**NovoSeven® RT**

Coagulation Factor VIIa (Recombinant)

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use NovoSeven® RT safely and effectively. See full prescribing information for NovoSeven® RT. NovoSeven® RT, Coagulation Factor VIIa (Recombinant) For Intravenous Use Only. Lyophilized Powder for Solution for Injection Initial U.S. Approval: 1999

**WARNINGS AND PRECAUTIONS**

- Serious arterial and venous thrombotic events following administration of NovoSeven® RT have been reported. (5.1)
- 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. (5.1)

**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 (1)
- Treatment of bleeding episodes and perioperative management in adults with acquired hemophilia (1)

**DOSAGE AND ADMINISTRATION**

For intravenous bolus 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>
<tr>
<td>Acquired Hemophilia</td>
<td>70-90 mcg/kg every 2-3 hours until hemostasis is achieved</td>
</tr>
<tr>
<td>Congenital Factor VII Deficiency</td>
<td>15-30 mcg/kg every 4-6 hours until hemostasis is achieved</td>
</tr>
<tr>
<td>Glanzmann’s Thrombasthenia</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>
<tr>
<td>Major:</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 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 2-6 hours for the duration of surgery and until hemostasis is achieved</td>
</tr>
<tr>
<td>Glanzmann’s Thrombasthenia</td>
<td>90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure</td>
</tr>
<tr>
<td></td>
<td>90 mcg/kg every 2-6 hours to prevent post-operative bleeding</td>
</tr>
</tbody>
</table>

**ADVERSE REACTIONS**

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

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-877-668-6777 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

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

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

Revised: 10/2015
**Dose and Initial:** 70-90 mcg/kg

**Congenital Hemophilia A or B with Inhibitors**

*The minimum effective dose has not been determined.*

**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>Minimal</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2-3 hours</td>
<td>Until hemostasis is achieved</td>
</tr>
<tr>
<td></td>
<td>Post-surgical: 90 mcg/kg every 2-3 hours</td>
<td>For the duration of the surgery</td>
</tr>
<tr>
<td>Acquired Hemophilia</td>
<td>Initial: 70-90 mcg/kg immediately before surgery and repeat every 4-6 hours</td>
<td>Until hemostasis is achieved</td>
</tr>
<tr>
<td></td>
<td>Post-surgical: 90 mcg/kg every 4-6 hours</td>
<td>For the duration of the surgery</td>
</tr>
<tr>
<td>Glanzmann's Thrombasthenia</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours</td>
<td>Effective treatment has been achieved with doses as low as 10 micrograms per kg body weight</td>
</tr>
<tr>
<td></td>
<td>Post-surgical: 90 mcg/kg every 2-6 hours</td>
<td>To prevent post-operative bleeding</td>
</tr>
</tbody>
</table>

*The minimum effective dose has not been determined.*

**2. DOSAGE AND ADMINISTRATION**

**For intravenous bolus administration only**

**2.1 Dose**

- Treatment with NovoSeven® RT should be initiated under the direction of a qualified healthcare professional experienced in the treatment of bleeding disorders.
- 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.

**Treatment of Acute Bleeding Episodes**

NovoSeven® RT dosing for the treatment of acute bleeding episodes is provided in Table 1.

<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>Initial: 90 mcg/kg immediately before surgery and repeat every 2-3 hours</td>
<td>Until hemostasis is achieved</td>
</tr>
<tr>
<td></td>
<td>Post-surgical: 90 mcg/kg every 2-3 hours</td>
<td>For the duration of the surgery</td>
</tr>
<tr>
<td>Glanzmann's Thrombasthenia</td>
<td>Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours</td>
<td>Effective treatment has been achieved with doses as low as 10 micrograms per kg body weight</td>
</tr>
<tr>
<td></td>
<td>Post-surgical: 90 mcg/kg every 2-6 hours</td>
<td>To prevent post-operative bleeding</td>
</tr>
</tbody>
</table>

**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 explain 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 activation of the coagulation system and for thrombosis. [See Warnings and Precautions (5.1)]

**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 vial.

**Pre-filled syringe with diluent**

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

**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 mL Histidine diluent
  - 2 mg (2000 micrograms) vial + 2 mL Histidine diluent
  - 5 mg (5000 micrograms) vial + 5 mL Histidine diluent
  - 8 mg (8000 micrograms) vial + 8 mL Histidine diluent
- 3. Remove caps from the NovoSeven® RT vials. Cleanse the rubber stoppers with an alcohol swab and allow to dry prior to use.
- 4. Peel back the protective paper from the vial adapter. Do not remove the vial adapter from the package.
- 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 of NovoSeven RT (1000 micrograms per mL).

