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
Bleeding Episodes (2.1)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Hemophilia A or B with Inhibitors</td>
<td>90 mcg/kg every 2 hours, adjustable based on severity of bleeding until hemostasis is achieved</td>
</tr>
<tr>
<td></td>
<td>90 mcg/kg every 3-6 hours after hemostasis is achieved for severe bleeds</td>
</tr>
</tbody>
</table>

Acquired Hemophilia

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70-90 mcg/kg every 2-3 hours until hemostasis is achieved</td>
</tr>
</tbody>
</table>

Congenital Factor VII Deficiency

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15-30 mcg/kg every 4-6 hours until hemostasis is achieved</td>
</tr>
</tbody>
</table>

Glanzmann’s Thrombasthenia

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>90 mcg/kg every 2-6 hours until hemostasis is achieved</td>
</tr>
</tbody>
</table>

Peri-operative Management (2.1)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Hemophilia A or B with Inhibitors</td>
<td>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>
</tbody>
</table>

Major:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>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 5 days, then every 4 hours or by continuous infusion at 50 mcg/kg/hr until healing has occurred</td>
</tr>
</tbody>
</table>

Acquired Hemophilia

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70-90 mcg/kg every 2-3 hours for the duration of surgery and until hemostasis is achieved</td>
</tr>
</tbody>
</table>

Congenital Factor VII Deficiency

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></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>
</tbody>
</table>

Glanzmann’s Thrombasthenia

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></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>

—- DOSAGE FORMS AND STRENGTHS —-
Available as lyophilized powder in single-dose vials of 1, 2, 5, or 8 mg recombinant coagulation factor VIIa (FVIIa). After reconstitution with specified volume of histidine diluent, the final solution contains 1 mg per mL (1000 micrograms per mL) of recombinant FVIIa

—- CONTRAINDICATIONS —-
None known

—- WARNINGS AND PRECAUTIONS —-
• Hypersensitivity reactions, including anaphylaxis, can occur with NOVOSEVEN® RT. Discontinue infusion and administer appropriate treatment if symptoms appear
• 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

—- 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

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-877-668-6777 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)
• Do not administer NOVOSEVEN® RT with coagulation factor XIII (FXIII)

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

Revised: 7/2020
1 INDICATIONS AND USAGE
NOVOSEVEN® RT, Coagulation Factor VIII (Recombinant), is indicated for:
- Treatment of bleeding episodes and peri-operative management in adults and children with hemophilia A or B with inhibitors, congenital Factor VII (FVII) deficiency, and Glanzmann’s thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets.
- Treatment of bleeding episodes and peri-operative management in adults with acquired hemophilia.

2 DOSAGE AND ADMINISTRATION

For intravenous administration only

2.1 Dose
- Use hemostasis evaluation to determine the effectiveness of NOVOSEVEN® RT and to provide a basis for modification of the NOVOSEVEN® RT treatment schedule.
- Coagulation parameters do not necessarily correlate with or predict the effectiveness of NOVOSEVEN® RT.

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>Acquired Hemophilia</td>
<td>70-90 mcg/kg every 2-3 hours</td>
<td>Until hemostasis is achieved*</td>
</tr>
<tr>
<td>Congenital Hemophilia</td>
<td>15-30 mcg/kg every 4-6 hours</td>
<td>Until hemostasis is achieved*</td>
</tr>
</tbody>
</table>

*The minimum effective dose has not been determined

NOVOSEVEN® RT dosing for prevention of bleeding in surgical interventions or invasive procedures (perioperative management) is provided in Table 2.

Table 2: Dosing for Perioperative Management

<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>Minor</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2-3 hours for the duration of the surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post surgical: 90 mcg/kg every 2 hours for 48 hours then every 2-6 hours until healing occurs</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 surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post surgical: 90 mcg/kg every 2 hours for 5 days then every 4 hours or by continuous infusion at 50 mcg/kg/h until healing occurs</td>
<td></td>
</tr>
</tbody>
</table>

Doses as low as 10 micrograms per kg body weight can be effective

Higher doses of 100-140 micrograms per kg can be used for surgical patients who have clinical refractoriness with or without platelet-specific antibodies

Corresponding to the amount of NOVOSEVEN® RT 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 admir air into the syringe. It is recommended to use syringes of needle size 20-26.

