### Dosage and Administration

#### For intravenous injection only

<table>
<thead>
<tr>
<th>Bleeding Episodes (2.1)</th>
<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>
<td>90 mcg/kg every 3-6 hours after hemostasis is achieved for severe bleeds</td>
</tr>
<tr>
<td>Acquired Hemophilia</td>
<td>70-90 mcg/kg every 2-3 hours until hemostasis is achieved</td>
<td></td>
</tr>
<tr>
<td>Congenital Factor VII Deficiency</td>
<td>15-30 mcg/kg every 4-6 hours until hemostasis is achieved</td>
<td></td>
</tr>
<tr>
<td>Glanzmann's Thrombasthenia</td>
<td>90 mcg/kg every 2-6 hours until hemostasis is achieved</td>
<td></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>Minor: 90 mcg/kg immediately before surgery, repeat every 2 hours during surgery 90 mcg/kg every 2 hours after surgery for 48 hours, then every 2-6 hours until healing has occurred Major: 90 mcg/kg immediately before surgery, repeat every 2 hours during surgery 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>
<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 90 mcg/kg every 2-6 hours to prevent post-operative bleeding</td>
</tr>
</tbody>
</table>

### Dosing Recommendation

*Initial U.S. Approval: 1999

**NOVOSEVEN® RT (coagulation Factor VIIa, recombinant) lyophilized powder for solution, for intravenous use**

*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

**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.

**Recent Major Changes**

Dosing and Administration (2.1, 2.3) 10/2018

Warnings and Precautions (5.1, 5.2) 10/2018

**Indications and Usage**

NOVOSEVEN® RT, Coagulation Factor VIIa (Recombinant) is indicated for:

- Treatment of bleeding episodes and perioperative 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 perioperative management in adults with acquired hemophilia

**Dosage Forms and Strengths**

Available as lyophilized powder in single-use 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® RT 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: 1/2019

### Full Prescribing Information: Contents

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FULL PRESCRIBING INFORMATION

WARNING: THROMBOSIS

- Serious arterial and venous thrombotic events following administration of NOVOSEVEN® RT have been reported. [See Warnings and Precautions (5.1)]
- Discuss the risks and the signs and symptoms of thrombotic and thromboembolic events to patients who will receive NOVOSEVEN® RT. [See Warnings and Precautions (5.1)]
- Monitor patients for signs or symptoms of the coagulation system and for thrombosis. [See Warnings and Precautions (5.1)]

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 Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Hemophilia A or B with Inhibitors</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2-3 hours for the duration of the surgery. Post surgical: 90 mcg/kg every 2 hours for 48 hours then every 2-6 hours until healing occurs.</td>
</tr>
<tr>
<td>Acquired Hemophilia</td>
<td>Initial: 70-90 mcg/kg immediately before surgery and repeat every 2-3 hours for the duration of the surgery and until hemostasis is achieved.</td>
</tr>
<tr>
<td>Congenital Factor VII Deficiency</td>
<td>Initial: 15-30 mcg/kg immediately before surgery and repeat every 4-6 hours for the duration of the surgery and until hemostasis is achieved.* Adjust dose and frequency of injections to each individual patient.</td>
</tr>
<tr>
<td>Glanzmann’s Thrombasthenia</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure. Post surgical: 90 mcg/kg every 2-6 hours to prevent post-operative bleeding.*</td>
</tr>
</tbody>
</table>

*The minimum effective dose has not been determined.

Concentrations are provided in Table 1.

Additional Dosing

- For patients treated for joint or muscle bleeds, a decision on dose and administration interval may be adjusted to the individual patient based on the severity of the bleeding.1
- For patients treated for joint or muscle bleeds, a decision on dose and administration interval may be adjusted to the individual patient based on the severity of the bleeding.1
- For patients treated for joint or muscle bleeds, a decision on dose and administration interval may be adjusted to the individual patient based on the severity of the bleeding.1

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.

Table 2: Dosing for Perioperative Management

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Dose and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2-3 hours for the duration of the surgery. Post surgical: 90 mcg/kg every 2 hours for the duration of the surgery.</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. Post surgical: 90 mcg/kg every 2 hours for 48 hours then every 4 hours or by continuous infusion at 50 mcg/kg/hr until healing occurs.</td>
</tr>
</tbody>
</table>

Additional bolus doses can be given.

