NovoSeven®
1 mg (50 KIU) powder and solvent for solution for injection
2 mg (100 KIU) powder and solvent for solution for injection

Qualitative and quantitative composition

eptacog alfa (activated) 1 mg/vial (corresponds to 50 KIU/vial), 1mg/ml after reconstitution
eptacog alfa (activated) 2 mg/vial (corresponds to 100 KIU/vial), 1mg/ml after reconstitution
1 KIU equals 1000 IU (International Units)
eptacog alfa (activated) is recombinant coagulation factor VIIa (rFVIIa) with a molecular mass of approximately 50,000 Daltons produced in baby hamster kidney cells (BHK Cells) by recombinant DNA technology.

After reconstitution, the product contains 1mg/ ml eptacog alfa (activated) when reconstituted with solvent.

For a full list of excipients, see *List of excipients*.

Pharmaceutical form

Powder and solvent for solution for injection.
White lyophilized powder. Solvent: clear colourless solution. The reconstituted solution has a pH of approximately 6.0.

Clinical particulars

Therapeutic indications

NovoSeven® is indicated for the treatment of bleeding episodes and for the prevention of bleeding in those undergoing surgery or invasive procedures in the following patient groups:
• in patients with congenital haemophilia with inhibitors to coagulation factors VIII or IX > 5 Bethesda Units (BU)
• in patients with congenital haemophilia who are expected to have a high anamnestic response to factor VIII or factor IX administration
• in patients with acquired haemophilia

Posology and method of administration

Treatment should be initiated under the supervision of a physician experienced in the treatment of haemophilia and/or bleeding disorders.
Posology

Haemophilia A or B with inhibitors or expected to have a high anamnestic response
Dose
NovoSeven® should be given as early as possible after the start of a bleeding episode. The recommended initial dose, administered by intravenous bolus injection, is 90 µg per kg body weight.
Following the initial dose of NovoSeven® further injections may be repeated. The duration of treatment and the interval between injections will vary with the severity of the haemorrhage, the invasive procedures or surgery being performed.

Dosing in children
Current clinical experience does not warrant a general differentiation in dosing between children and adults, although young children have faster clearance than

adults. Therefore, higher doses of rFVIIa may be needed in paediatric patients to achieve similar plasma concentrations as in adult patients, see *Pharmacokinetic properties*.

Dose interval
Initially 2 - 3 hours to obtain haemostasis.
If continued therapy is needed, the dose interval can be increased successively once effective haemostasis is achieved to every 4, 6, 8 or 12 hours for as long as treatment is judged as being indicated.

Mild to moderate bleeding episodes (including home therapy)
Early intervention has been shown to be efficacious in the treatment of mild to moderate joint, muscle and mucocutaneous bleeds. Two to three injections of 90 µg per kg body weight administered at three-hour intervals. If further treatment is required, one additional dose of 90 µg per kg body weight can be administered. The duration of the home therapy should not exceed 24 hours.Only after consultation with the haemophilia treatment centre can continued home treatment be considered.

Serious bleeding episodes
An initial dose of 90 µg per kg body weight is recommended and could be administered on the way to the hospital where the patient is usually treated. The following dose varies according to the type and severity of the haemorrhage. Dosing frequency should initially be every second hour until clinical improvement is observed. If continued therapy is indicated, the dose interval can then be increased to 3 hours for 1 - 2 days. Thereafter, the dose interval can be increased successively to every 4, 6, 8 or 12 hours for as long as treatment is judged as being indicated. A major bleeding episode may be treated for 2 - 3 weeks but can be extended beyond this if clinically warranted.

Invasive procedure/surgery
An initial dose of 90 µg per kg body weight should be given immediately before the intervention. The dose should be repeated after 2 hours and then at 2 - 3 hour intervals for the first 24 - 48 hours depending on the intervention performed and the clinical status of the patient. In major surgery, the dose should be continued at 2 - 4 hour intervals for 6 - 7 days. The dose interval may then be increased to 6 - 8 hours for another 2 weeks of treatment. Patients undergoing major surgery may be treated for up to 2 - 3 weeks until healing has occurred.

Acquired Haemophilia
Dose and dose interval
NovoSeven® should be given as early as possible after the start of a bleeding episode. The recommended initial dose, administered by intravenous bolus injection, is 90 µg per kg body weight. Following the initial dose of NovoSeven® further injections may be given if required. The duration of treatment and the interval between injections will vary with the severity of the haemorrhage, the invasive procedures or the surgery being performed.
The initial dose interval should be 2 - 3 hours. Once haemostasis has been achieved, the dose interval can be increased successively to every 4, 6, 8, or 12 hours for as long as treatment is judged to be indicated.

