**NOVOSEVEN® RT Coagulation Factor VIIa (Recombinant)**

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use NOVOSEVEN® RT safely and effectively. See full prescribing information for NOVOSEVEN® RT. NOVOSEVEN® RT (coagulation Factor VIIa, recombinant) lyophilized powder for solution, for intravenous use. Initial U.S. Approval: 1999

**DOSAGE AND ADMINISTRATION**

For intravenous injection only

<table>
<thead>
<tr>
<th>Bleeding Episodes (2.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td>Congenital Hemophilia A or B with Inhibitors</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Acquired Hemophilia</td>
</tr>
<tr>
<td>Congenital Factor VII Deficiency</td>
</tr>
<tr>
<td>Glanzmann's Thrombasthenia</td>
</tr>
</tbody>
</table>

**Peri-operative Management (2.1)**

<table>
<thead>
<tr>
<th><strong>Indication</strong></th>
<th><strong>Dosing Recommendation</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Hemophilia A or B with Inhibitors</td>
<td>Minor: 90 mcg/kg immediately before surgery, repeat every 2 hours during surgery</td>
</tr>
<tr>
<td></td>
<td>90 mcg/kg every 2 hours after surgery for 48 hours, then every 2-6 hours until healing has occurred</td>
</tr>
<tr>
<td></td>
<td>Major: 90 mcg/kg immediately before surgery, repeat every 2 hours during surgery</td>
</tr>
<tr>
<td></td>
<td>90 mcg/kg every 2 hours after surgery for 3 days, then every 4 hours or by continuous infusion at 50 mcg/kg/hr until healing has occurred</td>
</tr>
<tr>
<td>Acquired Hemophilia</td>
<td>70-90 mcg/kg immediately before surgery and every 2-3 hours for the duration of surgery and until hemostasis is achieved</td>
</tr>
<tr>
<td>Congenital Factor VII Deficiency</td>
<td>15-30 mcg/kg immediately before surgery and every 4-6 hours for the duration of surgery and until hemostasis is achieved</td>
</tr>
<tr>
<td>Glanzmann's Thrombasthenia</td>
<td>90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure</td>
</tr>
<tr>
<td></td>
<td>90 mcg/kg every 2-6 hours to prevent post-operative bleeding</td>
</tr>
</tbody>
</table>

**WARNING: THROMBOSIS**

*See full prescribing information for complete boxed warning*

- Serious arterial and venous thrombotic events following administration of NOVOSEVEN® RT have been reported.
- Discuss the risks and explain the signs and symptoms of thrombotic and thromboembolic events to patients who will receive NOVOSEVEN® RT
- Monitor patients for signs or symptoms of activation of the coagulation system and for thrombosis.

**CONTRAINDICATIONS**

None known (4)

**WARNINGS AND PRECAUTIONS**

- Hypersensitivity reactions, including anaphylaxis, can occur with NOVOSEVEN® RT. Discontinue infusion and administer appropriate treatment if symptoms appear (5.2)
- Antibody to FVII may occur in FVII deficient patients. Monitor Factor VII deficient patients for prothrombin time (PT) and FVII coagulant activity, and for antibody formation to NOVOSEVEN® RT (5.3)

**ADVERSE REACTIONS**

The most common and serious adverse reactions in clinical trials are thrombotic events. Thrombotic adverse reactions following the administration of NOVOSEVEN® RT in clinical trials occurred in 4% of patients with acquired hemophilia and 0.2% of bleeding episodes in patients with congenital hemophilia (6)

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-877-868-6777 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

- Avoid simultaneous use of NOVOSEVEN® RT and aPCCs (activated prothrombin complex concentrates) (7)
- Do not administer NOVOSEVEN® RT with coagulation factor XIII (FXIII) (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2018

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2.3 Administration

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*Sections or subsections omitted from the full prescribing information are not listed.*
CONGENITAL HEMOPHILIA A OR B WITH INHIBITORS

Table 1: Dosing for Treatment of Acute Bleeding Episodes

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Dose and Frequency</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Hemophilia A or B with Inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemostatic plug</td>
<td>90 mcg/kg immediately before surgery and repeat every 4-6 hours for 48 hours then every 2-6 hours until healing occurs</td>
<td></td>
</tr>
<tr>
<td>Hemostatic plug</td>
<td>90 mcg/kg every 2 hours for 48 hours then every 2-6 hours until healing occurs</td>
<td></td>
</tr>
<tr>
<td>Acquired Hemophilia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the surgery</td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2-3 hours for the duration of the surgery and until hemostasis is achieved*</td>
<td></td>
</tr>
<tr>
<td>Congenital Factor VII Deficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>15-30 mcg/kg immediately before surgery and repeat every 4-6 hours for the duration of the surgery and until hemostasis is achieved*</td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure</td>
<td></td>
</tr>
<tr>
<td>Glanzmann’s Thrombasthenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure</td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure</td>
<td></td>
</tr>
</tbody>
</table>

*The minimum effective dose has not been determined.

2.2 Reconstitution

- Follow the procedures below for the preparation and reconstitution of NOVOSEVEN® RT. For questions regarding reconstitution, please contact Novo Nordisk at 1-877-NOVO-777.

- Calculate the NOVOSEVEN® RT dosage and select the appropriate NOVOSEVEN® RT package provided with either 1 histidine diluent vial or 1 pre-filled histidine diluent syringe.

- Reconstitute only with the histidine diluent provided with NOVOSEVEN® RT.