3.0 Administration

- Always use aseptic technique.
- 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. 1 mg (1000 micrograms) vial + 1.1 mL Histidine diluent
  2. 2 mg (2000 micrograms) vial + 2.1 mL Histidine diluent
  3. 5 mg (5000 micrograms) vial + 5.2 mL Histidine diluent
  4. 8 mg (8000 micrograms) vial + 8.1 mL Histidine diluent
- 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.
- 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.
- Insert the needle of the syringe into the Histidine diluent vial. Inject air into the vial and withdraw the quantity required for reconstitution.
- 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.
- 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.

4.0 Administration

- Vial with NovoSeven® RT powder
- Vial adapter
- Pre-filled syringe with diluent
- Plunger rod
- Protective cap
- Protective paper
- Syringe tip (under syringe cap)
- Scale

- Always use aseptic technique.
- 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. 1 mg (1000 micrograms) vial + 1 mL Histidine diluent
  2. 2 mg (2000 micrograms) vial + 2 mL Histidine diluent
  3. 5 mg (5000 micrograms) vial + 5 mL Histidine diluent
  4. 8 mg (8000 micrograms) vial + 8 mL Histidine diluent
- Remove caps from the NOVOSEVEN® RT vial. Cleanse the rubber stopper with an alcohol swab and allow to dry prior to use.
- Peel back the protective paper from the vial adapter. Do not remove the vial adapter from the 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 vial 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 in syringes.
- Administer within 3 hours after reconstitution.
- Do not mix with other infusion 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 needleless 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 vial.
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 needless 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®/Biojector®), 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) 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 DOSEAGE 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) reconstituted coagulation Factor VII (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.
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 hematostatic 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 (7.1) 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 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) 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 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.

Data from 75 patients with factor FVII deficiency treated with NOVOSEVEN® RT 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® on bleeding times/volumes in models of clinically-induced bleeding in healthy volunteers who had received Warfarin, when laboratory parameters (PT/INR, aPTT, thromboelastogram) have normalized.

While administration of NOVOSEVEN® shortens the prolonged aPTT in hemophilia A/B patients with inhibitors, normalization 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® administration of 35 micrograms per kg body weight and 90 micrograms per kg body weight following hemostatic dosing at two-hour intervals. Average steady state levels were 11 and 28 units per mL for the two dose levels, respectively.

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® 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># of adverse reactions (n=1,939 treatments)</th>
<th># of patients (n=298 reactions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a whole</td>
<td>Fever</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Platelets, Bleeding, and Clotting</td>
<td>Fibrinogen plasma decreased</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Hypertension</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Immune reactivity</td>
<td>Thrombotic events (see Table 3 below)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immune reactivity</td>
<td>Severe, serious adverse reactions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Serious adverse reactions included thrombosis, pain, thrombophilies, deep pulmonary embolism, decreased therapeutic response, 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® administration 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 hemorrhage (n=1), decreased therapeutic response (n=4).

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

Congenital 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).
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 HTS registry, and the published literature showed that 139 patients with acquired hemophilia received NOVOSEVEN® for 264 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 thrombocytopenic events (n=6) which included cerebral artery occlusion, cerebral ischemia, angina pectoris, myocardial infarction, peptic ulcer and 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 HTS registry showed that 140 patients with Glanzmann’s thrombasthenia received NOVOSEVEN® RT for 516 bleeding episodes, surgeries, and traumatic injuries. Of these 140 patients, 6 patients experienced 8 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, peptic ulcer and thrombosis. Three of the serious adverse reactions had a fatal outcome.

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 per kg body weight and 5 mg/kg per kg body weight respectively. At 6 mg/kg per 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 23 litters. Forty-three out of 25 female rats given 6 mg 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.

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 condition. In general, breastfeeding should be considered along with the mother’s clinical condition. Breastfeeding should be considered along with the mother’s clinical condition. Breastfeeding should be considered along with the mother’s clinical condition.

