Scheduling Status

S4

Proprietary name (and dosage form)

NovoSeven® 1 mg - Powder and solvent for solution for injection

NovoSeven® 2 mg - Powder and solvent for solution for injection

NovoSeven® 5 mg - Powder and solvent for solution for injection

Composition

- NovoSeven® 1 mg (corresponds to 50 KIU) contains 1 mg/vial activated recombinant coagulation factor VIIa (eptacog alfa).
- NovoSeven® 2 mg (corresponds to 100 KIU) contains 2 mg/vial activated recombinant coagulation factor VIIa (eptacog alfa).
- NovoSeven® 5 mg (corresponds to 250 KIU) contains 5 mg/vial activated recombinant coagulation factor VIIa (eptacog alfa).

The activated recombinant coagulation factor VIIa (eptacog alfa) is[1] produced in baby hamster kidney cells (BHK) by recombinant DNA technology.

After reconstitution 1 ml solution contains 1 mg eptacog alfa (activated).

1 KIU equals 1000 IU (International units).

Excipients:

After reconstitution 1 ml solution contains 10 mg sucrose, 25 mg mannitol and 0,5 mg (0,05 % m/v) methionine (an antioxidant).

1. **The activated recombinant coagulation factor VIIa (eptacog alfa) is**
Anchor Name: The activated recombinant coagulation factor VIIa (eptacog alfa) is *[Agency Jcostello@rti.org]*

Pharmacological classification

A 8.1 Coagulants, Haemostatics

Pharmacological action

Pharmacodynamic properties:

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, localised 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. Accordingly, 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 Disseminated Intravascular Coagulation (DIC) cannot be totally excluded.

Pharmacokinetic properties:

Healthy subjects

Using the FVII clotting assay, the pharmacokinetics of NovoSeven® were 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

[no notes on this page]

40, 80 and 160 µg NovoSeven® per kg body weight and /or placebo (3 doses each). 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/kg/h, and the mean terminal half-life ranged from 3,9 to 6,0 hours.

Haemophilia A and B with inhibitors

Using the FVIIa assay, the pharmacokinetic properties of NovoSeven® 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). Mean clearance was approximately 50 % higher in paediatric patients relative to adults (78 versus 53 ml/kg/h), 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 %.

Factor VII deficiency

Single dose pharmacokinetics of NovoSeven®, 15 and 30 µg per kg body weight, showed no significant difference, between the two doses used with regard to dose-independent parameters: total body clearance (70,8 – 79,1 ml/h x kg), volume of distribution at steady state (280 - 290 ml/kg), mean residence time (3,75 – 3,80 h), and half-life (2,82 – 3,11 h). The mean *in vivo* plasma recovery was approximately 20 %.

[no notes on this page]

Glanzmann's thrombasthenia

Pharmacokinetics of NovoSeven® in patients with Glanzmann's thrombasthenia has not been investigated, but is expected to be similar to the pharmacokinetics in haemophilia A and B patients.

Indications

- NovoSeven® is intended for use in the treatment of patients with haemophilia with inhibitors to coagulation factor VIII and factor IX. The use of NovoSeven® is indicated for patients suffering life- or limb-threatening bleeds or requiring surgery and in home-treatment setting for early intervention to treat mild to moderate bleeding episodes.
- NovoSeven® is indicated for the treatment of bleeding episodes and for the prevention of bleeding in patients with congenital FVII deficiency undergoing surgery or invasive procedures.
- NovoSeven® is indicated for the treatment of bleeding episodes and for the prevention of bleeding in those patients undergoing surgery or invasive procedures with Glanzmann's thrombasthenia with antibodies to GP IIb-IIIa and/or HLA, and with past or present refractoriness to platelet transfusion.
- NovoSeven® is indicated for the treatment of bleeding episodes and for the prevention of bleeding in those patients with acquired haemophilia undergoing surgery or invasive procedures.

[no notes on this page]

Contra-indications

Known hypersensitivity to the active ingredient, the excipients, or to mouse, hamster or bovine protein.

Warnings

Arterial thromboembolic events outside approved indications

When NovoSeven® is administered to patients outside current approved indications, arterial thromboembolic events are common (≥1/100 to <1/10).

A higher risk of arterial thromboembolic adverse events (5,6 % in patients treated NovoSeven® 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.

Thromboembolic events may lead to cardiac arrest.

Safety and efficacy of NovoSeven® have not been established outside the approved indications and therefore NovoSeven® is not recommended.

Patients receiving NovoSeven® after major surgery or in pathological conditions in which tissue factor may be expressed more extensively than considered normal e.g. conditions like advanced atherosclerotic disease, crush injury, liver failure, malignancy or septicemia, there may be a potential risk of development of thrombotic events or induction of disseminated intravascular coagulation (DIC) in association with NovoSeven® treatment. Patients in such conditions receiving NovoSeven® should be kept under close observation for signs and symptoms of untoward activation of the coagulation system or thrombosis.

[no notes on this page]

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 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. As recombinant coagulation factor VIIa, NovoSeven® may contain trace amounts of mouse IgG, bovine IgG and other residual culture proteins (hamster and bovine serum protein), the remote possibility exists that patients treated with this product may develop hypersensitivity to these proteins. If allergic or anaphylactic-type reactions occur, the administration should be discontinued immediately. In case of 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 and contact their physician.

In case of severe bleeds the product should be administered in hospitals preferably specialised 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.

In case of mild to moderate bleeding episodes, the product may be administered at home; however this should only be done in close collaboration with a haemophilia centre where the patient is regularly followed up.

There is no clinical experience with administration of a single dose of 270 µg per kg body weight in elderly patients.

The duration of home treatment should not exceed 24 hours.

[no notes on this page]

If bleeding is not kept under control, hospital care is mandatory. Patients with rare hereditary problems of fructose intolerance, glucose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Interactions

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 NovoSeven® treatment is however limited.

Pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Lactation

It is not known whether NovoSeven® is excreted in human breast milk.

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 benefit of NovoSeven® therapy to the woman.

Women of Childbearing Potential:

It is not known whether NovoSeven® can affect reproduction capacity.

[no notes on this page]

Fertility:

It is not known whether NovoSeven® can affect reproduction capacity.

Dosage and directions for use

NovoSeven® is for intravenous bolus administration only. Favourable clinical results have been observed after administration of a dose of 3 - 6 KIU (60 - 120 µg) per kg body weight given at intervals of 2 hours or more according to the type of bleeding and the effect obtained in the treatment of life- and limb-threatening bleeds and in connection with surgery.

Haemophilia A or B with inhibitors

(i) Serious bleeding episodes:

The dosage varies according to the type and severity of the haemorrhages. As a guideline an initial dosage of 4,5 KIU (90 µg) per kg body weight is recommended. 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.

(ii) *Surgery/invasive procedure:*

An initial dose of 4,5 KIU (90 µg) per kg body weight should be given immediately before the procedure. The dose should be repeated after 2 hours and then 2 - 3

[no notes on this page]

hours intervals for the first 24 - 48 hours depending on the surgery performed and the clinical status of the patient.

In major surgery, the dosage 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 two weeks of treatment. Patients undergoing surgery may be treated for up to 2 - 3 weeks until healing has occurred.
For patients with factor IX inhibitors or acquired antibodies to factor VIII, only experience of the use of NovoSeven® in minor surgery exists.

(iii) Mild to moderate bleeding episodes (Including home treatment setting):
Early intervention has shown to be efficacious in the treatment of mild to moderate joint, muscle and mucocutaneous bleeds.

Two dosing regimens can be recommended:

1. One to three injections of 90 µg (4,5 KIU) 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.
2. One single injection of 270 µg per kg body weight.

The duration of the home treatment should not exceed 24 hours.

Dosing in children
Current clinical experience does not warrant a general differentiation in dosing between children and adults, although 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.

[no notes on this page]

Factor VII deficiency

The recommended dose range for treatment of bleeding episodes and for the prevention of bleeding in patients undergoing surgery or invasive procedures is 15 – 30 µg per kg body weight every 4 - 6 hours until haemostasis is achieved. Dose and frequency of injections should be adequate to each individual.

Glanzmann's thrombasthenia

The recommended dose range for treatment of bleeding episodes and for the prevention of bleeding in patients undergoing surgery or invasive procedures is 90 µg (range 80 - 120 µg) per kg body weight at intervals of two hours (1,5 – 2,5 hours). At least three doses should be administered to secure effective haemostasis. The recommended route of administration is bolus injection as lack of efficacy may appear in connection with continuous infusion.

For those patients who are not refractory, platelets are the first line treatment for Glanzmann's thrombasthenia.

Acquired Haemophilia

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.