1. Always use aseptic technique.
2. Bring NOVOSEVEN® RT (white, lyophilized powder) and the specified volume of histidine (diluent) to room temperature, but not above 37° C (98.6° F). The specified volume of diluent corresponding to the amount of NOVOSEVEN® RT is as follows:
   - 1 mg (1000 micrograms) vial + 1.1 mL Histidine diluent
   - 2 mg (2000 micrograms) vial + 2.1 mL Histidine diluent
   - 5 mg (5000 micrograms) vial + 5.2 mL Histidine diluent
   - 8 mg (8000 micrograms) vial + 8.1 mL Histidine diluent
3. Remove caps from the NOVOSEVEN® RT vials to expose the central portion of the rubber stopper. Cleanse the rubber stoppers with an alcohol swab and allow to dry prior to use.
4. Draw back the plunger of a sterile syringe (attached to sterile needle) and admit air into the syringe. It is recommended to use syringe needles of gauge size 20-26.
5. Insert the needle of the syringe into the Histidine diluent vial. Inject air into the vial and withdraw the quantity required for reconstitution.
6. Insert the syringe needle containing the diluent into the NOVOSEVEN® RT vial through the center of the rubber stopper, aiming the needle against the side so that the stream of liquid runs down the vial wall (the NOVOSEVEN® RT vial does not contain a vacuum). Do not inject the diluent directly into the NOVOSEVEN® RT powder.
7. Gently swirl the vial until all the material is dissolved.

The reconstituted solution is a clear, colorless solution which may be stored either at room temperature or refrigerated for up to 5 hours after reconstitution. After reconstitution with the specified volume of diluent, each vial contains approximately 1 mg per mL NOVOSEVEN® RT (1000 micrograms per mL).

NOVOSEVEN® RT package containing 1 vial of NOVOSEVEN® RT powder and 1 pre-filled histidine diluent syringe with vial adapter for needleless reconstitution:

Vial with NovoSeven® RT powder

Vial adapter

Pre-filled syringe with diluent

Plunger rod

Syringe cap

1. Always use aseptic technique.
2. Bring NOVOSEVEN® RT (white, lyophilized powder) and the specified volume of histidine (diluent) to room temperature, but not above 37° C (98.6° F). The specified volume of diluent corresponding to the amount of NOVOSEVEN® RT is as follows:
   - 1 mg (1000 micrograms) vial + 1.1 mL Histidine diluent in pre-filled syringe
   - 2 mg (2000 micrograms) vial + 2.1 mL Histidine diluent in pre-filled syringe
   - 5 mg (5000 micrograms) vial + 5.2 mL Histidine diluent in pre-filled syringe
   - 8 mg (8000 micrograms) vial + 8.1 mL Histidine diluent in pre-filled syringe
3. Remove caps from the NOVOSEVEN® RT vial. Cleanse the rubber stopper with an alcohol swab and allow to dry prior to use.
4. Peel back the protective paper from the vial adapter. Do not remove the vial adapter from the package.
2. Administration
For intravenous injection only

- Inspect the reconstituted NOVOSEVEN® RT visually for particulate matter or discoloration prior to administration. Solution and container should be clear and colorless. Do not use if particulate matter or discoloration is observed.
- Do not freeze reconstituted NOVOSEVEN® RT or store it in syringes.
- Administer within 3 hours after reconstitution.
- Do not mix with other infusions.
- Discard any unused solution.

Perform the following procedures immediately prior to administration:

NOVOSEVEN® RT package containing 1 vial of NOVOSEVEN® RT powder and 1 vial of histidine diluent:

1. Always use aseptic technique.
2. Draw back the plunger of a sterile syringe (attached to needle) and admit air into the syringe.
3. Insert needle into the vial of reconstituted NOVOSEVEN® RT. Inject air into the vial and then withdraw the appropriate amount of reconstituted NOVOSEVEN® RT into the syringe.
4. Remove and discard the needle from the syringe.

NOVOSEVEN® RT package containing 1 vial of NOVOSEVEN® RT powder and 1 pre-filled histidine diluent syringe with vial adapter for needleless reconstitution:

1. Always use aseptic technique.
2. Invert the NOVOSEVEN® RT vial. 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 mixed solution into the syringe. Tap the syringe to remove air bubbles and withdraw the required dose amount of reconstituted NOVOSEVEN® RT into the syringe.
3. Unscrew the vial adapter with the vial. Discard the empty NOVOSEVEN® RT vial with the vial adapter attached.

Caution:
- The pre-filled diluent syringe is made of glass with an internal tip diameter of 0.037 inches, and is compatible with a standard Luer-lock connector.
- Some needleless connectors for intravenous catheters are incompatible with the glass diluent syringes (for example, certain connectors with an internal spike, such as Clave®/MicroClave® and InVision-Plus®), and their use can damage the connector and affect administration. To administer product through incompatible needleless connectors, withdraw reconstituted product into a standard 10 mL sterile Luer-lock plastic syringe.
- If you have encountered any problems with attaching the pre-filled diluent syringe to any Luer lock compatible device, please contact Nova Nordisk at (877) 968-6777.

Administer NOVOSEVEN® RT bolus infusion using the following procedures:

1. Administer as a slow bolus injection over 2 to 5 minutes, depending on the dose administered.
2. If line needs to be flushed before or after NOVOSEVEN® RT administration, use 0.9% Sodium Chloride Injection, USP.
3. Discard any unused reconstituted NOVOSEVEN® RT after 3 hours.

Administer NOVOSEVEN® RT continuous infusion for perioperative management using the following procedures:

1. Administer as a continuous infusion at 50 mcg/kg/hr using an infusion pump.
2. If line needs to be flushed before or after NOVOSEVEN® RT administration, use 0.9% Sodium Chloride Injection, USP.
3. Discard any unused reconstituted NOVOSEVEN® RT after 3 hours.

3. DOSAGE FORMS AND STRENGTHS

NOVOSEVEN® RT is available as a white lyophilized powder in single-use vials containing 1 mg (1000 micrograms), 2 mg (2000 micrograms), 5 mg (5000 micrograms), or 8 mg (8000 micrograms) recombinant coagulation Factor VIIa (FVIIa) per vial. The diluent for reconstitution of NOVOSEVEN® RT is a 10 mmol solution of L-histidine in water for injection. It is a clear colorless solution provided in a vial or a pre-filled diluent syringe and is referred to as the histidine diluent in this product information.

