Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Esperoct® 1000 IU
Powder and solvent for solution for injection

Active ingredient
Turoctocog alfa pegol (pegylated human coagulation factor VIII (rDNA))
Each vial of Esperoct contains 1000 IU turoctocog alfa pegol.
After reconstitution with the solvent supplied with the pack (sodium chloride 9 mg/mL (0.9%) solution for injection), the prepared solution for injection contains 250 IU turoctocog alfa pegol per mL.

Inactive ingredients and allergens: See section 2 "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?

Esperoct is intended for treatment and prophylaxis of haemorrhages in previously treated patients with haemophilia A (congenital factor VIII deficiency).
Esperoct does not contain von Willebrand factor, and must therefore not be used to treat von Willebrand's disease.
Therapeutic group: coagulation factors, coagulation factor VIII.
Esperoct contains the active ingredient turoctocog alfa pegol, a long-acting recombinant coagulation factor VIII. Coagulation factor VIII is a blood protein assisting in blood clotting.
In haemophilia A patients, factor VIII is missing or does not work properly. Esperoct replaces the missing or faulty factor VIII and helps to form a blood clot at the site of bleeding.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active substance or to any of the other ingredients in this medicine (see section 6)
- You are sensitive (allergic) to hamster proteins.

Special warnings about using this medicine
Previous use of a factor VIII medicine
Tell your doctor if you have used factor VIII medicines previously, especially if you developed inhibitors (antibodies) against the medicine, since there might be a risk of recurrent development of inhibitors.

Allergic reactions
There is a risk that you may experience a severe and sudden allergic reaction (e.g. anaphylactic reaction) to Esperoct.
Stop the injection and contact your doctor or an emergency unit immediately if you experience early signs of allergic reactions. These early signs may include rash, hives, local skin oedemas, itching on large areas of skin, redness and/or swelling of the lips, tongue, face or hands, difficulties swallowing or breathing, wheezing, tightness in the chest, pale and cold skin, fast heartbeat or dizziness, headache, nausea and vomiting.

Development of factor VIII inhibitors (antibodies)
Inhibitors (antibodies) can develop during treatment with all factor VIII medicines

- These inhibitors, especially at high levels, stop the proper treatment activity
- You will be monitored carefully for development of these inhibitors
- If your bleeding is not being controlled with Esperoct, tell your doctor immediately
- Do not increase the total dose of Esperoct to control bleeding without talking to your doctor.

Catheter-related problems
If you have a catheter where medicines can be injected into your blood (central venous access device), you may develop infections or blood clots at the site of the catheter.

Heart disease
Talk to your doctor or pharmacist if you have a heart disease or are at risk of heart disease.

Children
Esperoct is suitable for use in children of any age. See section 3 "How to use this medicine?".

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

Pregnancy and breastfeeding
There is no experience with the use of coagulation factor VIII during pregnancy and breastfeeding. Do not use the medicine without consulting your doctor before starting treatment. If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines
Esperoct has no or negligible influence on your ability to drive and use machines.

Important information about some of this medicine's ingredients
This medicine contains 30.5 mg sodium (main component of cooking/table salt) per reconstituted vial. This quantity is equivalent to 1.5% of the recommended maximum daily dietary intake of sodium for an adult.

Decreased factor VIII activity in previously treated patients
A decreased factor VIII activity may occur in the beginning of your treatment. If you think your medicine works less than expected, tell your doctor.

3. How to use this medicine?

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

How is Esperoct given
Esperoct is given as an injection into a vein (intravenously), see “Instructions for use of Esperoct” for more information.

How much to use
Your doctor will calculate your dosage for you. The dosage will depend on your body weight and whether it is used to prevent or to treat bleeding.

To prevent bleeding
Adults and adolescents (12 years of age and above): The recommended dosage is 50 IU of Esperoct per kg body weight every 4 days. Your doctor may choose another dosage or another frequency of injections, based on your need.
Children (below 12 years of age): The recommended initial dosage is between 50 IU-75 IU of Esperoct per kg body weight. The medicine is administered twice a week.