Method of administration
Reconstitute the solution as described under NovoSeven® user instructions and slowly administer as an intravenous bolus injection over 2-5 minutes.

Monitoring of treatment – Laboratory Tests
There is no requirement for monitoring of NovoSeven® therapy. Severity of bleeding condition and clinical response to NovoSeven® administration must guide dosing requirements.
After administration of rFVIIa, prothrombin time (PT) and activated partial thromboplastin time (aPTT) have been shown to shorten, however no correlation has been demonstrated between PT and aPTT and clinical efficacy of rFVIIa.

Contraindications
Hypersensitivity to the active substance orto any of the excipients listed in List of excipients, or to mouse, hamster or bovine protein.

Special warnings and precautions for use
In pathological conditions in which tissue factor may be expressed more extensively than considered normal, there may be a potential risk of development of thrombotic events or induction of Disseminated Intravascular Coagulation (DIC) in association with NovoSeven® treatment.

Such situations may include patients with advanced atherosclerotic disease, crush injury, septicaemia or DIC. Because of the risk of thromboembolic complications, caution should be exercised when administering NovoSeven® to patients with a history of coronary heart
disease, to patients with liver disease, to patients Post-operatively, to neonates, or to patients at risk of thromboembolic phenomena or
disseminated intravascular coagulation. In each of these situations, the potential benefit of treatment with NovoSeven® should be weighed against the risk of these complications.

If allergic or anaphylactic-type reactions occur, the administration should be discontinued immediately. In case of anaphylactic shock, standard medical treatment for shock should be implemented. Patients should be informed of the early signs of hypersensitivity reactions. If such symptoms occur, the patient should be advised to discontinue use of the product immediately and contact their physician.

In case of severe bleeds, the product should be administered in hospitals preferably specialized in treatment of haemophilia patients with coagulation factor VIII or IX inhibitors, or if not possible in close collaboration with a physician specialized in haemophilia treatment.

If bleeding is not kept under control, hospital care is mandatory. Patients/carers should inform the physician/supervising hospital at the earliest possible opportunity about all usages of NovoSeven®.

Interaction with other medicinal products and other forms of interaction
The risk of a potential interaction between NovoSeven® and coagulation factor concentrates is unknown. Simultaneous use of prothrombin complex concentrates, activated or not, should be avoided.

Anti-fibrinolytics have been reported to reduce blood loss in association with surgery in haemophilia patients, especially in orthopaedic surgery and surgery in regions rich in fibrinolytic activity, such as the oral cavity. Experience with concomitant administration of anti-fibrinolytics and rFVIIa treatment is however limited.

Based on a non-clinical study (see *Preclinical safety data*) it is not recommended to combine rFVIIa and rFXIII.
There are no clinical data available on interaction between rFVIIa and rFXIII.

Pregnancy and lactation
Pregnancy
As a precautionary measure it is preferable to avoid the use of NovoSeven® during pregnancy. Data on a limited number of exposed pregnancies within approved indications indicate no adverse effects of rFVIIa on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development,

Breastfeeding
It is unknown whether rFVIIa is excreted in human breast milk. The excretion of rFVIIa in milk has not been studied in animals. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with NovoSeven® should be made taking into account the benefit of breast-feeding to the child and the benefit of NovoSeven® therapy to the woman.

Fertility
Data from non-clinical studies as well as post-marketing data show no indication that rFVIIa has a harmful effect on male or female fertility.

Effects on ability to drive and use machines
No studies on the effect on the ability to drive and use machines have been performed.

Undesirable effects
Summary of the safety profile
The most frequently reported adverse drug reactions are decreased therapeutic response, pyrexia, rash, venous thromboembolic events, pruritus and urticaria. These reactions are reported as uncommon (≥ 1/1,000, < 1/100).

Summary of adverse reactions
Adverse reactions reported during clinical trials and from spontaneous (post-marketing) reports are listed below. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Adverse drug reactions reported post-marketing only (i.e. not in clinical trials) are presented with a frequency of 'not known'.

Clinical trials conducted in 484 patients (including 4297 treatment episodes) with haemophilia A and B, acquired haemophilia, factor VII deficiency or Glanzmann's thrombasthenia have shown that adverse drug reactions are common (≥ 1/100 to < 1/10). As the total number of treatment episodes in clinical trials is below 10,000, the lowest possible frequency of adverse drug reactions that can be assigned is rare (≥ 1/10,000 to < 1/1,000).