2.3 Administration

For intravenous bolus 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 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 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 needless 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 admitting 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. Unscrew the vial adapter with the vial. Discard the empty vial adapter. Administer 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®, 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, contact Novo Nordisk (at 877) 968-7677.

Administer NovoSeven RT 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.

3 DOSAGE FORMS AND STRENGTHS

NovoSeven RT is available as a white lyophilized powder in single-use vials containing 1 mg (1000 micrograms), 2 mg (2000 micrograms), 5 mg (5000 micrograms), or 8 mg (8000 micrograms) recombinant coagulation Factor VIIa (FVII:C) per vial. The diluted solution of L-histidine in water for injection, it contains 0.9% sodium chloride 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 disseminated intravascular coagulation (DIC), advanced atherosclerotic disease, crush injury, sepsis, or coagulant treatment with aPCs/PCsC (activated or nonactivated prothrombin complex concentrates) and uncontrolled post-partum hemorrhage have an increased risk of developing thromboembolic events due to circulating tissue factor (TF) or predisposing coagulopathy (See Adverse Reactions (6.1) and Drug Interactions (7)).

• Exercise caution when administering NovoSeven RT to patients with an increased risk of thromboembolic complications. These include, but are not limited to, patients with a history of coronary heart disease, liver disease, disseminated intravascular coagulation, elderly patients, and neonates. In each of these situations, the potential benefit of treatment with NovoSeven RT should be weighed against the risk of these complications.

• Monitor patients who receive NovoSeven RT for development of signs or symptoms of activation of the coagulation system or thrombosis. When there is laboratory evidence 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 have been reported with NovoSeven RT. Administer NovoSeven RT only if clearly needed in patients with known hypersensitivity to NovoSeven RT or any of its components, or in patients with known hypersensitivity to mouse, hamster, or bovine proteins. Should symptoms occur, discontinue NovoSeven RT, administer appropriate treatment and weigh the benefit/risk priors to restarting treatment with NovoSeven RT.

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 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 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 following graph shows the PT in patients with Factor VII deficiency.

PT (sec)  PT versus FVII:C

<table>
<thead>
<tr>
<th>FVII:C (unit per mL)</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aPTT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6 ADVERSE REACTIONS

The most common and serious adverse reactions in clinical trials are thrombotic events. Thrombotic adverse reactions following the administration of NovoSeven RT in clinical trials occurred in 4% of patients with known hemophilia A/B 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 22% of the patients who were treated with NovoSeven RT for 1,959 bleeding episodes (See Table 3 below).

<table>
<thead>
<tr>
<th>Body System</th>
<th>Reactions</th>
<th># of adverse reactions</th>
<th># of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a whole</td>
<td>Fever</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Platelets, Bleeding, and Clotting</td>
<td>Fibrogen plasma decreased</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Hypertension</td>
<td>9</td>
<td>6</td>
</tr>
</tbody>
</table>

Serious adverse reactions included thrombosis, pain, thrombophlebitis, deep, pulmonary embolism, decreased therapeutic response, cerebral vasoconstriction disorder, anagia pectoris, DIC, anaphylactic shock and anaphylaxis. Several adverse reactions of DIC and therapeutic response decreased had a fatal outcome.

In two clinical trials evaluating safety and efficacy of NovoSeven RT administration in the perioperative setting in hemophilia A or B patients with inhibitors (N=51), the following serious adverse reactions were reported: acute post-operative hemorrhaxis (n=1), internal jugular thrombosis adverse reaction (n=1), decreased therapeutic response (n=4).

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.

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 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 FVIIa and FVII (n=1), localized phlebitis (n=1).

Immunogenicity

In 73 patients with factor VII deficiency treated with NovoSeven RT, one patient developed a IgG antibody against FVIIa 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, sampling handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to NovoSeven® RT with the incidence of antibodies to other products may be misleading.

Acquired Hemophilia

Data collected from four compassionate use programs, the HTSR registry, and the published literature showed that 139 patients with acquired hemophilia received NovoSeven® RT for 204 bleeding episodes, surgeries and traumatic injuries. Of these 139 patients, 6 patients experienced 8 serious adverse reactions. Serious adverse reactions included shock (n=1), cerebrovascular accident (n=1) and thromboembolic events (n=6) which included cerebral arterial occlusion, cerebral ischaemia, angiitis pectoris, myocardial infarction, pulmonary embolism and deep vein thrombosis. Three of the serious adverse reactions had fatal outcome.