5. Insert the needle of the syringe into the Histidine diluent vial. Inject air into the vial and withdraw the quanity 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 on 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 3 hours after reconstitution. After reconstitution with the specific 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

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 cap 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 vial and package.

5. Place the NOVOSEVEN® RT vial on a flat surface. While holding the vial adapter package, place the vial adapter over the NOVOSEVEN® RT vial and press down firmly on the package until the vial adapter spike penetrates the rubber stopper.

6. Attach the plunger rod to the syringe. Turn the plunger rod clockwise into the plunger inside the pre-filled diluent syringe until resistance is felt. Remove the syringe cap from the pre-filled diluent syringe and screw onto the vial adapter.

7. Push the plunger rod to slowly inject all the diluent into the vial. Keep the plunger rod pressed down and swirl the vial gently until the powder is dissolved. The reconstituted solution is a clear, colorless solution which may be stored fully assembled either at room temperature or refrigerated for up to 3 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).
2.3 Administration
For intravenous injection only
- Inspect the reconstituted NOVOSEVEN® RT visually for particulate matter and discoloration prior to administration, whenever solution and container permit. 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 solutions.
- 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 sterile 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 spike of 0.037 inches, and is compatible with a standard Luer-lock connector.
- Some needless connectors for intravenous catheters are incompatible with the glass diluent syringe (for example, certain connectors with an internal spike, such as Clave®/MicroClave®, InVision-Plus®, InVision-Plus® CS®, InVision-Plus® Junior®, Bionector®, and their use can damage the connector and affect administration. To administer product through incompatible needless 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 histidine diluent syringe to any Luer lock compatible device, please contact Novo Nordisk at (877) 668-6777.

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 DOSAGE FORMS AND STRENGTHS
NOVOSEVEN® RT is available as a white lyophilized powder in single-dose vials containing 1 mg (1000 micrograms), 2 mg (2000 micrograms), 5 mg (5000 micrograms), or 8 mg (8000 micrograms) recombinant coagulation Factor VIIa (rFVIIa) per vial.
The diluent for reconstitution of NOVOSEVEN® RT is a 10 mmol/L 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.
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 (6.1) and Drug Interactions (7)).

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 appropriate 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), activated partial thromboplastin time (aPTT), and factor VII coagulant activity before and after administration of NOVOSEVEN® RT. If the factor VII activity fails to reach the expected level, or prothrombin time is not corrected, or bleeding is not controlled 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® RT 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 in PT. The clinical relevance of prothrombin time shortening following NOVOSEVEN® RT administration is unknown.
- aPTT: While administration of NOVOSEVEN® RT shortens the prolonged aPTT in hemophilia A/B patients with inhibitors, proportionately has usually not been observed in doses shown to induce clinical improvement. Data indicate that clinical improvement was associated with a shortening of aPTT of 15 to 20 seconds.
- FVII:C: FVII:C levels were measured two hours after NOVOSEVEN® RT administration of 35 micrograms per kg body weight and 90 micrograms per kg body weight following two days of dosing at two hour intervals. Average steady state levels were 11 and 28 units per mL for the two dose levels, respectively.

5.5 Laboratory Coagulation Parameters
Food and Drug Administration (FDA) and EMEA labeling contain a brief summary of the following parameters:
- INR: NOVOSEVEN® RT has demonstrated the ability to normalize INR. However, INR values have not been shown to directly predict bleeding outcomes, nor has it been possible to demonstrate the impact of NOVOSEVEN® RT on bleeding times/volume in models of clinically-induced bleeding in a healthy volunteers who has received NOVOSEVEN® RT, Coagulation Factor VIIa (Recombinant) with the incidence of antibodies to NOVOSEVEN® RT.