[no notes on this page]

NovoSeven® Powder in vial/Histidine solvent in pre-filled syringe:

Reconstitution:

Always use aseptic technique

- The NovoSeven® powder vial and pre-filled syringe with solvent should be at room temperature at reconstitution. Remove the plastic cap from the vial. If the 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 after wiping it.
- Remove the protective paper from the vial adaptor. Do not take the vial adaptor out of the protective cap. If the protective paper is not fully sealed or it is broken do not use the vial adaptor. Turn over the protective cap, and snap the vial adaptor onto the vial. Lightly squeeze the protective cap with the thumb and index finger. Remove the protective cap from the vial adaptor.
- Screw the plunger rod 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 adaptor until resistance is felt. Hold the pre-filled syringe slightly tilted with the vial pointing downwards. Make sure not to aim the stream of solvent directly at the NovoSeven® powder as this will cause foaming. 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.

[no notes on this page]

If a larger dose is needed, repeat the procedure with additional vials, pre-filled syringes and vial adaptors.

The NovoSeven® reconstituted solution is colourless and should be inspected visually for particulate matter and discoloration prior to administration.

It is recommended to use NovoSeven® immediately after reconstitution.

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 to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Administration

- 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 mixed solution into the syringe.
  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.

If the entire dose is not required, use the scale on the syringe to see how much mixed solution is withdrawn.

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- Unscrew the vial adaptor with the vial.

- NovoSeven® is now ready for injection. Locate a suitable site, and slowly inject NovoSeven® into a vein over a period of 2 – 5 minutes without removing the needle from the injection site.

Safely dispose of the used materials. Any unused product or waste material should be disposed of as instructed by your healthcare professional.

Side-Effects and Special Precautions

Side effects

Clinical trials conducted in 484 patients (including 4297 treatment episodes) with haemophilia A and B, acquired haemophilia, factor VII deficiency and Glanzmann's thrombasthenia have shown that adverse reactions are common (≥1/100 to <1/10). As the total number of treatment episodes is below 10 000, the lowest possible frequency of adverse reactions that can be assigned is rare (≥1/10 000, <1/1000).

The most frequent adverse reactions are pyrexia and rash, and the most serious adverse reaction are thromboembolic events.
The frequencies of both serious and non-serious adverse reactions are listed by system organ classes in the table below:

[no notes on this page]

System Organ Class	Side effects
Blood and lymphatic disorders	Rare (≥1/10 000, <1/1000) • Disseminated intravascular coagulation and related laboratory findings including elevated levels of D-dimer and decreased levels of AT-III • Coagulopathy
Immune system disorders	Rare (≥1/10 000, <1/1000) • Hypersensitivity *Not known • Anaphylactic reaction
Gastrointestinal disorders	Rare (≥1/10 000, <1/1000) • Nausea
Nervous system disorders	Rare (≥1/10 000, <1/1000) • Headache
Vascular disorders	Rare (≥1/10 000, <1/1000) • 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 Uncommon (≥1/1000, <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 *Arterial thromboembolic events in patients with acquired*

[no notes on this page]

	haemophilia have a frequency of common (≥1/100 to <1/10). Not known • Intracardiac thrombus
Skin and subcutaneous tissue disorders	Uncommon (≥1/1000, <1/100) • Rash (including allergic dermatitis and rash erythematous) • Pruritus and urticaria *Not known • Flushing • Angioedema
General disorders and administration site conditions	Uncommon (≥1/1000; <1/100) • Therapeutic response decreased (It is important that the dosage regimen of NovoSeven® is compliant with recommended dosage.) • Pyrexia Rare (≥1/10 000, <1/1000) • Injection site reaction including injection site pain
Investigations	Rare (≥1/10 000, <1/1000) • Increase of alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase and prothrombin levels have been reported • Increased fibrin degradation products

**Adverse reactions reported post-marketing only (i.e. not in clinical trials) are presented with a frequency of not known.*

Special precautions

There have been no reports of antibodies against factor VII in haemophilia patients.

[no notes on this page]

Patients with Factor VII deficiency

Formation of antibodies against NovoSeven® and FVII is the only adverse reaction reported in these clinical trials of patients with factor VII deficiency exposed to NovoSeven® (frequency: common ≥1/100 to <1/10). In two out of five patients with reported antibody formation against NovoSeven® and FVII, reported in clinical trials and post-marketing, 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®, were present.

Patients with factor VII deficiency treated with NovoSeven® should be monitored for factor VII antibodies.

Factor VII deficient patients should be monitored for prothrombin time and factor VII coagulant activity before and after administration of NovoSeven®. In case the factor VIIa activity fails to reach the expected level or bleeding is not controlled after treatment with the recommended doses, antibody formation may be suspected and analysis for antibodies should be performed.

The risk of thrombosis in factor VII deficient patients treated with NovoSeven® is unknown.

Glanzmann's thrombasthenia

One case of angioneurotic oedema has been reported spontaneously in a patient with Glanzmann's thrombasthenia after administration of NovoSeven®.

[no notes on this page]

Effects on ability to drive and use machines

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

Known symptoms of overdosage and particulars of its treatment

Dose limiting toxicities of NovoSeven® have not been investigated in clinical trials. A few cases of overdose have been reported in patients with haemophilia. 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 or Glanzmann's thrombasthenia.

In patients with factor VII deficiency, where the recommended dose is 15 - 30 µg/kg rFVIIa, one episode of overdose has been associated with a thrombotic event (occipital stroke) in an elderly (>80 year) male patient treated with 10 – 20 times the recommended dose. In addition, the development of antibodies against NovoSeven® and FVII has been associated with overdose in one patient with factor VII deficiency.

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.

Treatment is symptomatic and supportive.

[no notes on this page]

Identification

Freeze-dried powder: A white, homogenous lyophilisate

Histidine solvent: A clear, colourless solution

Reconstituted product: A clear, colourless solution

Presentation

NovoSeven® Packages:

(a) NovoSeven® 1 mg (vial/syringe presentation):

- 1 x 2 ml clear colourless, type I glass vial containing 1 mg (50 KIU) freeze-dried recombinant coagulation factor VIIa. The vial is closed with grey chlorobutyl rubber stopper, which is sealed with gold coloured aluminium cap covered with yellow red tamper-evident snap-off polypropylene cap.
- 1 x 3 ml clear colourless, type I glass pre-filled syringe containing 1 ml Histidine solvent for reconstitution. The syringe consists of a glass barrel with a polypropylene backstop and bromobutyl rubber plunger. The syringe cap consists of bromobutyl rubber and polypropylene tamper evident seal. The plunger rod is made of polypropylene.

(b) NovoSeven® 2 mg (vial/syringe presentation):

- 1 x 2 ml clear colourless, type I glass vial containing 2 mg (100 KIU) freeze-dried recombinant coagulation factor VIIa. The vial is closed with grey chlorobutyl rubber stopper which is sealed with a gold coloured aluminium cap covered with light blue tamper-evident snap-off polypropylene cap.

[no notes on this page]

- 1 x 3 ml clear colourless, type I glass pre-filled syringe containing 2 ml Histidine solvent for reconstitution. The syringe consists of a glass barrel with a polypropylene backstop and bromobutyl rubber plunger. The syringe cap consists of bromobutyl rubber and polypropylene tamper evident seal. The plunger rod is made of polypropylene.

(c) NovoSeven® 5 mg (vial/syringe presentation):

- 1 x 13 ml clear colourless, type I glass vial containing 5 mg (250 KIU) freeze-dried recombinant coagulation factor VIIa. The vial is closed with grey chlorobutyl rubber stopper, which is sealed with a gold coloured aluminium cap covered with dark blue tamper-evident snap-off polypropylene cap.
- 1 x 10 ml clear colourless, type I glass pre-filled syringe containing 5 ml Histidine solvent for reconstitution. The syringe consists of a glass barrel with a polypropylene backstop and bromobutyl rubber plunger. The syringe cap consists of bromobutyl rubber and polypropylene tamper evident seal. The plunger rod is made of polypropylene.

The NovoSeven® Powder in vial/Histidine solvent in syringe product presentations come with a vial adaptor.

Storage instructions

Store powder and solvent at or below 25 °C.

Store powder and solvent protected from light.

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Do not remove powder and solvent vials or pre-filled syringe from the original outer carton to protect from light.

Avoid freezing to prevent damage to the solvent vial or pre-filled syringe.

Do not freeze the reconstituted solution.

After reconstitution, chemical and physical stability have been demonstrated for 6 hours at 25 °C and 24 hours at 2 - 8 °C.

Safely dispose of any unused product as instructed by your healthcare professional.

Do not use after expiry date.

Keep out of the reach and sight of children.