The frequencies of both serious and non-serious adverse drug reactions are listed by system organ classes below.

Blood and lymphatic system disorders
Rare (> 1/10,000, < 1/1,000)
Disseminated intravascular coagulation and related laboratory findings including elevated levels of D-dimer and decreased levels of AT, see Special warnings and precautions for use.

Coagulopathy.

Gastrointestinal disorders
Rare (≥ 1/10,000, < 1/1,000)
– Nausea

General disorders and administration site conditions
Uncommon (≥ 1/1,000, < 1/100)
– Therapeutic response decreased*
– Pyrexia

Rare (≥ 1/10,000, < 1/1,000)
– Injection site reaction including injection site pain

Immune system disorders
Rare (> 1/10,000, < 1/1,000)
- Hypersensitivity (see Contraindications and Special warnings and precautions for
use).
Frequency not known
- Anaphylactic reaction.

Investigations
Rare (≥ 1/10,000, < 1/1,000)
– Increased fibrin degradation products
– Increase of alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase and prothrombin

Nervous system disorders
Rare (> 1/10,000, < 1/1,000)
- Headache.

Skin and subcutaneous tissue disorders
Uncommon (≥ 1/1,000, < 1/100)
– Rash (including allergic dermatitis and rash erythematous)
– Pruritus and urticaria

Frequency not known
– Flushing
– Angioedema

Vascular disorders

Uncommon (> 1/1,000, < 1/100)
Venous thromboembolic events: (deep vein thrombosis, thrombosis at i.v. site, pulmonary embolism, thromboembolic events of the liver including portal vein thrombosis, renal vein thrombosis, thrombophlebitis, superficial thrombophlebitis and intestinal ischaemia).

Rare (≥ 1/10,000, < 1/1,000)
– Arterial thromboembolic events (myocardial infarction, cerebral infarction, cerebral ischaemia, cerebral artery occlusion, cerebrovascular accident, renal artery thrombosis, peripheral ischaemia, peripheral arterial thrombosis and intestinal ischaemia)
– Angina pectoris

Frequency not known

– Intracardiac thrombus

*Lack of efficacy (therapeutic response decreased) has been reported. It is important that the dosage regimen of NovoSeven® is compliant with the recommended dosage as stated in Posology and method of administration.

Description of selected adverse reactions
Inhibitory antibody formation
In post-marketing experience, there have been no reports of inhibitory antibodies against NovoSeven® RT or FVII in patients with haemophilia A or B. Development of inhibitory antibodies to NovoSeven® RT has been reported in a post-marketing observational registry of patients with congenital FVII deficiency.

In clinical trials of patients with factor VII deficiency, formation of antibodies against NovoSeven® RT and FVII is the only adverse drug reaction reported (frequency: common (≥ 1/100 to < 1/10)). In some cases, the antibodies showed inhibitory effect *in vitro.* Risk factors that may have contributed to antibody development including previous treatment with human plasma and/or plasma-derived factor VII, severe mutation of FVII gene, and overdose of NovoSeven® RT, were present. Patients with factor VII deficiency treated with NovoSeven® RT should be monitored for factor VII antibodies (see *Special warnings and precautions for use*).

Thromboembolic events – arterial and venous
When NovoSeven® RT is administered to patients outside approved indications, arterial thromboembolic events are common (≥ 1/100 to < 1/10). A higher risk of arterial thromboembolic adverse events (see *Undesirable effects; Vascular disorders*) (5.6% in patients treated with NovoSeven® RT versus 3.0% in placebo-treated patients) has been shown in a meta-analysis of pooled data from placebo-controlled trials conducted outside current approved indications in various clinical settings, each of these having distinct patient characteristics and hence different underlying risk profiles.

Safety and efficacy of NovoSeven® RT have not been established outside the approved indications, and therefore NovoSeven® RT should not be used.

Thromboembolic events may lead to cardiac arrest.

Other Special Populations
Patients with acquired haemophilia
Clinical trials conducted in 61 patients with acquired haemophilia with a total of 100 treatment episodes, showed that certain adverse drug reactions were reported more frequent (1% based on treatment episodes):
Arterial thromboembolic events (cerebral artery occlusion, cerebrovascular accident), venous thromboembolic events (pulmonary embolism and deep vein thrombosis), angina pectoris, nausea, pyrexia, erythematous rash and investigation of increased levels of fibrin degradation products.