5.6 Laboratory Coagulation Parameters
- APTT: The aPTT of patients with Factor VII-deficient inhibitor disease treated with NOVOSEVEN® RT in the peri-operative setting in hemophilia A or B patients with inhibitors (n=51), the following serious adverse reactions were reported: acute post-operative hemorrhagic (n=1), internal jugular thrombosis adverse reaction (n=1), decreased therapeutic response (n=4).
- FVII:C: The FVII:C levels two hours following NOVOSEVEN® RT administration are unknown.

5.7 Laboratory Coagulation Parameters

6 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.

6.1 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 episodes that were treated with NOVOSEVEN® RT for 1,939 bleeding episodes (see Table 3 below).

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>No of adverse reactions</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fever</td>
<td>16</td>
<td>13</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>

Serious adverse reactions included thrombosis, pain, thromboembolic events, deep, pulmonary, cerebrovascular disorder, angina pectoris, DIC, anaphylactic shock and abnormal hepatic function. The serious adverse reactions of DIC and therapeutic response decreased had a fatal outcome.

In two clinical trials evaluating safety and efficacy of NOVOSEVEN® RT in the peri-operative setting in hemophilia A or B patients with inhibitors (n=51), the following serious adverse reactions were reported: acute post-operative hemorrhagic (n=1), decreased therapeutic response (n=4).

6.2 Immunogenicity
There have been no confirmed reports of inhibitory antibodies against NOVOSEVEN® RT 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.

6.3 Concomitant 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 patients with Factor VII deficiency had received NOVOSEVEN® RT: 70 patients for 124 bleeding episodes, surgeries, 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).

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

6.5 Acquired Hemophilia
Data collected from four compassionate use programs, the HTRS registry, and the published literature showed that 139 patients with acquired hemophilia received NOVOSEVEN® RT for 204 bleeding episodes, surgeries and traumatic injuries. Of these 139 patients, 6 experienced serious adverse reactions. Serious adverse reactions included shock (n=1), cerebrovascular accident (n=1)
and thrombocytopenic events (n=6) which included cerebral artery occlusion, cerebral ischemia, angina pectoris, myocardial infarction, pulmonary edema and deep vein 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 HTTS registry showed that 140 patients with Glanzmann’s thrombasthenia received NOVOSEVEN® for 516 bleeding episodes, surgurgic, and in surgical need. The following adverse reactions were reported: deep vein thrombosis (n=1), headache (n=2), fever (n=2), nausea (n=1), and dizziness (n=1).

6.2 Post marketing Experience

Adverse reactions reported during post marketing period were similar in nature to those observed during clinical trials and include reports of thrombotic and deep vein events.

7 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 XIII. [See Warnings and Precautions (5.1) and Nonclinical Toxicology (13.2)].

8 USE IN SPECIFIC POPULATIONS

8.1 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. Treatment of rats and rabbits with NOVOSEVEN® in reproduction studies has been associated with mortality at doses up to 6 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 body weight, the abortion rate was 2 out of 25 litters. Twenty-three out of 25 female rats given 6 mg/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 in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 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 need for NOVOSEVEN® RT and any potential adverse effects on the breastfed infant from NOVOSEVEN® RT or from the underlying maternal condition.

8.4 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 <6 years for 140 bleeding episodes, 43 children aged 6 to <12 years for 375 bleeding episodes and 30 children aged 12 to 16 years for 446 bleeding episodes. In a double-blind, randomized comparison trial of two dose levels of NOVOSEVEN® in the treatment of joint, muscle and mucocutaneous hemorrhages in hemophilia A and B patients with 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 per kg dose. Treatment was assessed as effective (definite relief of hemorrhage in hemophilia A and B patients with and without inhibitors was also used in 8 children aged >12 to 16 years for 111 bleeding episodes. In a dose comparison in congenital factor deficiencies, NOVOSEVEN® RT 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® RT was used in 8 children aged 12 to 16 years for 17 bleeding episodes and in 3 children aged >12 to 16 years for 3 surgical procedures. Efficacy of regimens including NOVOSEVEN® RT was evaluated by independent adjudicators as 93.6% and 100% for bleeding episodes in children aged 0 to 12 years and >12 to 16 years, respectively. Efficacy of surgical procedures was evaluated as 100% for all surgical procedures in children aged 0 to 16 years. No adverse reactions were reported in Glanzmann’s thrombasthenia children. [See Clinical Studies (14)].