Registration numbers

a) NovoSeven® 1 mg: Freeze-dried powder and 1 ml Histidine Solvent pre-filled syringe: 44/8.1/0550

b) NovoSeven® 2 mg: Freeze-dried powder and 2 ml Histidine Solvent pre-filled syringe: 44/8.1/0551

c) NovoSeven® 5 mg: Freeze-dried powder and 5 ml Histidine Solvent pre-filled syringe: 44/8.1/0552

Name and business address of the holder of the certificate of registration

Novo Nordisk (Pty) Ltd

2nd Floor, Building A

345 Rivonia Boulevard

Edenburg, Rivonia

Sandton, 2128

[no notes on this page]

Date of publication of this package insert

08 January 2014

NS2 NovoSeven® 2 mg - Namibia Reg. No.: 11/30.3/0214

[no notes on this page]

Skeduleringstatus

S4

Eiendomsnaam (en doseervorm)

- NovoSeven® 1 mg - Poeier en oplosmiddel vir oplossing vir inspuiting
- NovoSeven® 2 mg - Poeier en oplosmiddel vir oplossing vir inspuiting
- NovoSeven® 5 mg - Poeier en oplosmiddel vir oplossing vir inspuiting

Samestelling

- NovoSeven® 1 mg (wat ooreenstem met 50 KIU) bevat 1 mg/flessie geaktiveerde rekombinante stollingsfaktor VIIa (*eptacog alfa*).
- NovoSeven® 2 mg (wat ooreenstem met 100 KIU) bevat 2 mg/flessie geaktiveerde rekombinante stollingsfaktor VIIa (*eptacog alfa*).
- NovoSeven® 5 mg (wat ooreenstem met 250 KIU) bevat 5 mg/flessie geaktiveerde rekombinante stollingsfaktor VIIa (*eptacog alfa*).

Die geaktiveerde rekombinante stollingsfaktor VIIa (*eptacog alfa*) word deur middel van rekombinante DNS-tegnologie in baba-hamsters se nierselle (BHN) geproduseer.

Na hersamestelling bevat 1 ml oplossing 1 mg *eptacog alfa* (geaktiveer).

1 KIU is gelykstaande aan 1000 IU (internasionale eenhede).

Mengmiddels:

Na hersamestelling bevat 1 ml oplossing 10 mg sukrose, 25 mg mannitol en 0,5 mg (0,05 % m/v) metionien ('n anti-oksidant).

[no notes on this page]

Farmakologiese klassifikasie

A 8.1 Stolmiddels, Hemostatikums

Farmakologiese werking

Farmakodinamiese eienskappe:

NovoSeven® bevat geaktiveerde rekombinante stollingsfaktor VII.

Die werkingsmeganisme is onder meer die binding van faktor VIIa aan blootgestelde weefselfaktor. Hierdie samestelling aktiveer faktor IX na faktor IXa en faktor X na faktor Xa, wat lei tot die aanvanklike omskepping van klein hoeveelhede protrombien in trombien. Trombien lei weer tot die aktivering van plaatjies en faktore V en VIII by die plek van besering en tot die vorming van die hemostatiese prop deur fibrinogeen in fibrien te omskep.

Farmakologiese dosisse van NovoSeven® aktiveer faktor X direk op die oppervlak van geaktiveerde plaatjies plaaslik, rondom die plek van besering, en onafhanklik van weefselfaktor. Dit geen aanleiding tot die omskepping van protrombien in groot hoeveelhede trombien, onafhanklik van weefselfaktor. Dienooreenkomstig gee die farmakodinamiese effek van faktor VIIa gevolg aan 'n verhoogde vorming van faktor Xa, trombien en fibrien.

'n Teoretiese risiko vir die ontwikkeling van sistemiese aktivering van die stollingstelsel in pasiënte wat aan onderliggende siektes ly wat hulle vatbaar maak vir Gedissemineerde Intravaskulêre Stolling (GIS), kan nie heeltemal uitgesluit word nie.

Farmakokinetiese eienskappe:

Gesonde proefpersone

[no notes on this page]

Deur gebruik te maak van die FVII-stollingstoets, is die farmakokinetika van NovoSeven® in 35 gesonde Kaukasiese en Japanese proefpersone in 'n dosis-verhogende studie ondersoek. Proefpersone is gestratifiseer volgens geslag en etniese groep en gedoseer met 40, 80 en 160 µg NovoSeven® per kg liggaamsgewig en/of plasebo (3 dosisse elk). Die farmakokinetiese profiele het op dosis-eweredigheid gedui. Die farmakokinetika was soortgelyk oor geslags- en etniese groepe.

Die gemiddelde volume van verspreiding teen ewewigstoestand het gewissel van 130 tot 165 ml/kg, die gemiddelde waardes van opruiming het gewissel van 33,3 tot 37,2 ml/kg/uur, en die gemiddelde terminale halflewe het gewissel van 3,9 tot 6,0 uur.

Hemofilie A en B met inhibitors

Deur gebruik te maak van die FVII-stollingstoets, is die farmakokinetiese eienskappe van NovoSeven® in 12 pediatriese (2 - 12 jaar) en 5 volwasse pasiënte in nie-bloeiende toestand bestudeer. Dosis-eweredigheid is in kinders bevestig vir die ondersoekdosisse van 90 en 180 µg per kg liggaamgewig, wat ooreenstem met vorige bevindings teen laer dosisse (17,5 – 70 µg/kg rFVIIa). Gemiddelde opruiming was ongeveer 50 % hoër in pediatriese pasiënte vergeleke met volwassenes (78 teenoor 53 ml/kg/uur), waarenteen die gemiddelde terminale halflewe as 2,3 uur in albei groepe vasgestel is. Gemiddelde volume van verspreiding teen ewewigstoestand was 196 ml/kg in pediatriese pasiënte teenoor 159 ml/kg in volwassenes. Opruiming hou oënskynlik verband met ouderdom, en derhalwe kan opruiming in jonger pasiënte met meer as 50 % verhoog word.

[no notes on this page]

Faktor VII-gebrek

Enkeldosis-farmakokinetika van NovoSeven®, 15 en 30 µg per kg liggaamsgewig, het geen noemenswaardige verskil tussen die twee dosisse getoon met betrekking tot dosis-onafhanklike parameters nie: totale liggaamlike opruiming (70,8 – 79,1 ml/u x kg), volume van verspreiding teen ewewigstoestand (280 - 290 ml/kg), gemiddelde inblywingstyd (3,75 – 3,80 uur), en halflewe (2,82 – 3,11 uur). Die gemiddelde *in vivo*-plasmaverhaling was ongeveer 20 %.

Glanzmann se trombastenie

Die farmakokinetika van NovoSeven® in pasiënte met Glanzmann se trombastenie is nie ondersoek nie, maar sal na verwagting soortgelyk wees aan die farmakokinetika in pasiënte met hemofilie A en B.

Indikasies

- NovoSeven® is bedoel vir gebruik in die behandeling van pasiënte met hemofilie met inhibitors vir die stollingsfaktore VIII en IX. Die gebruik van NovoSeven® is aangewese vir pasiënte wat aan lewensgevaarlike of ledemaat-gevaarlike bloedings ly of wat chirurgie vereis, en in die tuis-behandelingsmilieu vir vroeë intervensie om ligte tot matige episodes van bloeding te behandel.
- NovoSeven® is aangewese vir die behandeling van bloedingepisodes en vir die voorkoming van bloeding in pasiënte met aangebore FVII-gebrek wat chirurgie of indringende prosedures ondergaan.
- NovoSeven® is aangewese vir die behandeling van bloedingepisodes en vir die voorkoming van bloeding in pasiënte wat chirurgie of indringende prosedures ondergaan en wat Glanzmann se trombastenie met

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teenliggaampies op GP IIb-IIIa en/of HLA het, en met vorige of huidige wederstrewigheid teen plaatjie-oortapping.

- NovoSeven® is aangewese vir die behandeling van bloedingepisodes en vir die voorkoming van bloeding in pasiënte met verworwe hemofilie wat chirurgie of indringende prosedures ondergaan.

Kontra-indikasies

Bekende hipersensitiwiteit vir die aktiewe bestanddeel, die mengmiddels, of vir muis-, hamster- of beesproteïen.

Waarskuwings

Arteriële tromboëmboliese voorvalle buite goedgekeurde indikasies

Waar NovoSeven® toegedien word aan pasiënte buite die tans goedgekeurde indikasies, is arteriële tromboëmboliese voorvalle algemeen (≥1/100 tot <1/10). 'n Hoër risiko van arteriële tromboëmboliese nadelige voorvalle (5,6 % in pasiënte behandel met NovoSeven® teenoor 3,0 % in plasebo-behandelde pasiënte) is getoon in 'n meta-ontleding van saamgevoegde data afkomstig van plasebo-gekontroleerde proewe uitgevoer buite die tans goedgekeurde indikasies in verskeie kliniese milieus, waarvan elkeen duidelik verskillende pasiëntkenmerke en dus verskillende onderliggende risiko-profiele gehad het. Tromboëmboliese voorvalle mag lei tot kardiale arres.