After reconstitution with the histidine diluent, the final solution contains approximately 1 mg per mL NOVOSEVEN® RT (1000 micrograms per mL).

4. CONTRAINDICATIONS

None known.

5. WARNINGS AND PRECAUTIONS

5.1 Thrombosis

Serious arterial and venous thrombotic events have been reported in clinical trials and postmarketing surveillance.

- Patients with congenital hemophilia receiving concomitant treatment with APCs (activated prothrombin complex concentrates), older patients particularly with acquired hemophilia and receiving other hemostatic agents, or patients with a history of cardiac, vascular disease or predisposed to thrombotic events may have an increased risk of developing thrombotic events (See Adverse Reactions (8.1) and Drug Interactions (7)).
- Monitor patients who receive NOVOSEVEN® RT for development of signs or symptoms of activation of the coagulation system or thrombosis. When there is laboratory confirmation of intravascular coagulation or presence of clinical thrombosis, reduce the dose of NOVOSEVEN® RT or stop the treatment, depending on the patient’s condition.

5.2 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, can occur with NOVOSEVEN® RT. Patients with a known hypersensitivity to mouse, hamster, or bovine proteins may be at a higher risk of hypersensitivity reactions. Discontinue infusion and administer a standard treatment when hypersensitivity reactions occur.

5.3 Antibody Formation in Factor VII Deficient Patients

Factor VII deficient patients should be monitored for prothrombin time (PT) and factor VII coagulant activity before and after administration of NOVOSEVEN® RT. If the factor VII activity falls to reach the expected level, or prothrombin time is not corrected, or bleeding is not controlled after treatment with the recommended doses, antibody formation may be suspected and analysis for antibodies should be performed.

5.4 Laboratory Tests

Laboratory coagulation parameters (PT/INR, aPTT, FVII:C) have shown no direct correlation to achieving hemostasis. Assays of prothrombin time (PT/INR), activated partial thromboplastin time (aPTT), and plasma FVII clotting activity (FVII:C) may give different results with different reagents. Treatment with NOVOSEVEN® has been shown to produce the following characteristics:

- PT: As shown below, in patients with hemophilia A/B with inhibitors, the PT shortened to about a 7-second plateau at a FVII:C level of approximately 5 units per mL. For FVII:C levels > 5 units per mL, there is no further change in PT. The clinical relevance of prothrombin time shortening following NOVOSEVEN® RT administration is unknown.

<table>
<thead>
<tr>
<th>PT (sec)</th>
<th>PT versus FVII:C</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVII:C</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td></td>
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<tr>
<td>40</td>
<td></td>
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<tr>
<td>50</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Adverse Reactions Reported in ≥2% of the 298 Patients with Hemophilia A or B with Inhibitors

<table>
<thead>
<tr>
<th>Body System</th>
<th>Reactions</th>
<th># of adverse reactions (n=1,939 treatments)</th>
<th># of patients (n=298 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fever</td>
<td>16</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Platelets, Bleeding, and Clotting</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular Hypertension</td>
<td>9</td>
<td>6</td>
</tr>
</tbody>
</table>

6. ADVERSE REACTIONS

The most common and serious adverse reactions in clinical trials are thrombotic events. Thrombotic adverse reactions following the administration of NOVOSEVEN® in clinical trials occurred in 4% of patients with acquired hemophilia and 0.2% of bleeding episodes in patients with congenital hemophilia.

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug product cannot be directly compared to rates in clinical trials of another drug and may not reflect rates observed in practice.

Adverse reactions outlined below have been reported from clinical trials and data collected in registries.

Hemophilia A or B Patients with Inhibitors

In two studies for hemophilia A or B patients with inhibitors treated for bleeding episodes (N=298), adverse reactions were reported in ≥2% of the patients that were treated with NOVOSEVEN® for 1,939 bleeding episodes (see Table 3 below).

Immunogenicity

There have been no confirmed reports of inhibitory antibodies against NOVOSEVEN® or FVII in patients with congenital hemophilia A or B with alloantibodies.

The incidence of antibody formation is dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to NOVOSEVEN® RT with the incidence of antibodies to other products may be misleading.

Concentrational Factor VII Deficiency

Data collected from the compassionate/emergency use programs, the published literature, a pharmacokinetics study, and the Hemophilia and Thrombosis Research Society (HTRS) registry showed that 75% of patients with Factor VII deficiency had received NOVOSEVEN® RT. Of these patients, 70% had 124 bleeding episodes, 3 surgicor, or prophylaxis, 5 patients in the pharmacokinetics trial. The following adverse reactions were reported: intracranial hypertension (n=1), IgG antibody against rFVIIa and FVII (n=1), localized phlebitis (n=1).

In 75 patients with factor FVII deficiency treated with NOVOSEVEN® RT, one patient developed IgG antibody against rFVIIa and FVII.

NovoSeven® RT, Coagulation Factor VIIa (Recombinant)
Patients with factor VII deficiency treated with NOVOSEVEN® RT should be monitored for factor VII antibodies.

The incidence of antibody formation is dependent on the sensitivity and specificity of the assay. Additionally, the incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to NOVOSEVEN® RT with the incidence of antibodies to other products may be misleading.

Acquired Hemophilia

Data collected from four compassionate use programs, the HTSR registry, and the published literature showed that 139 patients with acquired hemophilia received NOVOSEVEN® for 204 bleeding episodes, surgeries and traumatic injuries. Of these 139 patients, 6 patients experienced 8 serious adverse reactions. Serious adverse reactions included shock (n=1), cerebrovascular accident (n=1) and thrombomembolic events (n=6) which included cerebral artery occlusion, cerebral ischemia, angiia pectoris, myocardial infarction, pleural effusion, and renal thrombosis. Three of the serious adverse reactions had a fatal outcome.