8.5 Geriatric Use

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

10 OVERDOSAGE

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 micrograms/kg body weight). Following administration of NOVOSEVEN® RT 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 two doses of 324 micrograms per kg body weight (10-20 times the recommended dose) and experienced a thrombotic event (occipital stroke).
• One hemophilia B patient (16 years of age, 68 kg) received a single dose of 352 micrograms per kg body weight and one hemophilia A patient (2 years of age, 14.6 kg) received doses ranging from 246 micrograms per kg body weight to 986 micrograms per kg body weight on five consecutive days. There were no reported complications in either case.

11 DESCRIPTION

NOVOSEVEN® RT, Coagulation Factor VIIa (Recombinant) is a sterile, white lyophilized powder of recombinant human coagulation factor VIIa (rFVIIa) for reconstitution for intra-venous injection. The product is supplied as single-dose vials containing the following:

<table>
<thead>
<tr>
<th>Contents</th>
<th>1 mg Vial</th>
<th>2 mg Vial</th>
<th>5 mg Vial</th>
<th>8 mg Vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>rFVIIa</td>
<td>1000 mg</td>
<td>2000 mg</td>
<td>5000 mg</td>
<td>8000 mg</td>
</tr>
<tr>
<td>micrograms/kg body weight</td>
<td>micrograms</td>
<td>micrograms</td>
<td>micrograms</td>
<td>micrograms</td>
</tr>
<tr>
<td>sodium chloride</td>
<td>2.54 mg</td>
<td>4.80 mg</td>
<td>11.76 mg</td>
<td>17.82 mg</td>
</tr>
<tr>
<td>calcium chloride</td>
<td>1.47 mg</td>
<td>2.94 mg</td>
<td>7.35 mg</td>
<td>11.76 mg</td>
</tr>
<tr>
<td>Glycine</td>
<td>1.32 mg</td>
<td>2.64 mg</td>
<td>6.06 mg</td>
<td>10.56 mg</td>
</tr>
<tr>
<td>poly-L-lysine</td>
<td>0.07 mg</td>
<td>0.14 mg</td>
<td>0.35 mg</td>
<td>0.56 mg</td>
</tr>
<tr>
<td>Monocit</td>
<td>25 mg</td>
<td>50 mg</td>
<td>125 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td>Ssacrose</td>
<td>10 mg</td>
<td>20 mg</td>
<td>50 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.5 mg</td>
<td>1.0 mg</td>
<td>2.5 mg</td>
<td>4.0 mg</td>
</tr>
</tbody>
</table>

* per mg of rFVIIa: 0.4 mEq sodium, 0.01 mEq calcium
NOVOSEVEN® RT also contains trace amounts of proteins derived from the manufacturing and purification processes such as mouse IgG (maximum of 1.2 ng/mg), bovine IgG (maximum of 30 ng/mg), and protein from BHK-cells and media (maximum of 19 ng/mg).

The diluent for reconstitution of NOVOSEVEN® RT contains 10 mg/mL of solution of histidine in water for injection and is supplied as a clear colorless solution in a vial or pre-filled diluent syringe. After reconstitution with the appropriate volume of histidine diluent, each vial contains approximately 1 mg/mL NOVOSEVEN® RT (corresponding to 10 micrograms/mL). The reconstituted solution is a clear colorless solution with a pH of approximately 6.0 and contains no preservatives.

Recombinant coagulation Factor VIIa (rFVIIa), the active ingredient in NOVOSEVEN® RT, is a vitamin K-dependent glycoprotein consisting of 406 amino acid residues with an approximate molecular mass of 50 kDa. It is structurally similar to endogenous human coagulation factor VIIa.