8.3 Pediatric 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.

10 OVERDOSE

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® RT (20,800 micrograms per kg body weight). NOVOSEVEN® RT also contains trace amounts of proteins derived from bovine plasma and therefore may contain Bacillus cereus endotoxin.

11 DESCRIPTION

NOVOSEVEN® RT, Coagulation Factor VIIa (Recombinant) is a sterile, white lyophilized powder of recombinant human coagulation factor VIIa (rFVIIa) for reconstitution for intravenous injection. The product is supplied as single-use 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 micrograms</td>
<td>2000 micrograms</td>
<td>5000 micrograms</td>
<td>8000 micrograms</td>
</tr>
<tr>
<td>sodium chloride</td>
<td>2.34 mg</td>
<td>4.68 mg</td>
<td>11.7 mg</td>
<td>18.72 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>Glycosylglycine</td>
<td>1.32 mg</td>
<td>2.64 mg</td>
<td>6.60 mg</td>
<td>10.56 mg</td>
</tr>
<tr>
<td>polysorbate 80</td>
<td>0.07 mg</td>
<td>0.14 mg</td>
<td>0.35 mg</td>
<td>0.52 mg</td>
</tr>
<tr>
<td>Mannitol</td>
<td>25 mg</td>
<td>50 mg</td>
<td>125 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>Sodium Acetate</td>
<td>8 mg</td>
<td>10 mg</td>
<td>20 mg</td>
<td>30 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>

Dosage: 100-200 micrograms per kg body weight in newborns and infants, 50-100 micrograms per kg body weight in children, and 25-50 micrograms per kg body weight in adults. Each microgram of rFVIIa contains 1 microgram of NOVOSEVEN® RT. One microgram of rFVIIa contains 1 microgram of NOVOSEVEN® RT. Each microgram of rFVIIa contains 1 microgram of NOVOSEVEN® RT.
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>Formulation (n)</th>
<th>Healthy Subjects</th>
<th>Hemophilia A or B</th>
<th>FVII Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rFVIIa (n=35)</td>
<td>rFVIIa-25C (n=22)</td>
<td>rFVIIa (n=15)</td>
</tr>
<tr>
<td>Ages</td>
<td>20-45</td>
<td>22-44</td>
<td>15-63</td>
</tr>
<tr>
<td>Doses (mcg/kg)</td>
<td>40, 60, 160</td>
<td>90</td>
<td>17.5, 35, 70</td>
</tr>
<tr>
<td></td>
<td>3.0 (0.5)</td>
<td></td>
<td>3.0 (0.73)</td>
</tr>
<tr>
<td>AUC (h*U/mL)</td>
<td>71.46, 76.91*</td>
<td>113.26 (17.36)*</td>
<td>53.31 (20.27)**</td>
</tr>
<tr>
<td></td>
<td>5.31 (2.27)**</td>
<td></td>
<td>2.45 (0.73)</td>
</tr>
<tr>
<td>CL (mL/h)</td>
<td>1953-2516</td>
<td>3077 (438)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>2587 (385)</td>
<td></td>
<td>2767 (385)</td>
</tr>
<tr>
<td>CL (mL/kg/h)</td>
<td>33-37</td>
<td>40.43 (6.23)</td>
<td>33.84 (11.72)</td>
</tr>
<tr>
<td></td>
<td>34.11 (17.12)</td>
<td></td>
<td>37.6 (13.11)</td>
</tr>
<tr>
<td>t½ (h)</td>
<td>3.9-6.0</td>
<td>3.54 (0.28)</td>
<td>2.72 (0.54)</td>
</tr>
<tr>
<td></td>
<td>3.0 (0.3)</td>
<td></td>
<td>3.2 (0.3)</td>
</tr>
<tr>
<td>Vss (mL/kg)</td>
<td>130-165</td>
<td>122.96 (20.42)</td>
<td>108.96 (37.15)</td>
</tr>
<tr>
<td></td>
<td>121 (30)</td>
<td></td>
<td>121 (30)</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>3.66-4.98</td>
<td>3.05 (0.27)</td>
<td>3.33 (0.64)</td>
</tr>
<tr>
<td></td>
<td>3.31 (0.38)</td>
<td></td>
<td>3.31 (0.38)</td>
</tr>
<tr>
<td>IR ((U/L)/U(L/j))</td>
<td>0.89-1.04</td>
<td>1.18 (0.16)²</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>0.94 (0.15)</td>
<td></td>
<td>0.94 (0.15)</td>
</tr>
</tbody>
</table>