Overdose
Dose limiting toxicities of NovoSeven® have not been investigated in clinical trials.
Four cases of overdose have been reported in patients with haemophilia in 16 years. The only complication reported in connection with an overdose was a slight

transient increase in blood pressure in a 16- year-old patient receiving 24 mg rFVIIa instead of 5.5 mg.

No cases of overdose have been reported in patients with acquired haemophilia.

The dose schedule should not be intentionally increased above the recommended doses due to the absence of information on the additional risk that may be incurred.

Pharmacological properties
Pharmacodynamic properties
Pharmacotherapeutic group: Blood Coagulation factors, ATC code: B02BD08

Mechanism of Action
NovoSeven® contains activated recombinant coagulation factor VII. The mechanism of action includes the binding of factor VIIa to exposed tissue factor. This complex activates factor IX into factor IXa and factor X into factor Xa, leading to the initial conversion of small amounts of prothrombin into thrombin. Thrombin leads to the activation of platelets and factors V and VIII at the site of injury and to the formation of the haemostatic plug by converting fibrinogen into fibrin. Pharmacological doses of NovoSeven® activate factor X directly on the surface of activated platelets, localized to the site of injury, independently of tissue factor. This results in the conversion of prothrombin into large amounts of thrombin independently of tissue factor.

Pharmacodynamic effects
The pharmacodynamic effect of factor VIIa gives rise to an increased local formation of factor Xa, thrombin and fibrin.
A theoretical risk for the development of systemic activation of the coagulation system in patients suffering from underlying diseases predisposing them to DIC cannot be totally excluded.

Pharmacokinetic properties
Healthy subjects
Distribution, Elimination and Linearity
Using the FVII clotting assay, the pharmacokinetics of rFVIIawere investigated in 35 healthy Caucasian and Japanese subjects in a dose-escalation study. Subjects were stratified according to sex and ethnic group and dosed with 40, 80 and 160 µg rFVIIa per kg body weight (3 doses each) and/or placebo. The pharmacokinetic profiles indicated dose proportionality. The pharmacokinetics were similar across sex and ethnic groups. The mean steady state volume of distribution ranged from 130 to 165 mL/kg, the mean values of clearance ranged from 33.3 to 37.2 ml/h x kg, and the mean terminal half-life ranged from 3.9 to 6.0 hours.

Haemophilia A and B with inhibitors
Distribution, elimination and linearity
Using the FVIIa assay, the pharmacokinetic properties of rFVIIa were studied in 12 paediatric (2 - 12 years) and 5 adult patients in non-bleeding state. Dose proportionality was established in children for the investigated doses of 90 and 180 µg per kg body weight, which is in accordance with previous findings at lower doses (17.5 - 70 µg/kg rFVIIa). The mean clearance was approximately 50% higher in paediatric patients relative to adults (78 versus 53 ml/h x kg), whereas the mean terminal half-life was determined to 2.3 hours in both groups. Mean volume of distribution at steady state was 196 mL/kg in paediatric patients versus 159 mL/kg in adults. Clearance appears related with age, therefore in younger patients clearance may be increased by more than 50%.

Preclinical safety data
All findings in the preclinical safety programme were related to the pharmacological effect of rFVIIa.

A potential synergistic effect of combined treatment of rFXIII and rFVIIa in an advanced cardiovascular model in cynomolgus monkey resulted in exaggerated pharmacology (thrombosis and death) at a lower dose level than when administering the individual compounds.

Pharmaceutical Particulars
List of excipients
Powder
Sodium chloride, calcium chloride dihydrate, glycylglycine, polysorbate 80, mannitol, sucrose, methionine, hydrochloric acid (for pH-adjustment) and sodium hydroxide (for pH-adjustment).

Solvent
Histidine, hydrochloric acid (for pH-adjustment), sodium hydroxide (for pH-adjustment) and water for injections.

Incompatibilities
NovoSeven® must not be mixed with infusion solutions or be given in a drip.

Shelf life
After reconstitution, chemical and physical stability has been demonstrated for 6 hours at 30ºC and 24 hours at 5ºC.
From a microbiological point of view, the product should be used immediately. If not used immediately, storage time and storage conditions prior to use are the responsibility of the user, and should not be longer than 24 hours at 2°C - 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Special precautions for storage
- Store powder and solvent below 30°C
- Store powder and solvent protected from light
- Do not freeze
- For storage conditions of the reconstituted medicinal product, see *Shelf life*.