Glanzmann’s Thrombasthenia

Data collected from the Glanzmann’s Thrombasthenia Registry (GTR) and the HTSR registry showed that 140 patients with Glanzmann’s thrombasthenia received NOVOSEVEN® RT for 516 bleeding episodes, surgeries and traumatic injuries. Of these 139 patients, 6 patients experienced 8 serious adverse reactions. Serious adverse reactions included shock (n=1), cerebrovascular accident (n=1) and thrombomembolic events (n=6) which included cerebral artery occlusion, cerebral ischemia, angiia pectoris, myocardial infarction, pleural effusion, and renal thrombosis. Three of the serious adverse reactions had a fatal outcome.

Drug Interactions

Avoid simultaneous use of activated prothrombin complex concentrates.

Do not mix NOVOSEVEN® RT with infusion solutions.

Thrombosis may occur if NOVOSEVEN® RT is administered concomitantly with Coagulation Factor XII. [See Warnings and Precautions (5.1) and Nonclinical Toxicology (13.2)].

Use in Specific Populations

Pregnancy

Risk Summary

There are no adequate and well-controlled studies using NOVOSEVEN® RT in pregnant women to determine whether there is a drug-associated risk.

Recommendation: Treatment of rTF given to pregnant women with NOVOSEVEN® in reproduction studies has been associated with mortality at doses up to 4 mg/kg body weight and 5 mg/kg body weight respectively. At 6 mg/kg body weight in rats, the abortion rate was 0 out of 25 litters; in rabbits at 5 mg/kg per kg body weight, the abortion rate was 2 out of 20, and in rats born to 32% of females born at 9 mg/kg per kg body weight of NOVOSEVEN® gave birth successfully, however, two of the 23 litters died during the early period of lactation. No evidence of teratogenicity was observed after dosing with NOVOSEVEN®.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Lactation

Risk Summary

There is no information regarding the presence of NOVOSEVEN® RT in human milk, the effect on the breastfed infant, and the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical needs. NOVOSEVEN® RT and any potential adverse effects on the breastfed infant from NOVOSEVEN® RT or from the underlying maternal condition.

Pediatric Use

Clinical trials enrolling pediatric patients were conducted with dosing determined according to body weight and not according to age.

Hemophilia A or B with Inhibitors

During the investigational phase of product development NOVOSEVEN® was used in 16 children aged 0 to <2 years for 151 bleeding episodes, 27 children aged 2 to <5 years for 140 bleeding episodes, 43 children aged 6 to <12 for 375 bleeding episodes and 30 children aged 12 to 16 for 446 bleeding episodes.

In a double-blind, randomized comparison trial of two dose levels of NOVOSEVEN® (I) vs NOVOSEVEN® (II) in the treatment of joint, muscle and mucocutaneous hemorrhages in hemophilia A and B patients and without inhibitors 20 children aged 0 to <12 and 8 children aged 12 to 16 were treated with NOVOSEVEN® in doses of 35 or 70 micrograms/kg dose. Treatment was assessed as effective (definite relief of pain/tenderness as reported by the patient and/or a measurable decrease of the size of the hemorrhage and/or arrest of bleeding within 8 hours, rated as efficacy = 51%), within 8-14 hours (rated as efficacy = 18%) or after 14 hours (rated as partially effective = 25%) in 94% of the patients.

NOVOSEVEN® was used in two trials in surgery. In a dye comparison study 22 children aged 0 to 16 years were treated with NOVOSEVEN®. Three children did not participate due to underlying disease. For these reasons, comparison of the incidence of antibodies to NOVOSEVEN® RT with the incidence of antibodies to other products may be misleading.

Clinical trials enrolling pediatric patients were conducted with dosing of 60 mg/kg dose group and 9/12 (75%) in the 35 mcg/kg dose group at 5 days.

In the surgery trial comparing bolus (B) and continuous infusion (CI) 6 children aged 10 to 15 years participated, 3 in each group. Both regimens were 100% effective (defined as bleeding has stopped completely or decreased substantially) intra-operatively, through the first 24 hours and at day 5. At the end of the study period (Postoperative day 10 or discontinuation of therapy) hemostasis in two patients in the B group was rated ineffective and hemostasis in one patient was rated as ineffective (defined as bleeding is the same or has worsened). Hemostasis in all three patients in the CI group was rated as effective.

Adverse drug reactions in pediatric patients were similar to those reported for NOVOSEVEN® RT in adult patients including one thrombotic event in a 4 year old with internal jugular vein thrombosis after port-a-cath placement which resolved.

Congenital Factor VII deficiency

In published literature, compassionate use trials and registries on use of NOVOSEVEN® in congenital Factor VII deficiency, NOVOSEVEN® was used in 24 children aged 0 <12 years and 7 children aged 12 to 16 years for 38 bleeding episodes, 16 surgeries and 9 prophylaxis regimens. Treatment was effective in 95% of bleeding episodes (5% not rated) and 100% of surgeries. No thrombotic events were reported. A seven-month old exposed to NOVOSEVEN® and various plasma products developed antibodies against FVII and rFVIIa [See Adverse Reactions (6.1 and 7.7)].

Glanzmann’s Thrombasthenia

In the Glanzmann’s Thrombasthenia Registry, NOVOSEVEN® was used in 43 children aged 0 to 12 years for 157 bleeding episodes and in 15 children aged 0 to 12 years for 19 surgical procedures. NOVOSEVEN® was also used in 8 children aged >12 to 16 years for 17 bleeding episodes and in 3 children aged >12 to 16 years for 2 surgical procedures. Treatment was effective in 95% of bleeding episodes (5% not rated) and 100% of surgeries. Efficacy in surgical procedures was evaluated as 100% in 10 surgical procedures in children aged 0 to 16 years. No adverse reactions were reported in Glanzmann’s thrombasthenia patients. [See Clinical Studies (14)].

Geriatric Use

Clinical studies of NOVOSEVEN® RT in congenital factor deficiencies and Glanzmann’s thrombasthenia did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Oversdosage

Dose limiting toxicities of NOVOSEVEN® RT have not been investigated in clinical trials. The following are examples of accidental overdose.