The gene for human coagulation factor VII (FVII) is cloned and expressed in baby hamster kidney cells (BHK cells). Recombinant FVII is secreted into the culture media (containing newborn calf serum) in its single-chain form and then proteolytically converted by autocalytase to the active two-chain form, rFVIIa, during a chromatographic purification process. The purification process has been demonstrated to remove exogenous viruses (MuLV, SV40, Pox virus, Rousvirus, BEV, IBR virus). No human serum or other proteins are used in the production or formulation of NOVOSEVEN® RT.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

NOVOSEVEN® RT is recombinant Factor VIIa and, when combined with tissue factor can activate coagulation Factor X to Factor Xa, as well as coagulation Factor IX to Factor IXa. Factor Xa, in complex with other factors, then converts prothrombin to thrombin, which leads to the formation of a hemostatic plug by converting fibrinogen to fibrin and thereby inducing local hemostasis. This process may also occur on the surface of activated platelets.

12.2 Pharmacodynamics

The effect of NOVOSEVEN® RT upon coagulation in patients with or without hemophilia has been assessed in different model systems. In an in vitro model of tissue-factor-initiated blood coagulation (Figure A), the addition of rFVIIa increased both the rate and level of thrombin generation in normal and hemophilia A and B blood, with an effect shown at rFVIIa concentrations as low as 10 nM. In this model, fresh human blood was treated with corn trypsin inhibitor (CTI) to block the contact pathway of blood coagulation. Tissue factor (TF) was added to initiate clotting in the presence and absence of rFVIIa for both types of blood.

In a separate model, and in line with previous reports, escalating doses of rFVIIa in hemophilia plasma demonstrate a dose-dependent increase in thrombin generation (Figure B). In this model, platelet rich normal and hemophilia plasma was adjusted with autologous plasma to 200,000 platelets/microliter. Coagulation was initiated by addition of tissue factor and CaCl2. Thrombin generation was measured in the presence of a thrombin substrate and various added concentrations of rFVIIa.

![Figure A](https://example.com/figureA.png)

**TF-initiated clotting of normal blood and congenital hemophilia A blood in the presence of factor VIIa.**

Clotting of CTI-inhibited (0.1 mg/mL) normal blood initiated with 12.5 pM TF and addition of 10 nM factor VIIa (△) and of hemophilia A blood with (■) and without (○) addition of 10 nM factor VIIa. Figure A shows Thrombin Anti-Thrombin generation over time. Arrows indicate clotting times.
The pharmacokinetics of NOVOSEVEN® 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 NOVOSEVEN®. No effect of gender or ethnicity on the pharmacokinetics of NOVOSEVEN® was observed. Range of mean PK parameters across dose groups 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))

<table>
<thead>
<tr>
<th>Healthy Subjects</th>
<th>Hemophilia A or B</th>
<th>FVII Deficiency</th>
<th>Dose (mcg/kg)</th>
<th>CL (mL/h)</th>
<th>AUC (h*IU/mL)</th>
<th>t½ (h)</th>
<th>Vss (mL/kg)</th>
<th>CL (mL/h)</th>
<th>AUC (h*IU/mL)</th>
<th>t½ (h)</th>
<th>Vss (mL/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Subjects</td>
<td>40, 80, 160</td>
<td>90</td>
<td>17.5, 35, 70</td>
<td>90</td>
<td>30</td>
<td>20-43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemophilia A or B</td>
<td>113.26 (17.36)</td>
<td>3.51 (0.27)*</td>
<td>2.45 (0.73)</td>
<td>23.7 (2.73)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVII Deficiency</td>
<td>1000 (438)</td>
<td>3.0 (0.24)*</td>
<td>2.9 (0.3)</td>
<td>2.6 (0.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doses (mcg/kg)</td>
<td>30, 60, 90</td>
<td>90</td>
<td>30</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CL (mL/h)</td>
<td>3.0 (0.24)*</td>
<td>2.9 (0.3)</td>
<td>2.6 (0.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC (h*IU/mL)</td>
<td>1068.36 (20.35)</td>
<td>3.0 (0.24)*</td>
<td>2.9 (0.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t½ (h)</td>
<td>120 (30)</td>
<td>120 (30)</td>
<td>120 (30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vss (mL/kg)</td>
<td>5.0 (1.6)</td>
<td>5.0 (1.6)</td>
<td>5.0 (1.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on the 80 mcg/kg dose
**Based on the 70 mcg/kg dose
NA: Not available