Nature and contents of container
Each NovoSeven® package contains:
- 1 vial with white powder for solution for injection
– 1 pre-filled syringe with solvent for reconstitution.
– 1 plunger rod
– 1 vial adapter with an integrated particle filter.

The NovoSeven® package contains:
Vial: Type I glass vial closed with a chlorobutyl rubber stopper, covered with an aluminium cap. The closed vial is equipped with a polypropylene tamper-evident snap-off cap.

Pre-filled syringe: Type I glass barrel with a polypropylene backstop and bromobutyl rubber plunger. The syringe cap consists of bromobutyl rubber and polypropylene tamper evident seal.

Plunger rod: made of polypropylene.

Not all pack sizes may be marketed.

Product Owner
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

NovoSeven® is a trademark owned by Novo Nordisk Health Care AG, Switzerland.

Instructions on how to use NovoSeven®

READ THESE INSTRUCTIONS CAREFULLY BEFORE USING NOVOSEVEN®

NovoSeven® is supplied as a powder. Before injection (administration) it must be reconstituted with the solvent supplied in the syringe. The solvent is a histidine solution. The reconstituted NovoSeven® must be injected into your vein (intravenous injection). The equipment in this package is designed to reconstitute and inject NovoSeven®.

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 NovoSeven® 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 vein, it is important **to use a clean and germ free (aseptic) technique.** An 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 'Expiry' 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.

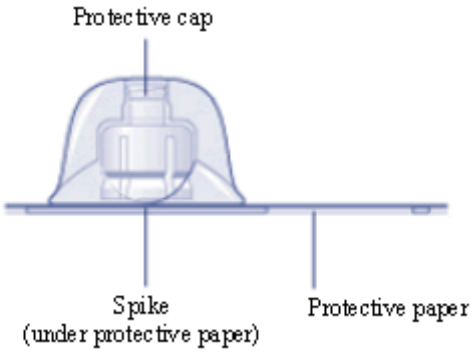
Contents

The package contains:
- 1 vial with NovoSeven® powder
- 1 vial adapter
- 1 pre-filled syringe with solvent
- 1 plunger rod (placed under the syringe)

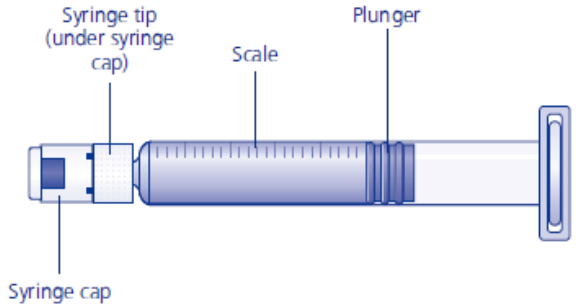
Overview

Vial with NovoSeven® powder

Vial adapter



Pre-filled syringe with solvent



Plunger rod

1. Prepare the vial and the syringe

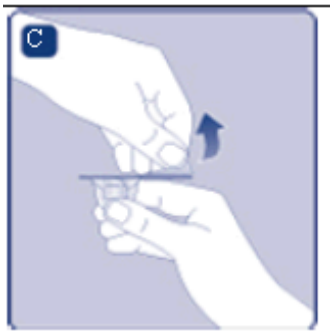
- **Take out the number of NovoSeven® packages you need.**
- **Check the expiry date.**
- **Check the name, stength and colour** of the package, to make sure it contains the correct product.
- **Wash your hands** and dry them properly using a clean towel or air dry.
- Take the vial, vial adapter and 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** (not above 37°C). 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** on the vial with a sterile alcohol swab and allow it to dry for a few seconds before use.
- **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.

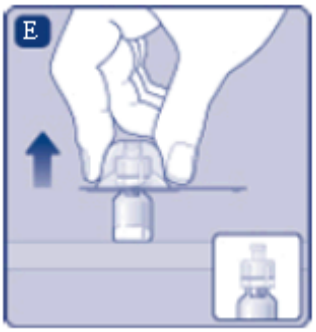


Do not take the vial adapter out of the protective cap. If you touch the spike on the vial adapter, germs from your fingers can be transferred.

- **Place the vial on a flat and solid surface.**
- **Turn over the protective cap,** and snap the vial adapter onto the vial.