Die veiligheid en doeltreffendheid van NovoSeven® is nie buite die goedgekeurde indikasies bevestig nie en daarom word NovoSeven® nie daarvoor aanbeveel nie.

Pasiënte wat NovoSeven® na groot chirurgie ontvang, of in patologiese toestande waar weefselfaktor dalk meer uitvoerig uitgedruk word as wat as normaal beskou

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word, bv. toestande soos gevorderde aterosklerotiese siekte, vergruisingsbesering, lewerversaking, kwaadaardigheid of septisemie, bestaan daar 'n potensiële risiko vir die ontwikkeling van trombotiese voorvalle of induksie van gedissemineerde intravaskulêre stolling (GIS) verbonde aan behandeling met NovoSeven®. Pasiënte in sulke toestande wat NovoSeven® ontvang, moet noukeurig waargeneem word vir tekens en simptome van problematiese aktivering van die stollingstelsel of trombose.

Weens die risiko van tromboëmboliese komplikasies, moet waaksaamheid uitgeoefen word waar NovoSeven® toegedien word aan pasiënte met 'n geskiedenis van kroonslagaarsiekte, pasiënte met lewersiekte, neonate, of pasiënte op risiko van tromboëmboliese voorvalle of gedissemineerde intravaskulêre stolling. In elkeen van hierdie situasies moet die potensiële voordeel van behandeling met NovoSeven® opgeweeg word teen die risiko van hierdie komplikasies. As rekombinante stollingsfaktor VIIa, mag NovoSeven® spore van muis-IgG, bees-IgG en ander residuele kultuurproteïene (hamster- en bees-serumproteïen) bevat, en bestaan daar 'n geringe moontlikheid dat pasiënte wat met hierdie produk behandel word, hipersensitiwiteit vir hierdie proteïene kan ontwikkel. Indien allergiese of anafilaktiese tipe reaksies intree, moet toediening onmiddellik gestaak word. In die geval van skok, moet mediese standaardbehandeling vir skok toegepas word. Pasiënte moet ingelig word van die vroeë tekens van hipersensitiwiteitsreaksies. Die pasiënt moet aangeraai word om dadelik gebruik van die produk te staak en sy/haar geneesheer te skakel indien sulke simptome sou voorkom.

In die geval van erge bloedings, moet die produk verkieslik toegedien word in hospitale wat gespesialiseer is in die behandeling van hemofiliese pasiënte met stollingsfaktor VIII- of IX-inhibitors of, indien dit nie moontlik is nie, in

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samewerking met 'n geneesheer wat in die behandeling van hemofilie gespesialiseer is.

In die geval van ligte tot matige bloedingepisodes, kan die produk by die huis toegedien word, maar dit moet slegs gedoen word in noue samewerking met 'n hemofiliesentrum waar die pasiënt gereeld opgevolg word.

Daar is geen kliniese ervaring met die toediening van 'n enkeldosis van 270 µg per kg liggaamsgewig in bejaarde pasiënte nie.

Die duur van tuisbehandeling mag nie 24 uur oorskry nie.
As bloeding nie onder beheer gehou word nie, is versorging in 'n hospitaal verpligtend. Pasiënte met seldsame aangebore probleme van fruktose-intoleransie, glukose-wanabsorpsie of sukrase-isomaltase-ontoereikendheid moet nie hierdie medikasie ontvang nie.

Interaksies

Die risiko van 'n potensiële interaksie tussen NovoSeven® en stollingsfaktor-konsentrate is onbekend.
Gelyktydige gebruik van protrombienkompleks-konsentrate, hetsy geaktiveer al dan nie, moet vermy word.
Daar is al aangemeld dat anti-fibrinolitikas bloedverlies verbonde aan chirurgie hemofiliese pasiënte verminder, veral in ortopediese chirurgie en chirurgie in areas ryk aan fibrinolitiese aktiwiteit, soos die mondholte. Ervaring met gelyktydige toediening van anti-fibrinolitikas en NovoSeven®-behandeling is egter beperk.

Swangerskap en borsvoeding

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Veiligheid tydens swangerskap en borsvoeding is nie bepaal nie.

Borsvoeding:

Dit is nie bekend of NovoSeven® in moedersmelk uitgeskei word nie.

'n Besluit om borsvoeding te staak of voort te sit, of om terapie met NovoSeven® te staak of voort te sit, moet geneem word met inagneming van die voordeel van borsvoeding vir die baba en die voordeel van NovoSeven®-terapie vir die vrou.

Vroue wat kinders kan hê:

Dit is nie bekend of NovoSeven® voortplantingsvermoë kan aantas nie.

Vrugbaarheid:

Dit is nie bekend of NovoSeven® voortplantingsvermoë kan aantas nie.

Dosering en gebruiksaanwysings

NovoSeven® is slegs vir intraveneuse bolustoediening. Gunstige kliniese resultate is waargeneem na toediening van 'n dosis van 3 - 6 KIU (60 - 120 µg) per kg liggaamsgewig, gegee teen tussenposes van 2 uur of meer, na gelang van die tipe bloeding en die uitwerking wat in die behandeling van lewensgevaarlike of ledemaat-gevaarlike bloedings en in verband met chirurgie verkry word.

Hemofilie A of B met inhibitors

(i) Ernstige bloedingepisodes:

Die dosis varieer na gelang van die tipe en erns van bloedings. As riglyn word 'n aanvanklike dosis van 4,5 KIU (90 µg) per kg liggaamsgewig aanbeveel. Die frekwensie van dosering moet aanvanklik elke tweede uur wees totdat kliniese

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verbetering waargeneem word. As voortgesette terapie aangewese is, kan die dosis-tussenpose verhoog word na 3 uur vir 1 - 2 dae. Daarna kan die dosis-tussenpose opeenvolgend verhoog word na elke 4, 6, 8 of 12 uur vir so lank as wat behandeling geoordeel word aangewese te wees.
'n Groot bloedingepisode kan vir 2 - 3 weke behandel word, maar kan langer as dit verleng word indien dit klinies regverdigbaar is.

(ii) *Chirurgie/indringende prosedure:*

'n Aanvanklike dosis van 4,5 KIU (90 µg) per kg liggaamsgewig moet onmiddellik voor die prosedure toegedien word. Die dosis moet na 2 uur herhaal word en dan teen tussenposes van 2 - 3 uur vir die eerste 24 – 48 uur, afhangende van die chirurgie wat uitgevoer word en die kliniese status van die pasiënt.

In groot chirurgie moet dosering voortgesit word teen tussenposes van 2 - 4 uur vir 6 - 7 dae. Die dosis-tussenpose kan dan verhoog word na 6 - 8 uur vir 'n verdere twee weke van behandeling. Pasiënte wat chirurgie ondergaan, kan vir tot 2 - 3 weke behandel word totdat genesing ingetree het.
Vir pasiënte met faktor IX-inhibitors of verworwe teenliggaampies op faktor VIII, is ervaring met die gebruik van NovoSeven® beperk tot slegs klein chirurgie.

(iii) Ligte tot matige bloedingepisodes (insluitend behandeling by die huis):

Daar is getoon dat vroeë intervensie doeltreffend werk vir die behandeling van ligte tot matige gewrigs-, spier- en mukokutane bloedings.

Twee doseringregimens kan aanbeveel word:

1. Een tot drie inspuitings van 90 µg (4,5 KIU) per kg liggaamsgewig toegedien teen tussenposes van 3 uur. Indien verdere behandeling vereis word, kan een addisionele dosis van 90 µg per kg liggaamsgewig toegedien word.

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2. Een enkele inspuiting van 270 µg per kg liggaamsgewig.

Die duur van tuisbehandeling moet nie 24 uur oorskry nie.

Dosering in kinders

Huidige kliniese ervaring regverdig nie 'n algemene differensiasie in dosering tussen kinders en volwassenes nie, alhoewel kinders 'n vinniger opruiming as volwassenes het. Derhalwe kan hoër dosisse van rFVIIa dalk in pediatriese pasiënte nodig wees om soortgelyke plasmakonsentrasies as in volwasse pasiënte te bewerkstellig.

Faktor VII-gebrek

Die aanbevole dosisreikwydte vir die behandeling van bloedingepisodes en vir die voorkoming van bloeding in pasiënte wat chirurgie of indringende prosedures ondergaan, is 15 – 30 µg per kg liggaamsgewig elke 4 – 6 uur totdat hemostase bewerkstellig word. Die dosis en frekwensie van inspuitings moet vir elke individu aangepas word.