To treat bleeding
The dosage of Esperoct is calculated depending on your body weight and the desired factor VIII levels. The target factor VIII levels will depend on the severity and location of bleeding. If you feel that the effect of Esperoct is insufficient, talk to your doctor.

Use in adolescents
Adolescents (12 years of age and above) can use the same dosage as adults.

Use in children
For treatment of children below 12 years of age, a higher dose or administration at a higher frequency compared to that recommended for adolescents above 12 years of age and adults may be required.

Do not exceed the recommended dose.

If you use more Esperoct than you should
If you use more Esperoct than you should, contact your doctor immediately.

If you have to significantly increase your usage of Esperoct to stop a bleed, talk to your doctor immediately. For further information, see “Development of factor VIII inhibitors (antibodies)” in section 2.
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to use Esperoct
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. Proceed with the next injection as scheduled and continue with the treatment as advised by your doctor. If you are in doubt, contact your doctor.
Adhere to the treatment as recommended by your doctor.

If you stop using Esperoct
Do not stop using Esperoct without talking to your doctor.
If you stop using Esperoct, you may no longer be protected against bleeding or the current bleed may not stop.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take a 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

Like with all medicines, using Esperoct may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Allergic reactions (hypersensitivity)
Stop the injection immediately if you develop severe and sudden allergic reactions (anaphylactic reactions). You must **contact your doctor or an emergency unit immediately** if you experience signs of an allergic reaction such as:

- difficulties swallowing or breathing
- wheezing
- chest tightness
- redness and/or swelling of the lips, tongue, face or hands
- rash, hives, local skin oedemas or itching
- pale and cold skin, fast heartbeat, or dizziness (low blood pressure)
- headache, nausea or vomiting.

Development of factor VIII inhibitors (antibodies)
If you have previously received more than 150 days of treatment with factor VIII, inhibitors (antibodies) may develop (may affect up to 1 in 100 users). If this happens, your medicine may stop working properly and you may experience persistent bleeding. If this happens, you should contact your doctor immediately. See “Development of factor VIII inhibitors (antibodies)” in section 2.

Additional side effects
Common side effects - affect up to 1 in 10 users

- skin reactions at the injection site
- itching
- redness of skin (erythema)
- rash.

Uncommon side effects - affect up to 1 in 100 users

- allergic reactions (hypersensitivity). These may become severe and could be life-threatening, see “Allergic reactions (hypersensitivity)” above for more information
- factor VIII inhibitors (antibodies) in patients previously treated with factor VIII.

Additional side effects (unknown frequency)

- Decreased factor VIII activity in the absence of factor VIII inhibitors.

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 links 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 reach and sight 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 pack, on the vial, and on the labels of pre-filled solvent syringes. The expiry date refers to the last day of that month.

Storage conditions

Before reconstitution (before the powder is mixed with the solvent):
Store in a refrigerator (2°C - 8°C). Do not freeze. Store in the original package in order to protect from light.
Esperoct can be kept

- at room temperature (≤30°C) for a single period for up to 12 months within the shelf life of the product **or**
- above room temperature (>30°C up to 40°C) for a single period for up to 3 months within the shelf life of the product.

When you start storing Esperoct outside the refrigerator, record the date and the storage temperature in the designated space on the carton box.
Once you have taken the product out of the refrigerator for storage, you must not store it again in the refrigerator.

After reconstitution (after the powder has been mixed with the solvent):
Once you have reconstituted Esperoct, it should be used immediately. If you cannot use the reconstituted solution immediately, it should be used within

- 24 hours when stored in a refrigerator (2°C - 8°C) **or**
- 4 hours at ≤30°C **or**
- 1 hour between >30°C and 40°C, only if the product was stored above room temperature (>30°C up to 40°C) before reconstitution for no longer than 3 months.

The colour of the powder in the vial is white to off-white. Do not use the powder if the colour has changed.