• One newborn female with congenital factor VII deficiency was administered an overdose of NOVOSEVEN® (single dose: 800 mcg/kg body weight per bolus infusion). Following an administration of NOVOSEVEN® VT and various plasma products, antibodies against rFVIIa were detected, but no thrombotic complications were reported.

• One Factor VII deficient male (83 years of age, 111.1 kg) received one newborn female with congenital factor VII deficiency was treated with NOVOSEVEN® RT, Coagulation Factor VIIIa (Recombinant)
1.3 Pharmacokinetics

The pharmacokinetics of NOVOSTEF® was investigated in 35 healthy subjects (17 Caucasian, 18 Japanese, 16 men, 19 women) in a dose-escalation study. Subjects were dosed with 40, 80, and 160 micrograms per kg NOVOSTEF®. No effect of gender or ethnicity on the pharmacokinetics of NOVOSTEF® was observed. Range of mean PK parameters across dose groups are shown in Table 4. The products NOVOSTEF® and NOVOSTEF® RT were found to be pharmacokinetically equivalent in a study of 22 patients receiving single doses of both formulations. Mean PK parameters for NOVOSTEF® RT are shown in Table 4.

| Table 4: Single Dose Pharmacokinetic Parameters in Healthy Subjects, Patients With Hemophilia A and B, and Patients With FVII Deficiency (Mean SD) |
|-----------------|----------------|----------------|----------------|----------------|----------------|
|                  | Healthy Subjects | Hemophilia A or B | FVII Deficiency |
| Formulation (n)  | rVIIa (n=35)° | rVIIa-25C (n=22)° | rVIIa (n=15)* | rVIIa (n=6)* | rVIIa (n=5)° |
| Ages              | 20-45          | 20-45           | 15-63         | 30-45         | 20-43         |
| Doses (mcg/kg)    | 40, 80, 160    | 90              | 17,5, 35, 70  | 90             | 30            |
| AUC (h*IU/mL)     | 71.46, 76.91*  | 113.26 (17.36)* | 53.31 (20.27)** | 2.45 (0.73)  | 23.70 (7.23)* |
| CL (mL/h)         | 1953-2516      | 3077 (438)      | NA            | 2767 (385)    | NA            |
| t½ (h)            | 3.9-6.0        | 3.54 (0.28)     | 2.72 (0.54)   | 3.2 (0.3)     | 2.62 (0.63)   |
| Vss (mL/kg)       | 130-165        | 122.96 (20.42)  | 108.86 (37.15) | 121 (30)      | 230 (70)      |
| MRT (h)           | 3.66-4.98      | 3.05 (0.27)     | 3.33 (0.64)   | 3.31 (0.38)   | 3.46 (0.64)   |
| IR ([IU/dL]/[U/kg]) | 0.89-1.04     | 1.18 (0.16)     | NA            | 0.94 (0.15)   | 0.53 (0.2)    |

*Based on the 80 mcg/kg dose
**Based on the 70 mcg/kg dose
NA: Not available
AUC: Area under the curve from time 0 to infinity; CL: Clearance; MRT: Mean residence time; IR: Incremental recovery; rFVIIa: NOVOSTEF® original formulation; rFVIIa-25C: NOVOSTEF® RT

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Two mutagenicity studies have given no indication of carcinogenic potential for NOVOSTEF®. The clastogenic activity of NOVOSTEF® was evaluated in both in vitro studies (i.e., cultured human lymphocytes) and in vivo studies (i.e., mouse micronucleus test). Neither of these studies indicated clastogenic activity of NOVOSTEF®. Other gene mutation studies have not been performed with NOVOSTEF® RT (e.g., Ames test). No chronic carcinogenicity studies have been performed with NOVOSTEF® RT. A reproductive study in male and female rats at dose levels up to 3.0 mg per kg per day had no effect on mating performance, fertility, or litter characteristics. Treatment of rats and rabbits with NOVOSTEF® in reproduction studies has been associated with mortality at doses up to 6 mg per kg and 5 mg per kg, respectively. Administration of NOVOSTEF® RT did not alter fertility, growth, or survival of offspring. In a study in rabbits (59 joint, 15 muscle and 5 mucocutaneous bleeding episodes) and 43 patients were treated at the 70 micrograms per kg dose (59 joint, 15 muscle and 5 mucocutaneous bleeding episodes) and 30 micrograms per kg dose (70 joint, 15 muscle and 14 muscle bleeding episodes). Dosing was repeated at 2.5 hour intervals but ranged up to four hours for some patients. Efficacy was assessed at 12±2 hours or at end of treatment, whichever occurred first. Based on a subjective evaluation by the investigator, the respective efficacy rates for the 35 and 70 micrograms per kg groups were excellent (definite relief of pain/tenderness as reported by the patient and/or a measurable decrease of the size of the hemorrhage and/or arrest of bleeding within 8 hours) 59% and 60%, effective (definite relief of pain/tenderness as reported by the patient and/or a measurable decrease of the size of the hemorrhage and/or arrest of bleeding within 8-14 hours) 12% and 11%, and partially effective (definite relief of pain/tenderness as reported by the patient and/or a measurable decrease of the size of the hemorrhage and/or arrest of bleeding after 14 hours) 17% and 20%. The average number of injections required to achieve hemostasis was 2.8 and 3.2 for the 35 and 70 micrograms per kg groups, respectively.
NovoSeven® RT, Coagulation Factor VII (Recombinant)

Two clinical trials were conducted to evaluate the safety and efficacy of NOVOSEVEN® administration during and after surgery in hemophilia A or B patients with inhibitors. One of the studies was a randomized, double-blind, parallel group clinical trial (28 patients with hemophilia A or B and inhibitors and one patient with acquired inhibitor to VII, undergoing major or minor surgical procedures). Patients received bolus intravenous NOVOSEVEN® (either 35 micrograms per kg, N=15; or 90 micrograms per kg, N=14) prior to surgery, intra-operatively as required, then every 2 hours for the following 48 hours beginning at closure of the wound. Additional doses were administered every 2 to 6 hours up to an additional 3 days to maintain hemostasis. After a total of 5 days of double blind treatment, therapy could be continued in an open-label manner if necessary (90 micrograms per kg NOVOSEVEN® every 2-6 hours) (Table 6). Efficacy was assessed during the intra-operative period, and post-operatively from the time of wound closure (Hour 0) through Day 5.