Glanzmann se trombastenie

Die aanbevole dosisreikwydte vir die behandeling van bloedingepisodes en vir die voorkoming van bloeding in pasiënte wat chirurgie of indringende prosedures ondergaan, is 90 µg (reikwydte 80 - 120 µg) per kg liggaamsgewig teen tussenposes van twee uur (1,5 – 2,5 uur). Minstens drie dosisse moet toegedien word om doeltreffende hemostase te bewerkstellig. Die aanbevole roete van toediening is bolusinspuiting, aangesien gebrek aan doeltreffendheid in verband met aanhoudende infusie kan voorkom.

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Vir pasiënte wat nie refraktêr is nie, is plaatjies die eerstelynse behandeling vir Glanzmann se trombastenie.

Verworwe hemofilie

NovoSeven® moet so gou moontlik na die aanvang van 'n bloedingepisode toegedien word. Die aanbevole aanvanklike dosis, toegedien deur middel van bolusinspuiting, is 90 µg per kg liggaamsgewig. Na die aanvanklike dosis van NovoSeven® kan verdere inspuitings toegedien word indien nodig. Die duur van behandeling en die tydsverloop tussen inspuitings sal varieer na gelang van die erns van die bloeding, die indringende prosedures of die chirurgie wat uitgevoer word. Die aanvanklike dosis-tussenpose behoort 2 – 3 uur te wees. Sodra hemostase bewerkstellig is, kan die dosis-tussenpose daarna verhoog word na elke 4, 6, 8 of 12 uur, vir so lank as wat dit as aangewese geoordeel word.

NovoSeven®-poeier in flessie/Histidien-oplosmiddel in voorafgevulde spuit:

Hersamestelling:

Gebruik altyd 'n aseptiese tegniek

- Die NovoSeven®-poeierflessie en voorafgevulde spuit met oplosmiddel moet by kamertemperatuur wees vir hersamestelling. Verwyder die plastiekdeksel van die flessie. As die deksel los is of ontbreek, moenie die flessie gebruik nie. Vee die rubber stopper op die flessie af met 'n steriele alkoholdepper en laat dit vir enkele sekondes droog word voor gebruik. Moenie weer aan die rubber raak nadat dit afgevee is nie.
- Verwyder die beskermende papier van die flessiepasstuk. Moenie die flessiepasstuk uit die beskermende hoedjie haal nie. As die beskermende papier nie ten volle verseël is nie, of gebreek is, moenie die flessiepasstuk gebruik nie. Draai die beskermende hoedjie en knip die flessiepasstuk op die

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flessie vas. Druk die beskermende hoedjie liggies tussen die duim en voorvinger vas. Verwyder die beskermende hoedjie van die flessiepasstuk.

- Skroef die suierstafie kloksgewys in die voorafgevulde spuit in totdat weerstand gevoel word. Verwyder die spuit se deksel van die voorafgevulde spuit deur dit af te buig totdat die perforasie breek. Moenie aan die spuit se punt onder die spuit se deksel raak nie. As die spuit se deksel los is of ontbreek, moenie die voorafgevulde spuit gebruik nie.
- Skroef die voorafgevulde spuit ferm aan die flessiepasstuk vas totdat weerstand gevoel word. Hou die voorafgevulde spuit effens gekantel met die flessie wat ondertoe wys. Maak seker om nie die stroom van oplosmiddel reguit op die NovoSeven®-poeier te mik nie, want dit sal skuim veroorsaak. Druk die suierstafie om al die oplosmiddel in die flessie te spuit. Hou die suierstafie afgedruk en draai die flessie saggies totdat al die poeier opgelos is. Moenie die flessie skud nie, want dit sal skuim veroorsaak.

As 'n hoër dosis benodig word, herhaal die prosedure met bykomende flessies, voorafgevulde spuite en flessiepasstukke.

Die NovoSeven®-hersaamgestelde oplossing is kleurloos en moet voor toediening visueel ondersoek word vir partikels en verkleuring.

Daar word aanbeveel dat NovoSeven® onmiddellik na hersamestelling gebruik word.

As dit nie onmiddellik gebruik word nie, is bewaringstyd en bewaringstoestande voor gebruik die verantwoordelikheid van die gebruiker, en moet nie langer as 24 uur teen 2 °C tot 8 °C wees nie, tensy hersamestelling onder beheerde en gesertifiseerde aseptiese toestande plaasgevind het.

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Toediening

- Hou die suierstafie heeltemal ingedruk. Draai die spuit met die flessie onderstebo. Hou op om die suierstafie te druk en laat dit vanself terug beweeg terwyl die hersaamgestelde oplossing die spuit vul. Trek die suierstafie effens ondertoe om die gemengde oplossing in die spuit in te trek. Terwyl die flessie onderstebo gehou word, tik die spuit liggies om enige lugborrels boontoe te laat styg. Druk die suierstafie stadig totdat alle lugborrels verdwyn het.

As die hele dosis nie vereis word nie, gebruik die skaal op die spuit om te kyk hoeveel gemengde oplossing uitgetrek is.

- Skroef die flessiepasstuk met die flessie af.
- NovoSeven® is nou gereed vir inspuiting. Bepaal 'n geskikte plek en spuit NovoSeven® stadig in 'n aar oor 'n tydperk van 2 – 5 minute, sonder om die naald uit die inspuitingplek te verwyder.

Gooi gebruikte materiaal veilig weg. Enige ongebruikte produk of afvalmateriaal moet volgens die instruksies van u professionele lid van die mediese beroep weggedoen word.

Newe-effekte en spesiale voorsorgmaatreëls

Newe-effekte

Kliniese proewe wat in 484 pasiënte (insluitend 4297 behandelingsepisodes) met hemofilie A en B, verworwe hemofilie, faktor VII-gebrek en Glanzmann se trombastenie uitgevoer is. het getoon dat nadelige reaksies algemeen is (≥1/100

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tot <1/10). Omdat die totale aantal behandelingsepisodes benede 10 000 is, is die laagste moontlike frekwensie van nadelige/ongewenste reaksies wat toegewys kan word, seldsaam (≥1/10 000, <1/1000).

Die algemeenste nadelige reaksies is pireksie en uitslag, en die ernstigste nadelige reaksie is tromboëmboliese voorvalle.
Die frekwensie van beide ernstige en nie-ernstige nadelige reaksies word in die tabel hieronder volgens stelseloorgaanklas aangedui:

Stelseloorgaanklas	**Newe-effekte**
Bloed- en limfatiese versteurings	Seldsaam (≥1/10 000, <1/1000) • Gedissemineerde intravaskulêre stolling en verwante laboratoriumbevindings, insluitend verhewe vlakke van D-dimer en verlaagde vlakke van AT-III • Koagulopatie
Immuunstelsel-versteurings	Seldsaam (≥1/10 000, <1/1000) • Hipersensitiwiteit *Onbekend • Anafilaktiese reaksie
Gastroïntestinale versteurings	Seldsaam (≥1/10 000, <1/1000) • Naarheid
Senuweestelsel-versteurings	Seldsaam (≥1/10 000, <1/1000) • Hoofpyn
Vaskulêre versteurings	Seldsaam (≥1/10 000, <1/1000) • Arteriële tromboëmboliese voorvalle: (miokardiale infarksie, serebrale infarksie, serebrale iskemie, serebrale arterie-okklusie, serebrovaskulêre ongeval, renale

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	arterie-trombose, perifere iskemie, perifere arteriële trombose en intestinale iskemie) • Angina pectoris Ongewoon (≥1/1000, <1/100) • Veneuse tromboëmboliese voorvalle: (diep-aar-trombose, trombose by i.v. plek, pulmonêre embolisme, tromboëmboliese voorvalle van die lewer, insluitend portale-aar- trombose, renale-aartrombose, tromboflebitis, oppervlakkige tromboflebitis en intestinale iskemie *Die frekwensie van arteriële tromboëmboliese voorvalle in pasiënte met verworwe hemofilie is algemeen (≥1/100 tot <1/10).* Onbekend • Intrakardiale trombus
Versteurings van die vel en subkutane weefsel	Ongewoon (≥1/1000, <1/100) • Uitslag (insluitend allergiese dermatitis en eritematose uitslag) • Pruritus en urtikaria *Onbekend • Gloede • Angioedeem
Algemene versteurings en toestande by die plek van toediening	Ongewoon (≥1/1000; <1/100) • Afname in terapeutiese reaksie (Dit is belangrik om behandeling met NovoSeven® ingevolge die aanbevole dosering toe te dien.) • Pireksie

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	Seldsaam (≥1/10 000, <1/1000) • Reaksie by die inspuitingplek, insluitend pyn by die inspuitingplek
Ondersoeke	Seldsaam (≥1/10 000, <1/1000) • Verhoging in die vlakke van alanien-aminotransferase, alkalienfosfatase, laktaatdehidrogenase en protrombien is al aangemeld • Toename in fibrien-afbreekprodukte

**Nadelige reaksies wat slegs ná bemarking aangemeld is (d.w.s. nie in kliniese proewe nie) word voorgehou met 'n onbekende frekwensie.*

Spesiale voorsorgmaatreëls

Daar was geen aanmeldings van teenliggaampies teen faktor VII in hemofiliese pasiënte nie.