The reconstituted solution must be clear and colourless. Do not use the reconstituted solution if you notice any particles or discolouration.

Do not throw away any medicine via wastewater or household waste. Ask the 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, this medicine also contains:
sodium chloride, sucrose, L-histidine, calcium chloride dihydrate, polysorbate 80, L-methionine, sodium hydroxide and hydrochloric acid.

- The ingredients of the solvent are

sodium chloride and water for injections.

What the medicine looks like and contents of the pack:
Esperoct is available in packs containing 1000 IU. Each pack of Esperoct contains a vial with white to off-white powder, a 4 mL pre-filled syringe with a clear colourless solvent, a plunger rod and a vial adapter.

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

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

Approved in 03/2023

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Esperoct 1000 IU 172-44-37440-00

Instructions for use of Esperoct 1000 IU

Read these instructions carefully before using Esperoct.

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

You will also need the following items:

- an infusion set (butterfly needle with tubing)
- sterile alcohol swabs
- gauze pads and plasters.

These items are not included in the Esperoct 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 a vein, it is **important to use a clean and germ-free (aseptic) technique.** An incorrect technique can introduce germs that may infect your 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 pack, 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.

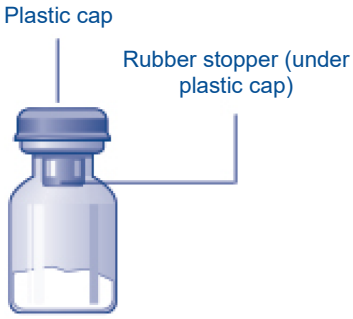
The equipment is for single use only.

Contents

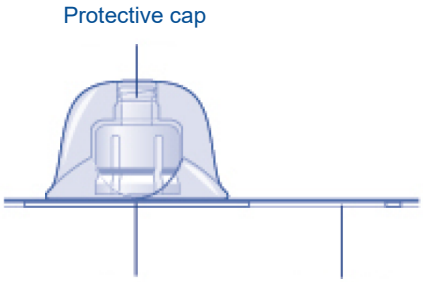
The package contains:

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

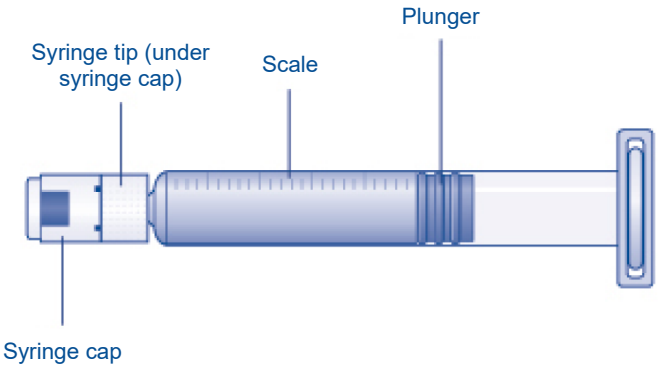
Overview
A vial with Esperoct powder



Vial adapter



Pre-filled syringe with solvent

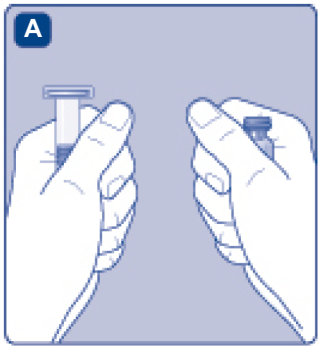


Plunger rod

1. Prepare the vial and the syringe

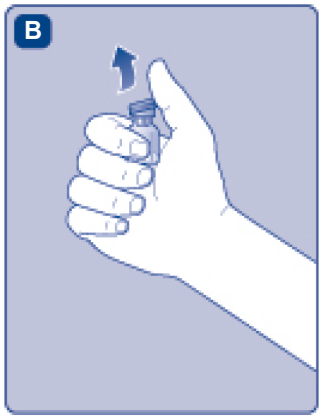
- **Take out the number of Esperoct packages you need.**
- **Check the expiry date.**
- **Check the name, strength and colour** of the package to make sure it contains the correct product.
- **Wash your hands** and dry them properly using a clean towel or let them air dry.
- Take the vial, the vial adapter and the pre-filled syringe out of the carton pack. **Leave the plunger rod untouched in the carton pack.**
- **Let the vial and the pre-filled syringe to reach room temperature**. You can do this by holding them in your hands until they feel as warm as your hands, see figure A.