Table 6: Dosing by Surgery Category

<table>
<thead>
<tr>
<th></th>
<th>Major Surgery</th>
<th>Minor Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of dosing, median</td>
<td>15 (2-28)</td>
<td>0 (0-11)</td>
</tr>
<tr>
<td>No. injections, median</td>
<td>135 (11-186)</td>
<td>81 (71-128)</td>
</tr>
<tr>
<td>Median total dose, mg</td>
<td>651 (35-839)</td>
<td>569 (107-698)</td>
</tr>
<tr>
<td>μg/kg = micrograms per kg body weight</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Intraoperative hemostasis was achieved in 28/29 (97%) patients. Satisfactory hemostasis was achieved in 14/14 (100%) patients in the 90 mcg/kg dose group and 11/15 (73%) in the 35 mcg/kg dose group at 48 hours; satisfactory hemostasis was achieved in 13/14 (93%) in the 90 mcg/kg dose group and 11/15 (73%) in the 35 mcg/kg dose group at 5 days. Twenty-three patients successfully completed the entire study including 13/14 (93%) achieving successful hemostasis through surgery completion (up to day 26) in the 90 mcg/kg dose group. Another open-label, randomized, parallel trial was conducted to compare the safety and efficacy of bolus intravenous (Bl) injection (N=12) and continuous intravenous (CI) infusion (N=12) administration of NOVOSEVEN® in 23 hemophilia A or B patients with inhibitors and one patient with acquired hemophilia who were undergoing elective major surgery. Table 7 provides the overview of dosing by treatment group for Bl and CI.

Table 7: Dosing by Treatment Group

<table>
<thead>
<tr>
<th></th>
<th>Continuous Infusion</th>
<th>Bolus Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of dosing, median (range)</td>
<td>10 (4-15)</td>
<td>10 (2-116)</td>
</tr>
<tr>
<td>No. bolus injections, median (range)</td>
<td>38 (36-42)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>No. of additional bolus injections, median (range)</td>
<td>0 (0-4)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Mean total dose, mg</td>
<td>237.5</td>
<td>292.2</td>
</tr>
</tbody>
</table>

1 Includes one patient with acquired hemophilia
2 Includes dosing during the follow-up period after the 10-day study period.

Intraoperative hemostasis was reported as effective in all Bl and CI treated patients. Bl regimen was 100% effective through the first 24 hours, and was 92% effective at day 5. CI regimen was 83% effective through day 24 hours, and was 83% effective at day 5. At the end of the study period (Post operative day 10 or discontinuation of therapy), hemostatic efficacy in the Bl and CI arms was 9/12 (75%) and 10/12 (83%), respectively.

14.2 Congenital Factor VII Deficiency

Data were collected from the published literature, compassionate use trials and registries for 70 patients with Factor VII deficiency treated with NOVOSEVEN® for 124 bleeding episodes, surgeries, or prophylaxis regimens. Thirty-two of these patients were enrolled in emergency and compassionate use trials conducted by Novo Nordisk (43 non-surgical bleeding episodes, 26 surgeries), 35 were reported in the published literature (20 surgeries, 10 non-surgical bleeding episodes, 4 cases of cesarean section or vaginal birth, and 10 cases of long-term prophylaxis, and 1 case of on-demand therapy; and 3 were from a registry maintained by the Hemophilia and Thrombosis Research Society (9 bleeding episodes, 1 surgery). Dosing ranged from 6 to 98 micrograms per kg administered every 2-12 hours (except for prophylaxis, where doses were administered from 2 times per day up to 2 times per week). Patients were treated with an average of 10-10 doses. Treatment was effective (bleeding stopped or treatment was rated as effective by the physician) in 93% of episodes (90% for trial patients, 98% for published patients, 90% for HTRS registry patients).

14.3 Acquired Hemophilia

Data were collected from four studies in a compassionate use program conducted by Novo Nordisk and the Hemophilia and Thrombosis Research Society (HTRS) registry. The studies were not designed to select doses or compare first-line efficacy or efficacy when used after failure of other hemostatic agents (salvage treatment). A total of 70 patients with acquired hemophilia were treated with NOVOSEVEN® for 113 bleeding episodes, surgeries, or traumatic injuries. Sixty-one of these patients were from the compassionate use program with 100 bleeding episodes (58 non-surgical and 32 surgical bleeding episodes) and 9 patients were from the HTRS registry with 13 bleeding episodes (8 non-surgical, 3 surgical and 2 episodes classified as other). Concomitant use of other hemostatic agents occurred in 29/70 (41%); 13 (19%) received more than one hemostatic agent. The most common hemostatic agents used were antiplatelet agents, Factor VIII and activated prothrombin complex concentrates. The mean dose of NOVOSEVEN® administered was 90 micrograms per kg (range: 31 to 197 micrograms per kg); the mean number of injections per day was 6 (range: 1 to 10 injections per day). Overall efficacy (i.e., effective and partially effective outcomes) was 87/112 (78%), with 77/110 (77%) efficacy in the compassionate use programs and 10/12 (83%) efficacy in the HTRS registry. In the compassionate use programs, overall efficacy for the first-line treatment was 38/46 (83%) compared to 39/56 (70%) when used as salvage therapy (Table 8).

Table 8: Efficacy of NOVOSEVEN® in Compassionate Use Programs and HTRS Registry

<table>
<thead>
<tr>
<th>Outcome*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective</td>
<td>67</td>
</tr>
<tr>
<td>Partial</td>
<td>20</td>
</tr>
<tr>
<td>Ineffective</td>
<td>17</td>
</tr>
<tr>
<td>Unknown</td>
<td>8</td>
</tr>
</tbody>
</table>

1 Outcome assessed at end of treatment, last observation carried forward
2 One patient in the HTRS registry was excluded from efficacy analysis since NOVOSEVEN® was used to maintain hemostasis after bleeding had been controlled.