Pasiënte met faktor VII-gebrek

Die vorming van teenliggaampies teen NovoSeven® en FVII is die enigste nadelige reaksie wat aangemeld is in kliniese proewe van pasiënte met faktor VII-gebrek wat aan NovoSeven® blootgestel is (frekwensie: algemeen ≥1/100 tot <1/10). In twee uit vyf pasiënte met aangemelde vorming van teenliggaampies teen NovoSeven® en FVII wat in sowel kliniese proewe as na bemarking gerapporteer is, het die teenliggaampies 'n inhiberende effek *in vitro* getoon. Risiko-faktore wat tot die ontwikkeling van teenliggaampies kon bygedra het, insluitend vorige behandeling met menslike plasma en/of plasma-afgeleide faktor VII, erge mutasie van die FVII-geen, en oordosering van NovoSeven®, was aanwesig.

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Pasiënte met faktor VII-gebrek wat met NovoSeven® behandel word, moet vir faktor VII-teenliggaampies gemonitor word.

Pasiënte met faktor VII-gebrek moet beide voor en na toediening van NovoSeven® vir protrombientyd en faktor VII-stollingsaktiwiteit gemonitor word. In die geval dat die faktor VIIa-aktiwiteit versuim om die verwagte vlak te bereik of bloeding nie na behandeling met die aanbevole dosisse beheer word nie, kan die vorming van teenliggaampies vermoed word en moet ontleding vir teenliggaampies uitgevoer word.

Die risiko van trombose in pasiënte met faktor VII-gebrek wat met NovoSeven® behandel word, is onbekend.

Glanzmann se trombastenie

Een geval van angioneurotiese edeem is in 'n pasiënt met Glanzmann se trombastenie na toediening van NovoSeven® spontaan aangemeld.

Uitwerking op vermoë om motor te bestuur en masjinerie te gebruik

Geen studies oor die vermoë om motor te bestuur en masjinerie te gebruik, is uitgevoer nie.

Bekende simptome van oordosering en besonderhede van die behandeling daarvan

Dosisbeperkende toksisiteite van NovoSeven® is nie in kliniese proewe ondersoek nie.

Enkele gevalle van oordosering is in pasiënte met hemofilie aangemeld. Die enigste komplikasie wat in verband met 'n oordosering aangemeld is, was 'n

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effense en verbygaande styging in bloeddruk in 'n pasiënt van 16-jaar oud wat 24 mg rFVIIa in plaas van 5,5 mg ontvang het.
Geen gevalle van oordosering is in pasiënte met verworwe hemofilie of Glanzmann se trombastenie aangemeld nie.

In pasiënte met faktor VII-gebrek, waar die aanbevole dosis 15 - 30 µg/kg rFVIIa is, is een episode van oordosering in verband gebring met 'n trombotiese voorval (oksipitale beroerte) in 'n bejaarde (>80 jaar) manspasiënt wat met 10 – 20 keer die aanbevole dosis behandel is. Verder is die ontwikkeling van teenliggaampies teen NovoSeven® en FVII in verband gebring met oordosering in een pasiënt met faktor VII-gebrek.

Die dosiskedule moet nie doelbewus bokant die aanbevole dosisse verhoog word nie, weens die afwesigheid van inligting oor die addisionele risiko wat aangegaan mag word.
Behandeling is simptomaties en ondersteunend.

Identifikasie

Vries-gedroogde poeier: 'n Wit, homogene liofilisaat
Histidien-oplosmiddel: 'n Helder, kleurlose oplossing
Hersaamgestelde produk: 'n Helder, kleurlose oplossing

Aanbieding

NovoSeven®-pakkies:

(a) NovoSeven® 1 mg (flessie/spuit-aanbieding):

- 1 x 2 ml helder, kleurlose, tipe I-glas flessie wat 1 mg (50 KIU) vries-gedroogde rekombinante stollingsfaktor VIIa bevat. Die flessie

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is toegemaak met 'n grys rubber stopper van chlorobutiel, wat verseël is met 'n goud gekleurde aluminium deksel bedek met 'n geel rooi peuter-duidelike afkniphoedjie van polipropileen.

- 1 x 3 ml helder, kleurlose, tipe I-glas voorafgevulde spuit wat 1 ml histidien-oplosmiddel vir hersamestelling bevat. Die spuit bestaan uit 'n glas romp met 'n polipropileen rugdop en bromobutiel rubber suier. Die spuit se deksel bestaan uit bromobutiel rubber en 'n polipropileen peuter-duidelike seël. Die suierstafie is gemaak van polipropileen.

(b) NovoSeven® 2 mg (flessie/spuit-aanbieding):

- 1 x 2 ml helder, kleurlose, tipe I-glas flessie wat 2 mg (100 KIU) vries-gedroogde rekombinante stollingsfaktor VIIa bevat. Die flessie is toegemaak met 'n grys rubber stopper van chlorobutiel, wat verseël is met 'n goud gekleurde aluminium deksel bedek met 'n ligblou peuter-duidelike afkniphoedjie van polipropileen.
- 1 x 3 ml helder, kleurlose, tipe I-glas voorafgevulde spuit wat 2 ml histidien-oplosmiddel vir hersamestelling bevat. Die spuit bestaan uit 'n glas romp met 'n polipropileen rugdop en bromobutiel rubber suier. Die spuit se deksel bestaan uit bromobutiel rubber en 'n polipropileen peuter-duidelike seël. Die suierstafie is gemaak van polipropileen.

(c) NovoSeven® 5 mg (flessie/spuit-aanbieding):

- 1 x 13 ml helder, kleurlose, tipe I-glas flessie wat 5 mg (250 KIU) vries-gedroogde rekombinante stollingsfaktor VIIa bevat. Die flessie is toegemaak met 'n grys rubber stopper van chlorobutiel,

[no notes on this page]

wat verseël is met 'n goud gekleurde aluminium deksel bedek met 'n ligblou peuter-duidelike afkniphoedjie van polipropileen.

- 1 x 10 ml helder, kleurlose, tipe I-glas voorafgevulde spuit wat 5 ml histidien-oplosmiddel vir hersamestelling bevat. Die spuit bestaan uit 'n glas romp met 'n polipropileen rugdop en bromobutiel rubber suier. Die spuit se deksel bestaan uit bromobutiel rubber en 'n polipropileen peuter-duidelike seël. Die suierstafie is gemaak van polipropileen.

Die NovoSeven®-poeier in flessie/histidien-oplosmiddel in spuitproduk-aanbieding kom met 'n flessiepasstuk.

Bewaringsinstruksies

Bewaar poeier en oplosmiddel teen of benede 25 °C.

Bewaar poeier en oplosmiddel met beskerming teen lig.

Moenie flessies met poeier en oplosmiddel of voorafgevulde spuit uit die oorspronklike buitenste kartondosie verwyder nie, om dit teen lig te beskerm.

Vermy bevriesing om skade aan die flessie met oplosmiddel of die voorafgevulde spuit te verhoed.

Moenie die hersaamgestelde oplossing bevries nie.

Na samestelling, is chemiese en fisiese bestendigheid vir 6 uur teen 25 °C en vir 24 uur teen 2 - 8 °C gedemonstreer.

Gooi enige ongebruikte produk veilig weg volgens die instruksies van u lid van die mediese beroep.

Moenie na die vervaldatum gebruik nie.

Hou buite die sig en bereik van kinders.

[no notes on this page]

Registrasienommers

d) NovoSeven® 1 mg: Vries-gedroogde poeier en 1 ml histidien-oplosmiddel voorafgevulde spuit: 44/8.1/0550

e) NovoSeven® 2 mg: Vries-gedroogde poeier en 2 ml histidien-oplosmiddel voorafgevulde spuit: 44/8.1/0551

f) NovoSeven® 5 mg: Vries-gedroogde poeier 5 ml histidien-oplosmiddel voorafgevulde spuit: 44/8.1/0552

Naam en besigheidsadres van die houer van die registrasiesertifikaat

Novo Nordisk (Edms) Bpk

2de Verdieping, Gebou A

345 Rivonia Boulevard

Edenburg, Rivonia

Sandton, 2128

Datum van publikasie van hierdie pakkievoubiljet

08 Januarie 2014

NS2 NovoSeven® 2 mg - Namibië se Regnr.: 11/30.3/0214

[no notes on this page]

Always use an aseptic technique

NOVOSEVEN® USER INSTRUCTIONS

NovoSeven® Powder in vial/Histidine solvent in syringe

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**. 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.