  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.

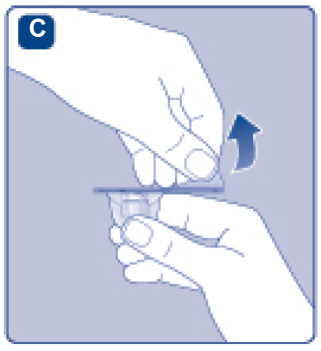


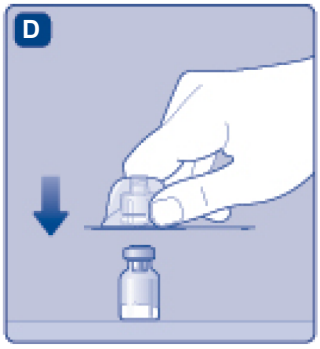
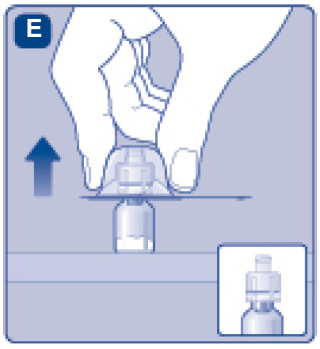
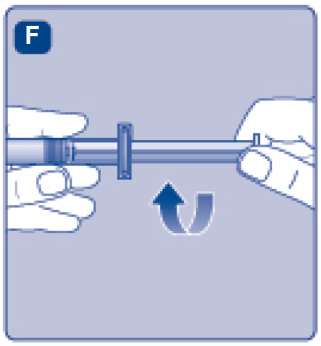
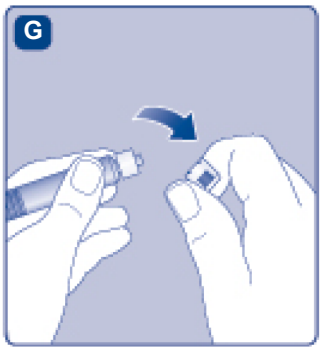
2. Attach the vial adapter

- **Remove the protective paper** from the vial adapter.

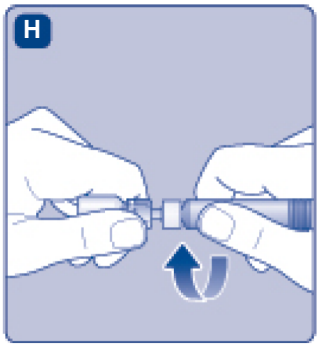
  If the protective paper is not fully sealed or if it is broken, do not use the vial adapter.

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.**	
• **Gently 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 pack. **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.**	

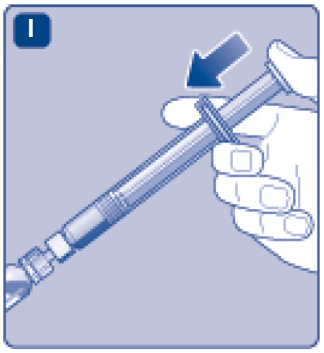
- **Screw the pre-filled syringe securely** onto the vial adapter until resistance is felt.



4. Reconstitute the powder with the solvent

- **Hold the pre-filled syringe slightly tilted** with the vial pointing downwards.