*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: NOVOSEVEN original formulation; rFVIIa-25C: NOVOSEVEN RT

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

<table>
<thead>
<tr>
<th>Formulation/ inhibitor status/ age group (n)</th>
<th>Healthy Subjects</th>
<th>Hemophilia A or B</th>
<th>Ferritin</th>
</tr>
</thead>
<tbody>
<tr>
<td>rFVIIa, without inhibitors, age ≤5 years</td>
<td>2.5</td>
<td>3-10</td>
<td>72-97</td>
</tr>
<tr>
<td>(n=3)</td>
<td></td>
<td></td>
<td>54-89</td>
</tr>
<tr>
<td>rFVIIa, with inhibitors, age ≤5 years</td>
<td>3-7</td>
<td>72-97</td>
<td>54-89</td>
</tr>
<tr>
<td>(n=2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doses (mcg/kg)</td>
<td>90, 180, 90, 180</td>
<td>90, 180, 90, 180</td>
<td>90</td>
</tr>
<tr>
<td>AUC (h*U/mL)</td>
<td>1.26 (0.09)*</td>
<td>1.51 (0.25)*</td>
<td>1.68 (0.24)*</td>
</tr>
<tr>
<td>CL (mL/h)</td>
<td>1131 (114)</td>
<td>1387 (75)</td>
<td>1688 (510)</td>
</tr>
<tr>
<td>CL (mL/kg)</td>
<td>73 (8)</td>
<td>61 (9)</td>
<td>52 (12)</td>
</tr>
<tr>
<td>t½ (h)</td>
<td>2.6 (0.9)</td>
<td>1.9 (0.6)</td>
<td>3.0 (0.5)</td>
</tr>
<tr>
<td>Vss (mL/kg)</td>
<td>191 (44)</td>
<td>145 (1)</td>
<td>149 (22)</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>2.6 (0.5)</td>
<td>2.4 (0.4)</td>
<td>2.9 (0.3)</td>
</tr>
<tr>
<td>IR ((U/L)/U(L/j))</td>
<td>0.59 (0.06)</td>
<td>0.75 (0.12)</td>
<td>0.76 (0.20)</td>
</tr>
</tbody>
</table>

*Based on the 90 mcg/kg dose

Nonclinical and clinical studies with the combination of excessive doses of Coagulation Factor XIII A-Subunit (Recombinant) (585 IU/kg, 17 times the expected human dose) in combination with rFVIIa (1000 mcg/kg, 11 times the expected human dose), one of the twelve monkeys died 4 hours after treatment due to thrombosis. Prorocacoaefactor ratios, including 6 indwelling catheters per monkey and the induction of anesthesia, may have complicated the study results. It is unclear whether the mortality was related to the overdose of one or both products, or a specific interaction between them. Nonclinical and clinical studies with the combination of rFVIIa and NOVOSEVEN RT at recommended human doses have not been performed.
Two clinical trials were conducted to evaluate the safety and efficacy of NOVOSEVEN® administration during and after surgery in hemophiliacs A or B patients with inhibitors. One of the studies was randomized, double-blind, parallel group clinical trial (28 patients with hemophilia A or B and inhibitors and one patient with acquired inhibitor to FVIII, undergoing major or minor surgical procedures).14 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 therapy, treatment 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.

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 (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 aminocaproic acid, 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 seen in 87/122 (72%), with 77/110 (70%) 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 seen in 38/44 (86%) compared to 39/56 (70%) when used as salvage treatment (Table 6).