### Table 5: Single Dose Pharmacokinetic Parameters in Hemophilia A Patients With and Without Inhibitors (Mean (SD))

<table>
<thead>
<tr>
<th>Hemophilia A Patients With Inhibitors</th>
<th>Hemophilia A Patients Without Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (mcg/kg)</td>
<td>CL (mL/h)</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Healthy Subjects</td>
<td>40, 80, 160</td>
</tr>
<tr>
<td>Hemophilia A</td>
<td>3.51 (0.27)*</td>
</tr>
</tbody>
</table>
with inhibitors and one patient with acquired hemophilia who were undergoing elective major surgery. Table 7 provides the overview of patients treated with NOVOSEVEN® RT and BI and CI.

Table 7: Dosing by Treatment Group

<table>
<thead>
<tr>
<th>Dosing Method</th>
<th>BI (n=38)</th>
<th>CI (n=166)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of dosing, median (range)</td>
<td>5 (2-12)</td>
<td>7 (2-12)</td>
</tr>
<tr>
<td>No. bolus injections, median (range)</td>
<td>10 (10-20)</td>
<td>10 (2-10)</td>
</tr>
<tr>
<td>No. of additional bolus injections, median (range)</td>
<td>0 (0-3)</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>

6 Includes one patient with acquired hemophilia

and therefore not designed to select doses. The GTR captured data for 218 Glinzmann's thrombathenia patients with 103 bleeding and 128 surgeries, and confirmed NOVOSEVEN® RT as effective treatment for these patients.

14.2 Congenital Factor VII Deficiency

Data were collected from four studies in a compassionate use trial, in registries with 13 bleeding episodes (8 non-surgical, 3 surgical and 2 cases of trauma) and 9 patients were from the HTRS Registry. The studies were not designed to select doses or compare first-line efficacy or efficacy with other therapies. Thirty-two of these patients were enrolled in emergency and compassionate use trials conducted by Novo Nordisk (43 non-surgical bleeding episodes, 6 surgeries), 35 were reported in the published literature (20 surgeries, 10 non-surgical bleeding episodes, 4 cases of caesarean 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).

Data ranged from 6 to 98 micrograms per kg administered every 2-12 hours (except for prophylaxis, where doses were administered from 2 times a day up to 2 times per week). Patients were treated with an average of 1-10 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 trial, in registries with 177 bleeding episodes (68 non-surgical and 32 surgical bleeding episodes) and 9 patients were from the HTRS Registry with 13 bleeding episodes, 8 with non-surgical and 5 with surgical bleeding episodes. The remainder received NOVOSEVEN® RT for 113 bleeding episodes, surgeries, or traumatic injuries. Sixty-one of these patients were from the compassionate use program with 100 bleeding episodes (68 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 platelet transfusions, 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 77/100 (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 regimen was 88/144 (61%) compared to 59/59 (70%) when used as salvage treatment (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>

No. of Bleeding Episodes

1 No. of patients are not additive. Patients may have episodes with different treatment regimens and have more than one antibody/refractory status

3 Anti-factor VIIa monoclonal antibodies were used in 9 patients. One patient in the HTRS registry was excluded from efficacy analysis since the patient was a non-clinical investigator.

NOVOSEVEN® RT, Coagulation Factor VIII (Recombinant)
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-dose vials, one single-dose vial per carton. The diluent supplied as a room temperature stable, white, lyophilized powder (RT) in a single-dose vial and pre-filled diluent syringe is provided in either a vial or pre-filled diluent syringe. The amount of rFVIIa in milligrams and in micrograms is stated on the label.