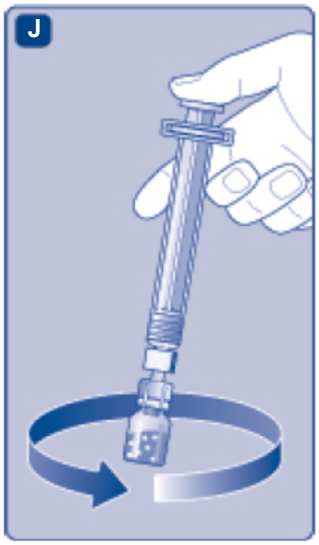
- **Push the plunger rod** to inject all the solvent into the vial.



- **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 and no particles should be visible. **If you notice particles or discolouration, do not use it.** Use a new package instead.



It is recommended to use Esperoct immediately after reconstitution.
If you cannot use the reconstituted Esperoct solution immediately, it should be used within

- 24 hours when stored in a refrigerator (2°C – 8°C) or
- 4 hours at a temperature not exceeding 30°C or
- 1 hour between >30°C and 40°C, only if the product was stored above room temperature (>30°C up to 40°C) before reconstitution for no longer than 3 months.

Store the reconstituted product in the vial.

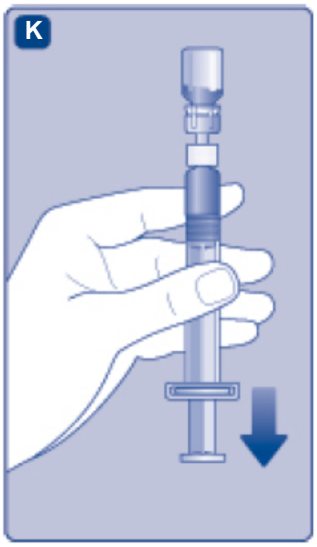
Do not freeze the reconstituted solution or store it in syringes.

Keep the reconstituted 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.

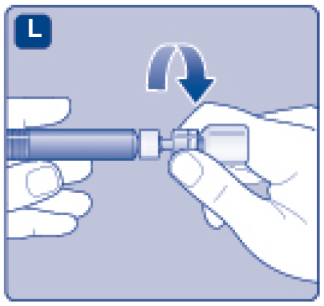
- **Keep the plunger rod pushed completely into the syringe.**
- **Turn the syringe with the vial** upside down, so that the vial is above the syringe.
- **Stop pushing the plunger rod and let it move back** on its own, while the reconstituted solution fills the syringe.
- **Pull the plunger rod gently downwards** to draw the reconstituted solution into the syringe.
- **If you do not need the entire amount of the reconstituted medicine from the vial**, use the scale on the syringe to withdraw the dose you need, 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 above the syringe, **tap the syringe gently** to let any air bubbles rise to the top.
- **Push the plunger rod** slowly until all the 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

Esperoct is now ready for injection into your vein.

- Inject the reconstituted solution as instructed by your doctor or nurse.
- Inject slowly over approximately 2 minutes.

Do not mix Esperoct with any other intravenous injections or medicines.

Injecting Esperoct 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 connectors. Some needleless connectors with an internal spike are incompatible with the pre-filled syringe. This incompatibility may prevent administration of the medicine and result in damage to the needleless connector.

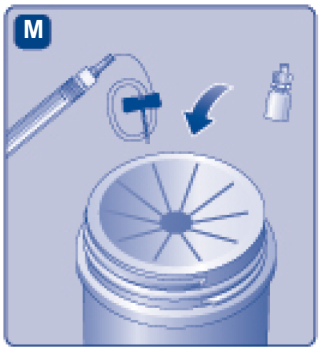
Injecting the solution via a central venous access device (CVAD) such as a central venous catheter or a subcutaneous port:

- Use a clean and germ-free (aseptic) technique. Follow the instructions for proper use of 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 the injection of Esperoct, use sodium chloride 9 mg/mL (0.9%) solution for injection.

Disposal

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

  Do not discard them into the ordinary household waste.



Do not disassemble the equipment before disposal.

Do not reuse the equipment.