Table 6: Dosing by Surgery Category

<table>
<thead>
<tr>
<th>Surgery Category</th>
<th>Major Surgery</th>
<th>Minor Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of dosing, median (range)</td>
<td>4 (2-6)</td>
<td>6 (4-13)</td>
</tr>
<tr>
<td>No. of patients, median (range)</td>
<td>135 (11-186)</td>
<td>65 (31-122)</td>
</tr>
</tbody>
</table>

Table 7: Dosing by Treatment Group

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Bolus Injection 90 micrograms/kg (n = 12)</th>
<th>Continuous Infusion 50 micrograms/kg/h (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of dosing, median (range)</td>
<td>10 (4-15)</td>
<td>10 (2-16)</td>
</tr>
<tr>
<td>No. bolus injections, median (range)</td>
<td>38 (36-42)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>Mean total dose, mg</td>
<td>237</td>
<td>292</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total</th>
<th>Effective</th>
<th>Partial</th>
<th>Ineffective</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Bleeding Episodes</td>
<td>112</td>
<td>67</td>
<td>20</td>
<td>17</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 9: Adjudicator Evaluation of Efficacy — Bleeding Episodes for GDT Data

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>All NOVOSEVEN®</th>
<th>NOVOSEVEN® only</th>
<th>NOVOSEVEN® + Platelets + Other hemostatic agents</th>
<th>Failure</th>
<th>Insufficient data</th>
<th>No Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>92</td>
<td>44</td>
<td>69</td>
<td>2 (1.8)</td>
<td>6 (2.3)</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>No. of episodes</td>
<td>266</td>
<td>109</td>
<td>157</td>
<td>101 (92.7)</td>
<td>101 (92.7)</td>
<td>101 (92.7)</td>
</tr>
<tr>
<td>Success</td>
<td>251 (94.4)</td>
<td>101 (92.7)</td>
<td>157 (99.3)</td>
<td>2 (1.8)</td>
<td>6 (2.3)</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>Failure</td>
<td>4 (1.5)</td>
<td>2 (1.8)</td>
<td>2 (1.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Table 10: Adjudicator Evaluation of Efficacy — Surgical Procedures for GDT Data

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>All NOVOSEVEN®</th>
<th>NOVOSEVEN® only</th>
<th>NOVOSEVEN® + Platelets + Other hemostatic agents</th>
<th>Failure</th>
<th>Insufficient data</th>
<th>No Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>77</td>
<td>35</td>
<td>57</td>
<td>26 (33.8)</td>
<td>24 (31.9)</td>
<td>24 (31.9)</td>
</tr>
<tr>
<td>No. of procedures</td>
<td>160</td>
<td>65</td>
<td>85</td>
<td>65 (98.5)</td>
<td>65 (98.5)</td>
<td>65 (98.5)</td>
</tr>
<tr>
<td>Failure</td>
<td>65 (98.5)</td>
<td>65 (98.5)</td>
<td>65 (98.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Insufficient data</td>
<td>6 (2.3)</td>
<td>6 (2.3)</td>
<td>6 (2.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

* Includes all treatment regimens that included treatment with NOVOSEVEN® only.
* Includes GPIb/IIa, HLA, and unspecified platelet-specific antibodies.
* Includes Platelet-specific antibodies.
* Includes Platelet-specific antibodies and antibody status.
* Includes Adjudicator-rated efficacy was consistent across treatment regimens, bleed and surgery types, age, and refractory/antibody status.

The majority of NOVOSEVEN® RT treated bleeding episodes were in pediatric patients (65%; children and adolescents, 0-16 yrs.). Of the 266 bleeding episodes treated with NOVOSEVEN® RT, the most common types of bleeding episodes were: epistaxis (116, 43.5%), gum bleeding (48, 18.0%), menorrhagia (36, 13.5%), tooth/dental extraction related (29, 10.9%), and gastrointestinal (23, 8.6%).

Of the patients treated with NOVOSEVEN® RT for surgical procedures, 86% were adults (> 16 years). Major surgery was defined as any invasive operative procedure in which, only skin, mucous membranes, or superficial connective tissue were manipulated. Surgical procedures treated with NOVOSEVEN® RT included minor (134/160, 83.8%) and major (26/160, 16.3%) procedures. Dental procedures were most common (106, 66.3%), followed by endoscopy (12*, 7.5%), nasal procedures (8, 5.0%), excision (7, 4.4%), GI surgery (7, 4.4%) and orthopedic procedures (6, 3.8%). Most surgeries were elective (147, 91.9%), with a few emergency (7, 4.4%) or unspecified (6). Overall, treatment with NOVOSEVEN® RT was successful in 94.4% of bleeding episodes (Table 9) and 99.4% of surgical procedures (Table 10). Adjudicator-rated efficacy was consistent across treatment regimens, bleed and surgery types, age, and refractory/antibody status. Treatment with NOVOSEVEN® RT was successful in patients with clinical refractoriness with or without platelet-specific antibodies in 94.9% of bleeding episodes and 98.6% of surgical procedures. In patients without refractoriness or platelet-specific antibodies, treatment with NOVOSEVEN® RT was comparable to treatment with platelets.
**NOVOSEVEN® RT, Coagulation Factor VIIa (Recombinant)**