Glanzmann’s Thrombasthenia

Data collected from the Glanzmann’s Thrombasthenia Registry (GTR) and the HTSR registry showed that 140 patients with Glanzmann’s thrombasthenia received NovoSeven® RT for 518 bleeding episodes, surgeries or traumatic injuries. The following adverse reactions were reported: deep vein thrombosis (n=1), headache (n=2), fever (n=2), nausea (n=1), and dyspnea (n=1).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of NovoSeven®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship.

Table 4: Post Marketing Experience

<table>
<thead>
<tr>
<th>MedDRA System Organ Class</th>
<th>Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td>Hypersensitivity (including anaphylactic shock, flushing, urticaria, rash, angioedema)</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Thromboembolic events (including hepatic artery thrombosis, myocardial infarction, cerebral infarction, intracranial thrombus, peripheral ischemia, portal vein thrombosis, myocardial infarction, renal artery thrombosis)</td>
</tr>
</tbody>
</table>

7 DRUG INTERACTIONS

• Avoid simultaneous use of activated prothrombin complex concentrates or prothrombin complex concentrates. The risk of a potential interaction between NovoSeven® RT and coagulation factor concentrates has not been adequately evaluated in preclinical or clinical studies.
• Do not mix NovoSeven® RT with infusion solutions.
• Thrombosis may occur if NovoSeven® RT is administered concomitantly with Coagulation Factor XIII. (See 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 of 6 mg per kg body weight and 5 mg per kg body weight respectively. At 6 mg per kg body weight, the abortion rate was 2 out of 25 litters. Twenty-three out of 25 female rats given 6 mg per kg body weight of NovoSeven® gave birth successfully. However, two of the 27 pregnant female rats 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 defect and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Breastfeeding

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.

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 and 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 given a single dose of NovoSeven® RT (4 mg/kg body weight) intravenously over 15 min. This resulted in an immediate increase of factor VII activity from 0 to 100% (the recommended dose) and experienced a thrombotic event (cerebral 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 (FVIIa) 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>2.94 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>Glycopyrrolate</td>
<td>1.32 mg</td>
<td>2.64 mg</td>
<td>6.09 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>0.56 mg</td>
</tr>
<tr>
<td>Mannitol</td>
<td>25 mg</td>
<td>50 mg</td>
<td>125 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td>Sucrose</td>
<td>10 mg</td>
<td>20 mg</td>
<td>50 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Methylparaben</td>
<td>0.1 mg</td>
<td>0.2 mg</td>
<td>0.4 mg</td>
<td>0.6 mg</td>
</tr>
<tr>
<td>* per mg of rFVIIa 0.4 mEq sodium, 0.01 mEq calcium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NovoSeven® RT also contains trace amounts of proteins derived from the manufacturing and purification processes such as mouse IgG (maximum of 1.2 mg/mg), bovine IgG (maximum of 30 ng/mg), and protein from BHK-cells and media (maximum of 19 mg/mg).

The diluent for reconstitution of NovoSeven® RT is a 10 mmol 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, use with the appropriate volume of histidine diluent. Each vial contains approximately 1 mg/mL NovoSeven® RT (corresponding to 1000 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 58 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 autotaxin to the active two-chain form, rFVIIa, during a chromatographic purification process. The purification process has been demonstrated to remove exogenous viruses (MuLV, SI140, Pox virus, RSV, and HIV-1) and Bacterial strains. 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 A1), the addition of rFVIIa increased both the rate and level of thrombin generation in normal and hemophilia A 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.
Table 5: Single Dose Pharmacokinetic Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>rFVIIa (n=35)</th>
<th>rFVIIa-25C (n=22)</th>
<th>rFVIIa (n=15)</th>
<th>rFVIIa (n=10)</th>
<th>rFVIIa (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>20-45</td>
<td>20-44</td>
<td>15-63</td>
<td>30-45</td>
<td>2-12</td>
</tr>
<tr>
<td>Doses (mcg/kg)</td>
<td>40, 80, 160</td>
<td>90</td>
<td>90</td>
<td>190</td>
<td>15</td>
</tr>
<tr>
<td>CL (mL/kg/h)</td>
<td>33-37</td>
<td>37-63</td>
<td>40-43</td>
<td>2-12</td>
<td>30-45</td>
</tr>
<tr>
<td>t½ (h)</td>
<td>3.9-6.0</td>
<td>3.48</td>
<td>3.54</td>
<td>3.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Vss (mL/kg)</td>
<td>130-165</td>
<td>111-136</td>
<td>121</td>
<td>126</td>
<td>280</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>ND</td>
<td>2.97</td>
<td>3.05</td>
<td>3.44</td>
<td>3.3</td>
</tr>
</tbody>
</table>