14.4 Glanzmann’s Thrombasthenia

Data were collected from the Glanzmann’s Thrombasthenia Registry (GTR), the Hemostasis and Thrombosis Research Society (HTRS) registry, and the published literature. The GTR was observational, and therefore not designed to select doses. The GTR captured data for 218 Glanzmann’s thrombasthenia patients with 1073 bleeding and surgical events. An independent adjudication committee assessed the bleeding severity, hemostasis and antibody status based on 5-days of data collected from investigators, patients, treatment, and treatment responses when only platelets were used. Adjudicators defined clinical refractoriness as lack of platelet response. Patients with apparent response to platelets only were not considered refractory, even if coded as such by investigators. Antibody status included GPIIb/IIIa, HLA, and unspecified platelet-specific antibodies. Efficacy was evaluated on a two-point scale (clinical assessment of success or failure). The median interval between doses of 3 hours.

Table 9: Adjudicator Evaluation of Efficacy – Bleeding Episodes for GTR Data

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>No. of patients</th>
<th>No. of episodes</th>
<th>Success</th>
<th>Failure</th>
<th>Insufficient data</th>
<th>No Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOVOSTENRT only</td>
<td>44</td>
<td>109</td>
<td>101 (92.7)</td>
<td>2 (1.8)</td>
<td>4 (3.7)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>NOVOSTENRT + Platelets + Other hemostatic agents</td>
<td>69</td>
<td>157</td>
<td>150 (95.5)</td>
<td>2 (1.3)</td>
<td>12 (7.6)</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>By Antibody/Refractor Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractoriness</td>
<td>31</td>
<td>79</td>
<td>75 (94.9)</td>
<td>2 (2.5)</td>
<td>2 (2.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Platelet-specific antibodies</td>
<td>8</td>
<td>10</td>
<td>10 (100.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>NA</td>
</tr>
<tr>
<td>Neither or unknown</td>
<td>57</td>
<td>177</td>
<td>168 (93.3)</td>
<td>2 (1.1)</td>
<td>4 (2.3)</td>
<td>5 (2.8)</td>
</tr>
</tbody>
</table>

1 All treatment regimens that included treatment with NOVOSTENRT
2 Includes GPIIb/IIIa, HLA, and unspecified platelet-specific antibodies
3 Assumes no platelet-specific antibodies or refractoriness or antibody and refractority status unknown
4 Patient numbers are not additive. Patients may have episodes with different treatment regimens and have more than one antibody/refractor status
5 Treatment was NOVOSTENRT only for 26/79 episodes with refractoriness with or without antibodies, 2/10 episodes with platelet-specific antibodies only, and 81/177 episodes with neither or unknown. The remainder received NOVOSTENRT with platelets and/or antiplatelet/anti-HLA agents.

Table 10: Adjudicator Evaluation of Efficacy – Surgical Procedures for GTR Data

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>No. of patients</th>
<th>No. of procedures</th>
<th>Success</th>
<th>Insufficient data*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOVOSTENRT only</td>
<td>35</td>
<td>36</td>
<td>35 (97.2)</td>
<td>1 (2.8)</td>
</tr>
<tr>
<td>NOVOSTENRT + Platelets + Other hemostatic agents</td>
<td>57</td>
<td>94</td>
<td>94 (100.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>By Antibody/Refractor Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractoriness</td>
<td>33</td>
<td>70</td>
<td>69 (98.6)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Platelet-specific antibodies</td>
<td>11</td>
<td>24</td>
<td>24 (100.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Neither or unknown</td>
<td>36</td>
<td>66</td>
<td>66 (100.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

1 All treatment regimens that included treatment with NOVOSTENRT
2 Includes GPIIb/IIIa, HLA, and unspecified platelet-specific antibodies
-Novoseven® RT, Coagulation Factor VIIa (Recombinant)

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

NOVOSEVEN® RT, Coagulation Factor VIIa (Recombinant), is supplied as a room temperature stable, white, lyophilized powder in single-use vials, one vial per carton. The diluent for reconstitution of NOVOSEVEN® RT is a 10 mmol solution of L-histidine in water for injection and is supplied as a clear colorless solution, and referred to as the histidine diluent. The histidine diluent is provided in either a vial or pre-filled diluted syringe.

The amount of rFVIIa in milligrams and in micrograms is stated on the label. NOVOSEVEN® RT package containing 1 vial of NOVOSEVEN® RT powder and 1 vial of histidine diluent.

Presentation Carton NDC Number Components
1 mg per vial (1000 micrograms/vial) NDC 0169 7010 01 • NOVOSEVEN® RT in a single-use vial (NDC 0169-7017-11) • Histidine diluent in vial, 1 mL (NDC 0169-7001-98)
2 mg per vial (2000 micrograms/vial) NDC 0169 7020 01 • NOVOSEVEN® RT in a single-use vial (NDC 0169-7027-11) • Histidine diluent in vial, 2.1 mL (NDC 0169-7002-98)
5 mg per vial (5000 micrograms/vial) NDC 0169 7050 01 • NOVOSEVEN® RT in a single-use vial (NDC 0169-7057-11) • Histidine diluent in vial, 5.2 mL (NDC 0169-7005-98)
8 mg per vial (8000 micrograms/vial) NDC 0169 7040 01 • NOVOSEVEN® RT in a single-use vial (NDC 0169-7047-11) • Pre-filled histidine diluent in syringe, 1 mL (NDC 0169-7011-98) • Vial adapter
drug administration.

Storage and Handling

Prior to reconstitution, store NOVOSEVEN® RT powder and histidine diluent between 2–25°C (36–77°F). Do not freeze. Store protected from light. Do not use past the expiration date.