**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 diluent syringe.

The amount of rFVIIa in milligrams and in micrograms is stated on the label.

16 **How Supplied/Storage and Handling**

**How Supplied**

NOVOSEVEN® RT package containing 1 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 7010 01</td>
<td>• NOVOSEVEN® RT in a single-use vial (NDC 0169-7017-11) • Histidine diluent in vial, 1.1 mL (NDC 0169-7001-98)</td>
</tr>
<tr>
<td>2 mg per vial (2000 micrograms/vial)</td>
<td>NDC 0169 7020 01</td>
<td>• NOVOSEVEN® RT in a single-use vial (NDC 0169-7027-11) • Histidine diluent in vial, 2.1 mL (NDC 0169-7002-98)</td>
</tr>
<tr>
<td>5 mg per vial (5000 micrograms/vial)</td>
<td>NDC 0169 7050 01</td>
<td>• NOVOSEVEN® RT in a single-use vial (NDC 0169-7057-11) • Histidine diluent in vial, 5.2 mL (NDC 0169-7005-98)</td>
</tr>
<tr>
<td>8 mg per vial (8000 micrograms/vial)</td>
<td>NDC 0169 7040 01</td>
<td>• NOVOSEVEN® RT in a single-use vial (NDC 0169-7047-11) • Vial adapter</td>
</tr>
</tbody>
</table>

**NOVOSEVEN® RT with MixPro® package containing 1 vial of NOVOSEVEN® RT powder and 1 pre-filled histidine diluent syringe with sterile vial adapter which serves as an alternative needleless reconstitution system:**

<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-use 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-use 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-use 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-use vial (NDC 0169-7218-11) • Pre-filled histidine diluent in syringe, 8 mL (NDC 0169-7018-98) • Vial adapter</td>
</tr>
</tbody>
</table>

**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**

Advising 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: 2019January-V19


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Bionector® is a registered trademark of VYGON.

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1-877-NOVO-777

www.NOVOSEVEN.com

Manufactured by: Novo Nordisk A/S

2880 Bapsgaard, Denmark

License Number: 1261

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US19INSN00010 1/19
NOVOSEVEN® RT is supplied as a powder. Before injection (administration) it must be mixed (reconstituted) with the liquid diluent supplied in the vial. 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

Vial adapter

Protective cap

Rubber stopper

(under plastic cap)

Scale

Plastic cap

Pre-filled syringe with diluent

Syringe tip

Rubber plunger

Plunger rod

Wide top end

Thread

Protective paper

Protective cap

Spike (under protective paper)

Rubber stopper

Scope (under plastic 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. If the protective paper is not fully sealed or if it is broken, don’t use the vial adapter.

- 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.
- Once attached, don’t remove the vial adapter from the vial.

- Lightly squeeze the protective cap with your thumb and index finger as shown.
- Remove the protective cap from the vial adapter.
- Don’t lift the vial adapter from the vial when removing the protective cap.

3. Attach the plunger rod and the syringe

- Grasp the plunger rod by the wide top end and take it out of the carton. 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.

- 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.

- Screw the pre-filled syringe securely onto the vial adapter until resistance is felt.
- Avoid touching the sides of the plunger rod at any time.

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 syringe.

- 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 be clear and colorless.
- If you notice visible particles or discoloration, don’t use it. Use a new package instead.

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

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.

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. Make sure you only need part of the entire dose, use the scale on the syringe to see how much mixed solution you withdraw. Instruct 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 10 mL sterile Luer-lock connector.

Some needless 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®, Bioclamp®), 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.