[no notes on this page]

The equipment is for single use only.

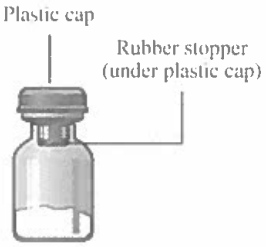
Contents

The package contains:

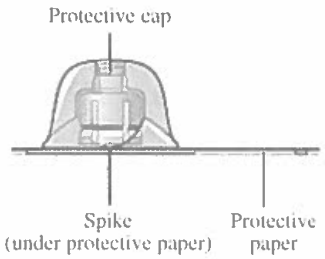
- 1 vial with NovoSeven® powder
- 1 vial adapter
- 1 pre-filled syringe with solvent
- 1 plunger rod (placed under the syringe)

Overview

Vial with NovoSeven powder



Vial adapter



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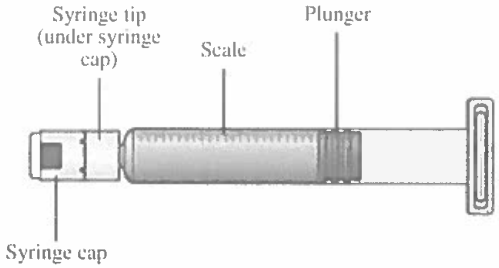
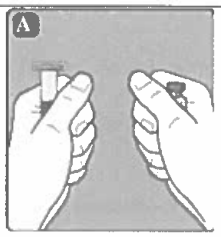
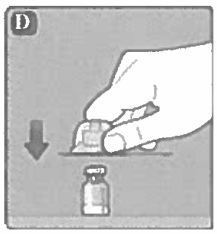
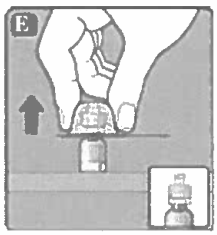
Pre-filled syringe with solvent



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, 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** (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** with a sterile alcohol	

[no notes on this page]

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	

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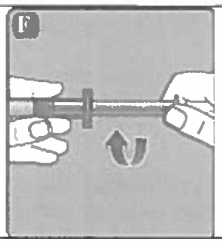
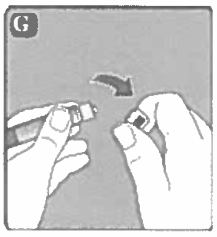
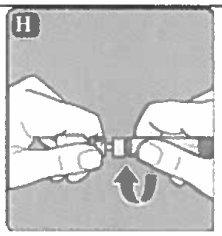
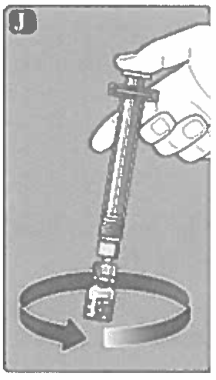
syringe by turning it clockwise into the plunger inside the pre-filled syringe until resistance is felt.	
• **Remove the syringe cap** from the pre-filled syringe by bending it down until the perforation breaks. **Do not touch the syringe tip under the syringe cap.** If you touch the syringe tip, germs 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 colourless. **If you notice visible particles or discolouration, do not use it.** Use a new package instead.	

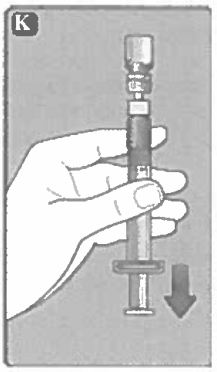
[no notes on this page]

Use the reconstituted NovoSeven® at once to avoid infections.

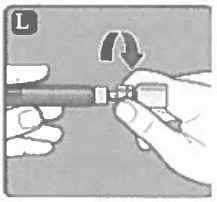
If you cannot use it at once, see section *Storage instructions* in the package insert. Do not store the reconstituted solution without advice from your doctor or nurse.

(I)
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 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 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.

[no notes on this page]

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.

[no notes on this page]

Gebruik altyd 'n aseptiese tegniek

GEBRUIKERSAANWYSINGS VIR NOVOSEVEN®

NovoSeven®-poeier in flessie/histidien-oplosmiddel in spuit

Aanwysings oor die gebruik van NovoSeven®

LEES HIERDIE AANWYSINGS NOUKEURIG DEUR VOORDAT NOVOSEVEN® GEBRUIK WORD

NovoSeven® word as 'n poeier voorsien. Voor inspuiting (toediening) moet dit hersaamgestel word met die oplosmiddel wat in die spuit voorsien word. Die oplosmiddel is 'n histidienoplossing. Die hersaamgestelde NovoSeven® moet in 'n aar (binneaarse inspuiting) ingespuit word. Die toerusting in hierdie pakkie is ontwerp vir die hersamestelling en inspuiting van NovoSeven®.

Jy sal 'n infusiestelletjie nodig hê (buisie en vlindernaald), steriele alkoholdeppers, gaaskussinkies en pleisters. Hierdie toerusting word nie by die NovoSeven®-pakkie ingesluit nie.

Moenie die toerusting sonder behoorlike opleiding van jou dokter of verpleegkundige gebruik nie.

Was altyd jou hande en maak seker dat die area om jou skoon is.

Wanneer jy medikasie voorberei en reguit in 'n aar inspuit, is dit belangrik om 'n **skoon en kiemvrye (aseptiese) tegniek te gebruik**. Onbehoorlike tegniek kan kieme laat inkom wat die bloed kan besmet.

[no notes on this page]

Moenie die toerusting oopmaak totdat jy gereed is om dit te gebruik nie.

Moenie die toerusting gebruik as dit geval het of beskadig is nie. Gebruik eerder 'n nuwe pakkie.

Moenie die toerusting gebruik as dit verval het nie. Gebruik eerder 'n nuwe pakkie. Die vervaldatum is na 'EXP' op die buitenste kartondosie gedruk, en ook op die flessie, op die flessiepasstuk en op die voorafgevulde spuit.

Moenie die toerusting gebruik as jy vermoed dat dit besoedel is nie. Gebruik eerder 'n nuwe pakkie.

Moenie enige van die items weggooi tot nadat jy die hersaamgestelde oplossing ingespuit het nie.

Die toerusting is slegs vir enkele gebruik.

Inhoud

Die pakkie bevat:

- 1 flessie met NovoSeven®-poeier
- 1 flessiepasstuk
- 1 voorafgevulde spuit met oplossing
- 1 suierstaaf (onder die spuit geplaas)

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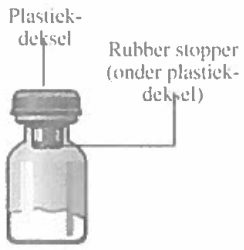
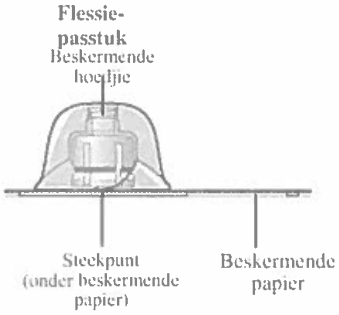
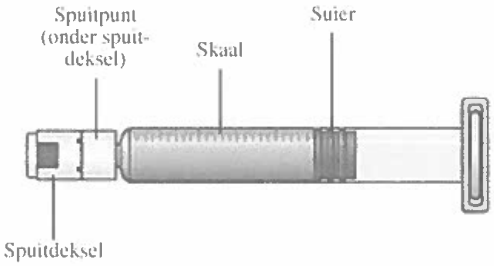
Oorsig

Flessie met NovoSeven-poeier

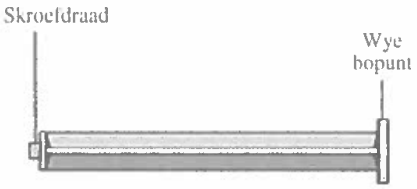




Voorafgevulde spuit met oplosmiddel



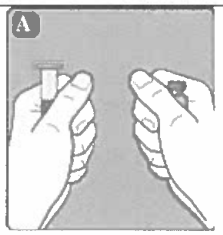
Suierstafie



[no notes on this page]

1. Berei die flessie en die spuit voor

- **Haal die aantal pakkies NovoSeven® wat u nodig het uit.**
- **Kontroleer die vervaldatum.**
- **Kontroleer die naam, sterkte en kleur** van die pakkie, om seker te maak dat dit die korrekte produk bevat.
- **Was u hande** en droog dit behoorlik af met 'n skoon handdoek of lugdroog.
- Haal die flessie, die flessiepasstuk en die voorafgevulde spuit uit die kartondosie. **Los die suierstafie onaangeraak in die kartondosie.**
- **Bring die flessie en voorafgevulde spuit na kamertemperatuur** (hoogstens 37 °C). U kan dit doen deur dit in u hande vas te hou totdat dit so warm as u hande voel.
- **Moenie enige ander manier gebruik om die** flessie en voorafgevulde spuit **warm te maak nie.**



- **Verwyder die plastiekdeksel** van die flessie. **As die plastiekdeksel los is of ontbreek, moenie die flessie gebruik nie.**
- **Vee die rubber stopper** af met 'n steriele alkoholdepper en laat dit vir 'n paar sekondes voor gebruik lugdroog word om te verseker dat dit so kiemvry as moontlik is.
- **Moenie met u vingers aan die rubber stopper raak nie, want dit kan kieme oordra.**

2. Heg die flessiepasstuk vas

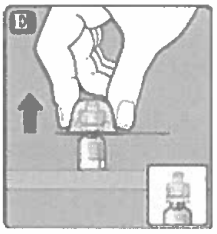
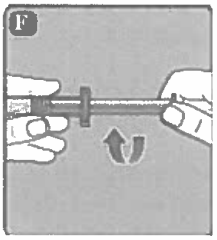
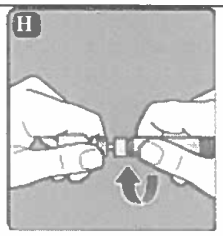
- **Verwyder die beskermende papier** van die flessiepasstuk.