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</td>
<td>4 (1-6)</td>
<td>2 (1-6)</td>
</tr>
<tr>
<td>No. injections</td>
<td>123 (101-144)</td>
<td>81 (71-128)</td>
</tr>
<tr>
<td>Median total dose, 35 mcg/kg</td>
<td>65 (31-639)</td>
<td>59 (107-638)</td>
</tr>
<tr>
<td>90 mcg/kg</td>
<td>45 (14-171)</td>
<td>67 (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</th>
<th>Continuous Infusion 50 micrograms/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of dosing, median</td>
<td>4 (1-6)</td>
<td>10 (6-12)</td>
</tr>
<tr>
<td>No. bolus injections</td>
<td>38 (36-42)</td>
<td>0 (0-12)</td>
</tr>
<tr>
<td>Median total dose</td>
<td>227.5</td>
<td>282.2</td>
</tr>
</tbody>
</table>

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

Intraoperative hemostasis was achieved in 28/29 (97%) patients. Satisfaction with hemostasis was assessed in 14/14 (100%) patients in the 90 mcg/kg dose group and 11/15 (73%) in the 35 mcg/kg dose group at 48 hours; satisfactory hemostasis was achieved in 13/14 (93%) in the 90 mcg/kg dose group and 11/15 (73%) in the 35 mcg/kg dose group at 5 days. Twenty-three patients successfully completed the entire study including 19/14 (93%) achieving successful hemostasis through study completion (up to day 26) in the 90 mcg/kg dose group.

Another open-label, randomized, parallel trial was conducted to compare the safety and efficacy of intravenous bolus injection (N=12) and continuous intravenous (CI) infusion (N=12) administration of NovoSeven in 23 hemophilia A or B patients with inhibitors and one patient with acquired hemophilia who were undergoing elective major surgery. Table 7 provides the overview of dosing by treatment group for BF and CI.

14.2 Congenital Factor VII Deficiency

Data were collected from the published literature, compassionate use trials and registries for 70 patients with Factor VII deficiency.
for all subjects, concomitant use of other hemostatic agents occurred in 157/266 (59%) bleeding episodes and 94/160 (59%) surgical bleeding episodes. 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, 43.6%), gum bleeding (48, 18.0%), menorrhagia (36, 13.5%), tooth/dental procedures (29, 10.7%), 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 body cavity was entered, mesenteric or bowel was entered, closed/facial plane was opened, organ was removed or normal anatomy was operated upon. Minor 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 (108, 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 urgent (7, 4.4%) or (6%) emergent procedures.

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, bleeding types, age, and refractoriness/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, treatment with platelet-specific antibodies, treatment with NovoSeven® RT was comparable to treatment with platelets.

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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. of patients</th>
<th>No. of episodes</th>
<th>Success</th>
<th>Failure</th>
<th>Insufficient data</th>
<th>No Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>NovoSeven®</td>
<td>92</td>
<td>266</td>
<td>251 (94.4)</td>
<td>4 (1.5)</td>
<td>6 (2.3)</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>NovoSeven® only</td>
<td>44</td>
<td>109</td>
<td>101 (92.7)</td>
<td>2 (1.8)</td>
<td>4 (3.7)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>NovoSeven® + Platelets + Other hemostatic agents</td>
<td>69</td>
<td>157</td>
<td>150 (95.5)</td>
<td>2 (1.3)</td>
<td>2 (1.3)</td>
<td>3 (1.9)</td>
</tr>
</tbody>
</table>

No. 11-90 mmHg

No. of Bleeding Episodes

<table>
<thead>
<tr>
<th>No. of bleeding episodes</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>21</th>
<th>25</th>
<th>25</th>
<th>41</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>Outcome</td>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effective % N (%)</td>
<td>100 (3.1)</td>
<td>3 (75)</td>
<td>5 (83)</td>
<td>10 (52)</td>
<td>13 (57)</td>
<td>10 (62)</td>
<td>7 (56)</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Partially N (%)</td>
<td>100 (3.1)</td>
<td>3 (75)</td>
<td>5 (83)</td>
<td>10 (52)</td>
<td>13 (57)</td>
<td>10 (62)</td>
<td>7 (56)</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Ineffective % N (%)</td>
<td>100 (3.1)</td>
<td>3 (75)</td>
<td>5 (83)</td>
<td>10 (52)</td>
<td>13 (57)</td>
<td>10 (62)</td>
<td>7 (56)</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Unknown % N (%)</td>
<td>100 (3.1)</td>
<td>3 (75)</td>
<td>5 (83)</td>
<td>10 (52)</td>
<td>13 (57)</td>
<td>10 (62)</td>
<td>7 (56)</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
</tbody>
</table>