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

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton NDC Number</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mg per vial (1000 micrograms/vial)</td>
<td>NDC 0169 7201 01</td>
<td>• NOVOSEVEN® RT in a single-dose vial (NDC 0169-7211-11) • Pre-filled histidine diluent in syringe, 1 mL (NDC 0169-7011-98) • Vial adapter</td>
</tr>
<tr>
<td>2 mg per vial (2000 micrograms/vial)</td>
<td>NDC 0169 7202 01</td>
<td>• NOVOSEVEN® RT in a single-dose vial (NDC 0169-7212-11) • Pre-filled histidine diluent in syringe, 2 mL (NDC 0169-7012-98) • Vial adapter</td>
</tr>
<tr>
<td>5 mg per vial (5000 micrograms/vial)</td>
<td>NDC 0169 7205 01</td>
<td>• NOVOSEVEN® RT in a single-dose vial (NDC 0169-7215-11) • Pre-filled histidine diluent in syringe, 5 mL (NDC 0169-7015-98) • Vial adapter</td>
</tr>
<tr>
<td>8 mg per vial (8000 micrograms/vial)</td>
<td>NDC 0169 7208 01</td>
<td>• NOVOSEVEN® RT in a single-dose vial (NDC 0169-7218-11) • Pre-filled histidine diluent in syringe, 8 mL (NDC 0169-7018-98) • Vial adapter</td>
</tr>
</tbody>
</table>

The NOVOSEVEN® RT and histidine diluent vials are made of glass closed with a chlorobutyl rubber stopper not made with natural rubber latex, and covered with an aluminum cap. The pre-filled diluent syringes are made of glass, with a siliconised bromobutyl rubber plunger not made with natural rubber latex. The closed vials and pre-filled diluent syringes are equipped with a tamper-evident snap-off cap which is made of polypropylene. A vial adapter with 25 micrometer filter is provided with the pre-filled diluent syringe.

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 either 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.

Version: 2020July-V20


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

Manufactured by:
Novo Nordisk A/S
2880 Bagsvaerd, Denmark
License Number: 1261
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US20NSVN00120  8/20
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 diluent 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. Single-dose vial. Discard unused portion.

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
Vial adapter
Rubber stopper
(under plastic cap)
Protective cap
Pre-filled syringe with diluent
Syringe tip
(under syringe cap)
Plunger rod
Rubber
Protection paper
Thread
Scale
Wide top
end
Syringe cap

1. Prepare the vial and the syringe
• Take out the number of NOVOSEVEN® RT packages you need.
• Check the expiry date.
• Check the name and the color 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 98.6°F (37°C)). You can do this by holding them in your hands until they feel as warm as your hands.

• Remove the plastic cap from the vial. If the plastic cap is loose or missing, don’t 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. Don’t touch the rubber stopper after wiping it.

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.

2. Attach the vial adapter
• Remove the protective paper from the vial adapter.
• Don’t take the vial adapter out of the protective cap.
• Place the vial on a flat and solid surface.
• Turn over the protective cap, and snap the vial adapter onto the vial.
• Don’t touch the spike on the vial adapter.

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

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 up until resistance is felt.

• Remove the syringe cap from the pre-filled syringe by bending it down until the perforation breaks. Don’t touch the syringe tip under the syringe cap.
• If the syringe cap is loose or missing, don’t use the pre-filled syringe.

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 vial.

• Keep the plunger rod pressed down and swirl the vial gently until all the powder is dissolved. Don’t shake the vial as this will cause foaming.
• Check the mixed solution. It must look clear. If you notice visible particles or discoloration, don’t use it. Use a new package instead.

NOVOSEVEN® RT is recommended to be used immediately after it is mixed.

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.
• It necessary, use 0.9% Sodium Chloride Injection, USP to flush the CVAD line before or after NOVOSEVEN® RT injection.

The peel-off label found on the NOVOSEVEN® RT vial can be used to record the lot number.

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.

• 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 mixture solution fills the syringe.
• Pull the plunger rod slightly downwards to draw the mixed solution into the syringe. In case 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.

• Unscrew the vial adapter with the vial.

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®, InVision-Plus®, InVision-Plus CS®, InVision-Plus® Junior®, Bionector®), 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 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.
For full Prescribing Information please read the other insert included in this package.

Revised: 07/2020


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2880 Bagsvaerd, Denmark
License Number: 1261
Version: 20200710-v8
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US20NSVN00120 8/20