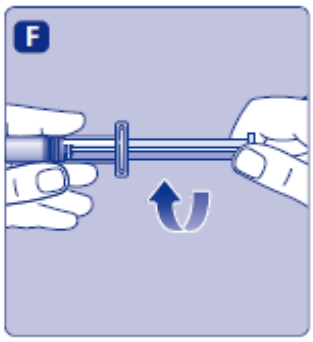
Once attached, do not remove the vial adapter from the vial.

- Lightly **squeeze the protective cap** with your thumb and index finger as shown.
  Remove the protective cap from the vial adapter.



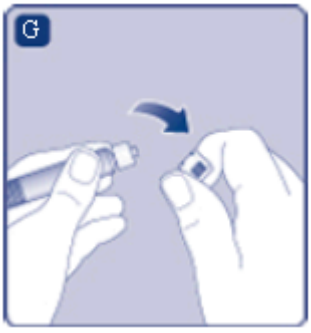
Do not lift the vial adapter from the vial when removing the protective cap.

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.

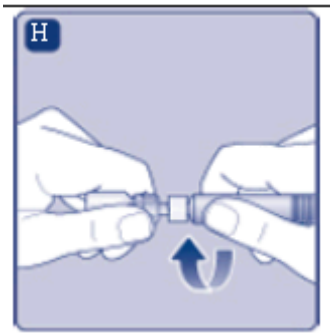
Immediately connect the plunger rod to the syringe by turning it clockwise into the plunger inside the pre-filled syringe until resistance is felt.



• **Remove the syringe cap** from the pre-filled syringe by bending it down until the perforation breaks.

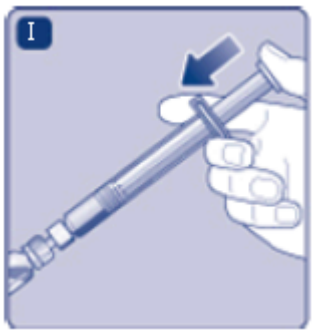
Do not touch the syringe tip under the syringe cap.

If 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 colourless. **If you notice visible particles or discolouration, do not use it.** Use a new package instead.

Use the reconstituted NovoSeven® at once to avoid infections.

If you cannot use it at once, see *Shelf life* on the other side of this leaflet.
Do not store the reconstituted solution without advice from your doctor or nurse.

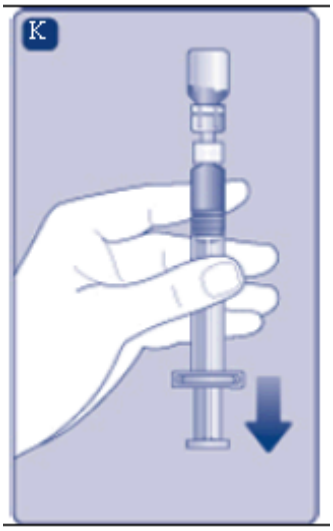
ⓘ If your dose requires more than one vial, repeat steps **A** to **J** with additional vials, vial adapters and prefilled syringes until you have reached your required dose.

- **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 mixed 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 reconstituted solution, use the scale on the syringe to see how much of the solution you withdraw, as instructed by your doctor or nurse.



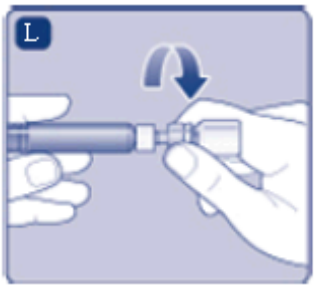
- If, at any point, there is too much air in the syringe, inject the air back into the vial.

- 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.



Injecting NovoSeven® with a pre-filled syringe 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 drug and/or result in damage to the needleless connector.

Follow the instructions for use for the needleless connector. Administration through a needleless connector may require withdrawal of the reconstituted solution into a standard 10 ml sterile luer-lock plastic syringe. This should be done right after step J.

5. Inject the reconstituted solution

NovoSeven® is now ready to inject into your vein.

• Inject the reconstituted solution as instructed by your doctor or nurse.

• Inject slowly over 2 to 5 minutes.

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.
• If the CVAD line needs to be flushed before or after NovoSeven® injection, use sodium chloride 9 mg/ml solution for injection.

Disposal

- **After injection, safely dispose** of the syringe with the infusion set, the vial with the vial adapter, any unused NovoSeven® and other waste materials as instructed by your doctor or nurse.
- Do not throw it out with the ordinary household waste.

Do not disassemble the equipment before disposal.

Do not reuse the equipment.