  As die beskermende papier nie heeltemal verseël is nie, of stukkend is, moenie die flessiepasstuk gebruik nie.

- **Moenie die flessiepasstuk met u vingers uit die beskermende hoedjie haal nie.** As u die skerp punt op die flessiepasstuk aanraak, kan kieme van u vingers oorgedra word.

- **Plaas die flessie op 'n plat en soliede**

[no notes on this page]

oppervlakte. • **Draai die beskermende hoedjie om,** en knip die flessiepasstuk aan die flessie vas. **Sodra vasgeheg, moenie die flessiepasstuk van die flessie verwyder nie.**	
• **Druk die beskermende hoedjie** liggies met u duim en voorvinger vas, soos getoon. **Verwyder die beskermende hoedjie** van die flessiepasstuk af. **Moenie die flessiepasstuk van die flessie aflig** wanneer die beskermende hoedjie verwyder word nie.	
3. Heg die suierstafie aan die spuit vas. • Hou die suierstafie aan die wye bopunt vas en haal dit uit die kartondosie. **Moenie aan die kante of die skroefdraad van die suierstafie vat nie.** As u aan die kante of die skroefdraad raak, kan kieme van u vingers oorgedra word. Maak die suierstafie **onmiddellik** aan die spuit vas deur dit kloksgewys in die voorafgevulde spuit in te draai totdat weerstand gevoel word.	
• **Veryder die spuitdeksel** van die voorafgevulde spuit deur dit afwaarts te buig totdat die perforasie breek. **Moenie aan die spuit se punt onder die spuitdeksel raak nie.** As u die punt van die spuit aanraak, kan kieme van u vingers oorgedra word. **As die spuitdeksel los is of ontbreek, moenie die voorafgevulde spuit gebruik nie.**	
• **Skroef die voorafgevulde spuit ferm aan die** flessiepasstuk vas totdat weerstand gevoel word.	

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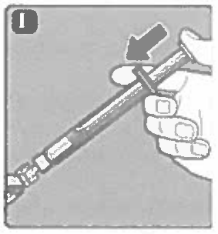
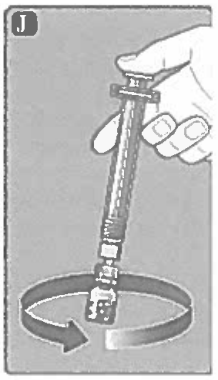
4. Hersamestelling van die poeier met die oplosmiddel

- **Hou die voorafgevulde spuit effens gekantel** met die flessie wat ondertoe wyse.
- **Druk die suierstafie in** om al die oplosmiddel in die flessie in te spuit.



- **Hou die suierstafie afgedruk en draai die** flessie saggies totdat al die poeier opgelos is. **Moenie die flessie skud nie, want dit sal skuim veroorsaak.**
- **Kontroleer die hersaamgestelde oplossing.** Dit moet kleurloos wees. **As u enige sigbare partikels of verkleuring opmerk, moet dit nie gebruik nie.** Gebruik eerder 'n nuwe pakkie.



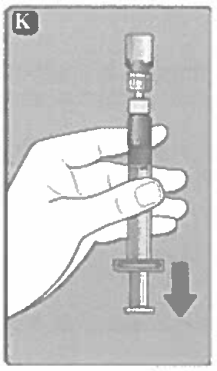
Gebruik die hersaamgestelde NovoSeven® dadelik om infeksie te vermy.

As u dit nie dadelik kan gebruik nie, verwys na die afdeling *Bewaringsinstruksies* in die pakkievoubiljet. Moenie die hersaamgestelde oplossing bewaar sonder om eers u dokter of verpleegkundige te raadpleeg nie.

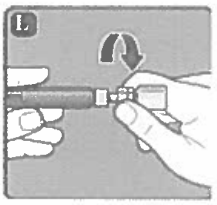
(I)
As u dosis meer as een flessie vereis, herhaal stappe **A** tot **J** met bykomende flessies, flessiepasstukke en voorafgevulde spuite totdat u u vereiste dosis bereik het.

[no notes on this page]

- **Hou die suierstafie heeltemal ingedruk.**
- **Draai die spuit** met die flessie onderstebo.
- **Hou op om die suierstafie te druk en laat dit vansself** terugbeweeg terwyl die hersaamgestelde oplossing die spuit vul.
- **Trek die suierstafie effens afwaarts** om die hersaamgestelde oplossing in die spuit in te trek.
- In die geval dat u net deel van die hersaamgestelde oplossing nodig het, gebruik die skaal op die spuit om te sien hoeveel van die oplossing u uittrek, volgens u dokter of verpleegkundige se instruksies.
- Indien daar op enige tydstip teveel lug in die spuit is, spuit die lug terug in die flessie in.
- Terwyl die flessie onderstebo gehou word, **tik die spuit saggies** om enige lugborrels boontoe te laat styg.
- **Druk die suierstafie** stadig totdat al die lugborrels weg is.



- **Skroef die flessiepasstuk** met die flessie af.
- **Moenie aan die punt van die spuit raak nie.** As u die spuit se punt aanraak, kan kieme van u vingers oorgedra word.



Inspuiting van NovoSeven® met voorafgevulde spuit deur middel van naaldlose koppelstukke/verbinders vir intraveneuse (IV) kateters

Waarskuwing: Die voorafgevulde spuit is gemaak van glas en is ontwerp om verenigbaar te wees met standaard-*luer*-slotverbinders. Party naaldlose koppelstukke met 'n interne steekpunt is nie met die voorafgevulde spuit verenigbaar nie. Hierdie onverenigbaarheid mag toediening van die medikasie verhoed en/of skade aan die naaldlose koppelstuk tot gevolg hê.

Volg die instruksies vir gebruik van die naaldlose koppelstuk. Toediening deur 'n naaldlose koppelstuk mag vereis dat die hersaamgestelde oplossing in 'n standaard- 10 ml steriele *luer*-slotplastiekspuit ingetrek word. Dit moet onmiddellik na stap J gedoen word.

5. Spuit die hersaamgestelde oplossing in

NovoSeven® is nou gereed om in u aar ingespuit te word.

[no notes on this page]

- Spuit die hersaamgestelde oplossing volgens u dokter of verpleegkundige se instruksies in.

- Spuit stadig oor 2 tot 5 minute in.

Inspuiting van die oplossing deur middel van 'n sentrale veneuse toegangtoestel (SVTT) soos 'n sentrale veneuse kateter of 'n subkutane poort:

- Gebruik 'n skoon en kiemvrye (aseptiese) tegniek. Volg die instruksies vir behoorlike gebruik van u verbinder en SVTT in konsultasie met u dokter of verpleegkundige.
- Inspuiting in 'n SVTT mag gebruik van 'n steriel 10 ml plastiekspuit vir onttrekking van die hersaamgestelde oplossing vereis.
- As die SVTT-lyn voor of na inspuiting van NovoSeven® uitgespoel moet word, gebruik natriumchloried 9 mg/ml oplossing vir inspuiting.

Wegdoening

- **Na inspuiting, raak veilig ontslae** van die spuit met die infusie-stelletjie, die flessie met die flessiepasstuk, enige ongebruikte NovoSeven® en ander afvalmateriaal volgens die opdrag van u dokter of verpleegkundige.

- Moenie enige hiervan in die gewone huishoudelike vullis weggooi nie.

Moenie die toerusting uitmekaar haal voordat dit weggegooi word nie.

Moenie die toerusting weer gebruik nie.

[no notes on this page]

[no notes on this page]