- A drug regimen that included treatment with NovoSeven® (n=45, 40%) was used in refractoriness bleeding episodes. Approximately 60% of treatment regimens that included treatment with NovoSeven® included platelets and/or other hemostatic agents (n=25, 23%).
- A drug regimen that included treatment with NovoSeven® (n=34, 31%) was used in refractoriness bleeding episodes. Approximately 50% of treatment regimens that included treatment with NovoSeven® included platelets and/or other hemostatic agents (n=25, 23%).
- A drug regimen that included treatment with NovoSeven® (n=23, 21%) was used in refractoriness bleeding episodes. Approximately 40% of treatment regimens that included treatment with NovoSeven® included platelets and/or other hemostatic agents (n=25, 23%).

In HTRS, there were 7 patients that were treated with NovoSeven® RT for bleeding episodes. Concomitant hemostatic agents were administered for 11 episodes (antifibrinolytics in 10 episodes). Treatment was reported effective in 21 of 23 (91.3%) episodes. In the other 2 episodes, bleeding was reported as slowed or no improvement; however in neither episode was further treatment reported. There were no surgical procedures reported in the HTRS registry.

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

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. NovoSeven® RT package containing 1 vial of NovoSeven® RT powder and 1 vial of histidine diluent.

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.

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 patients to read the FDA-approved patient labeling (Instructions for Use).
- Advise patients about the early signs of hypersensitivity reactions, including hives, urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis.
- Advise patients 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.
- Advise patients to immediately seek medical help if any of the above signs or symptoms occur.
- Advise patients to follow the recommendations in the FDA-approved patient labeling, regarding proper sharps disposal.

### How Supplied

<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 0169-7010-01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histidine diluent in vial, 1.1 mL</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 0169-7020-01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histidine diluent in vial, 2.1 mL</td>
</tr>
<tr>
<td>3 mg per vial (5000 micrograms/vial)</td>
<td>NDC 0169 7050 01</td>
<td>NovoSeven® RT in a single-use vial (NDC 0169-7050-01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histidine diluent in vial, 5.2 mL</td>
</tr>
<tr>
<td>5 mg per vial (8000 micrograms/vial)</td>
<td>NDC 0169 7040 01</td>
<td>NovoSeven® RT in a single-use vial (NDC 0169-7040-01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Histidine diluent in vial, 8.1 mL</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.
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 syringe to any Luer-lock compatible device, please contact Novo Nordisk at (877) 668-6777.

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®, 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 histidine diluent syringe to any Luer-lock compatible device, please contact Novo Nordisk at (877) 668-6777.

Do not mix NovoSeven® RT with any other intravenous infusions or medications.

Inject the mixed solution slowly over 2 to 5 minutes as instructed by your doctor or nurse.

Injecting the solution via a central venous access device (CVAD) such as a central venous catheter or subclavian port.

Use a clean and germ free (aseptic) technique. Follow the instructions for proper use for your connector and central venous access device in consultation with your doctor or nurse.

Injecting into a CVAD may require using a sterile 10 mL plastic syringe for withdrawal of the mixed solution and injection.

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

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 pre-filled syringe. If 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.

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 warm as your hands.

2. Attach the vial adapter

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

3. Attach the plunger rod and the syringe

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

4. Mix the powder with the diluent

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

• Use a clean and germ free (aseptic) technique. Follow the instructions for proper use for your connector and central venous access device in consultation with your doctor or nurse.

Injecting into a CVAD may require using a sterile 10 mL plastic syringe for withdrawal of the mixed solution and injection.

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

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.
For full Prescribing Information please read the other insert included in this package.

Revised: 03/2016
Version: 20160322-v7
NovoSeven® RT is covered by US Patent No. 8,299,029, and other patents pending.
Novo Nordisk® is a registered trademark of Novo Nordisk A/S.
NovoSeven® is a registered trademark of Novo Nordisk Health Care AG.
Clave® and MicroClave® are registered trademarks of ICU Medical Inc.
InVision-Plus®, InVision-Plus CS®, InVision-Plus® Junior® are registered trademarks of RyMed Technologies, Inc.
Bionector® is a registered trademark of Vygon.
Manufactured by:
Novo Nordisk A/S
2880 Bagsvaerd, Denmark
License Number: 1261
© 2016 Novo Nordisk
USA16HDM01748 5/16