After reconstitution, store NOVOSEVEN® RT at room temperature or refrigerated for up to 3 hours. Do not freeze reconstituted NOVOSEVEN® RT or store in syringes.

17 PATIENT COUNSELING INFORMATION

Advise the patient:
• To read the FDA-approved patient labeling (Instructions for Use).
• About the early signs of hypersensitivity reactions, including hives, urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis.
• About the signs of thrombosis, including new onset swelling and pain in the limbs or abdomen, new onset chest pain, shortness of breath, loss of sensation or motor power, or altered consciousness or speech.
• To immediately seek medical help if any of the above signs or symptoms occur.
• To follow the recommendations in the FDA-approved patient labeling, regarding proper sharps disposal.

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Bionector® is a registered trademark of VYGON.

For information contact:
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800 Scudders Mill Road
Plainsboro, NJ 08536, USA
1-877-NOVO-777
www.NOVOSEVENRT.com

Manufactured by:
Novo Nordisk A/S
2880 Bagsvaerd, Denmark
License Number: 1261
© 2018 Novo Nordisk
US18NSVN00091 11/18
FDA-approved patient labeling

Instructions for Use

NOVOSEVEN® RT
Coagulation Factor VIIa (Recombinant)

Instructions on how to use NOVOSEVEN® RT
READ THESE INSTRUCTIONS CAREFULLY BEFORE USING NOVOSEVEN® RT.

NOVOSEVEN® RT is supplied as a powder. Before injection (administration) it must be mixed (reconstituted) with the liquid diluent supplied in the syringe. The liquid diluent is a histidine solution. The mixed NOVOSEVEN® RT must be injected into your vein (intravenous injection). The equipment in this package is designed to mix and inject NOVOSEVEN® RT.

You will also need an infusion set (tubing and butterfly needle), sterile alcohol swabs, gauze pads, and bandages.

Don’t use the equipment without proper training from your doctor or nurse.

Always use a clean and germ free (aseptic) technique. It is important that you wash your hands and ensure that the area around you is clean.

Don’t open the equipment until you are ready to use it. The equipment is for single use only.

Content
The package contains:
• Vial with NOVOSEVEN® RT powder
• Vial adapter
• Pre-filled syringe with diluent
• Plunger rod (placed under the syringe)

Overview
Vial with NovoSeven® RT powder

2. Attach the vial adapter
• Remove the protective paper from the vial adapter.
Don’t take the vial adapter out of the protective cap. If the protective paper is not fully sealed or if it is broken, don’t use the vial adapter.

3. Attach the plunger rod and the syringe
• Grasp the plunger rod by the wide top end and take it out of the carton.
Be careful not to touch the sides or the thread of the plunger rod.
Keep holding the plunger rod at the wide top end.
Immediately connect the plunger rod to the syringe by turning it clockwise into the rubber plunger inside the pre-filled syringe until resistance is felt.

4. Mix the powder with the diluent
• Hold the pre-filled syringe slightly tilted with the vial pointing downwards.
• Push the plunger rod to inject all the diluent into the carton.

5. Inject the mixed solution
NOVOSEVEN® RT is now ready to inject into your vein.
• Do not mix NOVOSEVEN® RT with any other intravenous infusions or medications.
• Inject the mixed solution slowly over 2 to 5 minutes as instructed by your doctor or nurse.
Injecting the solution via a central venous access device (CVAD) such as a central venous catheter or subclavian port:
• Use a clean and germ free (aseptic) technique. Follow the instructions for proper use for your connector and central venous access device in consultation with your doctor or nurse.
• Injecting into a CVAD may require using a sterile 10 mL plastic syringe for withdrawal of the mixed solution and injection.
• If necessary, use 0.9% Sodium Chloride Injection, USP to flush the CVAD line before or after NOVOSEVEN® RT injection.

NOVOSEVEN® RT is recommended to be used immediately after it is mixed. If you cannot use the mixed NOVOSEVEN® RT solution immediately, it can be kept in the vial, still with the vial adapter and the syringe attached, at room temperature or refrigerated for no longer than 3 hours. Do not freeze mixed NOVOSEVEN® RT solution or store it in syringes.

Keep mixed NOVOSEVEN® RT solution out of direct light.

If your dose requires more than one vial, repeat step 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 mixed solution fills the syringe.

Pull the plunger rod slightly downwards to draw the mixed solution into the syringe. Be sure you only need part of the entire dose, use the scale on the syringe to see how much mixed solution you withdraw, as instructed by your doctor or nurse.

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.

Additional Tips

Don’t use the equipment if it has been dropped, or if it is damaged. Use a new package instead.

Don’t use the equipment if it is expired. Use a new package instead. The expiration date is printed on the outer carton and on the vial, the vial adapter and the pre-filled syringe.

Don’t dispose of any of the items until after you have injected the mixed solution.

Don’t disassemble the vial and vial adapter before disposal.

Don’t reuse the equipment.

Caution: The pre-filled diluent syringe is made of glass with an internal tip diameter of 0.037 inches, and is compatible with a standard Luer-lock connector.

Some needleless connectors for intravenous catheters are incompatible with the glass diluent syringes (for example, certain connectors with an internal spike, such as Clave®/MicroClave®, Invension-Plus®, Invision-Plus® CS®, Invision-Plus® Junior®, Biojector®), and their use can damage the connector and affect administration. To administer product through incompatible needleless connectors, withdraw reconstituted product into a standard 10 mL sterile Luer-latch plastic syringe.

If you have encountered any problems with attaching the pre-filled histidine diluent syringe to any Luer-lock compatible device, please contact Novo Nordisk at (877) 668-6777.

Disposal

• After injection, safely dispose of the syringe with the infusion set, the vial with the vial adapter, any unused NOVOSEVEN® RT and other waste materials as instructed by your doctor or nurse.

Don’t throw it out with the ordinary household trash.

Don’t disassemble the vial and vial adapter before disposal.

Don’t reuse the equipment.