the medicine?

Treatment with NovoEight will be started by a doctor who is experienced in the care of patients with haemophilia A. Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose and of how to use the medicine.
Only your doctor will determine your dose and how you should take this medicine.

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

The recommended dosage is usually:

- **Prevention of bleeding**

  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.

Do not exceed the recommended dose.

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. Adolescents (above the age of 12) can use the same dose as adults.

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

If you have accidentally taken a higher dose
If you have taken a higher dose than you should, an overdose or if a child has accidentally taken some medicine, see a doctor or go to a hospital emergency room straight away and bring the medicine package with you.
If you forget to take the medicine
You should contact your doctor if you have missed a dose and do not know how to compensate for it.
Adhere to the treatment as recommended by your doctor.

If you stop taking this medicine
If you stop using NovoEight you may no longer be protected against bleeding or a current bleed may not stop. Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

As with any medicine, using NovoEight may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of 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 any 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
- dizziness 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 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 medicine may stop working properly and you or your child may experience persistent bleeding. If this happens, you should contact your doctor immediately.

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

Common side effects (may affect up to 1 in 10 users) in patients who have not previously treated with Factor VIII medicines
- blushing of the skin
- inflammation of vein
- bleeding into joint spaces
- bleeding in muscle tissue
- cough
- redness around the site where you placed catheter
- vomiting

Uncommon side effects (may affect up to 1 in 100 users)
- tiredness
- headache
- dizziness
- 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
- heart attack.

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

Reporting side effects
If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which refers to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of the sight and reach of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the carton and on the vial and 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.
Store the vial in the outer carton in order to protect from light.

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, it 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 NovoEightit should be used immediatly. If you cannot use the reconstituted NovoEight solution immediately, it should be used within:
- 24 hours when stored at 2°C – 8°C.
- 4 hours when 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 when 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 immediatly 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. Additional information

– In addition to the active ingredient, the medicine also contains:
  Sodium chloride, sucrose, L-histadine, calcium chloride dihydrate, polysorbate 80, L-methionine, sodium hydroxide and hydrochloric acid.
– The ingridients in the solvent are: sodium chloride and water for injections.

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

What the medicine looks like and contents of the pack
NovoEight is a powder and solvent for solution for injection. Each pack of NovoEight contains a vial with white or slightly yellow powder, a 4 ml pre-filled syringe with a clear colourless solution, a plunger rod and a vial adapter.

Registration holder's name and address
Novo Nordisk Ltd.,
1 Atir Yeda,
Kfar Saba 4464301

Manufacturer's name and address
Novo Nordisk A/S,
Novo Allé DK-2880 Bagsværd, Denmark

This leaflet was revised in January 2022 according to MOH guidelines.

Registration numbers of the medicine in the Ministry of Health National Drug Registry:
NovoEight 500: 154-51-34373-00
NovoEight 1000: 154-52-34374-00
NovoEight 2000: 154-54-34376-00

NovoEight IL PIL JAN2022-Notification

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 medicine directly into the vein, 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 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.

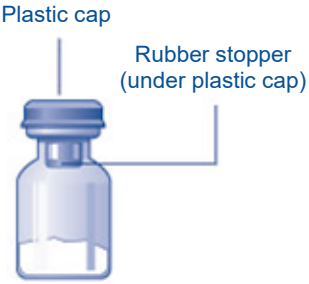
Contents

The package contains:

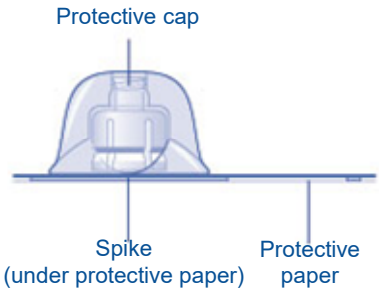
- 1 vial with NovoEight powder
- 1 vial adapter
- 1 pre-filled syringe with solvent
- 1 plunger rod (placed under the syringe)

Overview

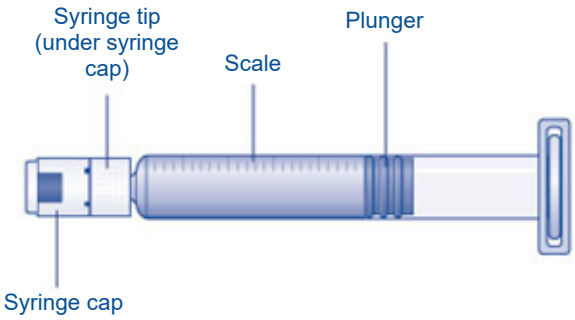
Vial with NovoEight powder



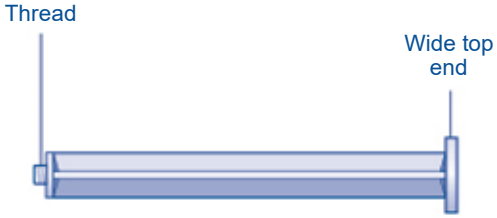
Vial adapter



Prefilled syringe with solvent

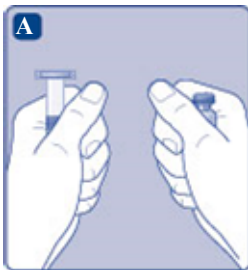


Plunger rod

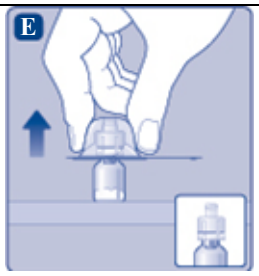
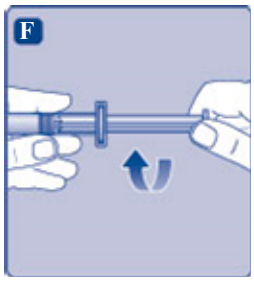
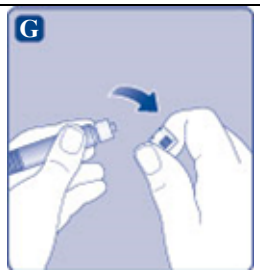
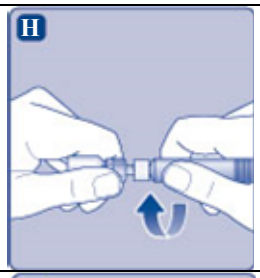
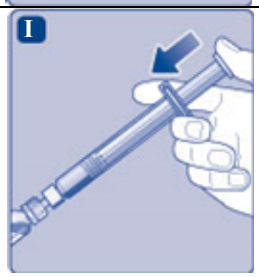


1. Prepare the vial and the syringe

- **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 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 heat** 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 in the illustration. **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 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 you do not use the reconstituted medicine immediately, it 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 medicine 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.

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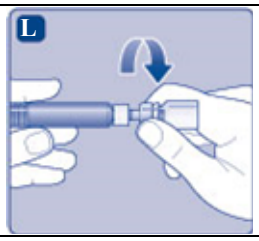
If your dose requires more than one vial, repeat steps **A** to **J** with additional vials, vial adapters and pre-filled syringes until you have reached your required dose.

• **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 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 medicines.

Injecting NovoEight 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 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.