WARNINGS AND PRECAUTIONS

• Anaphylaxis and severe hypersensitivity reactions are possible. Patients may develop hypersensitivity to hamster proteins, which are present in trace amounts in the product. Should symptoms occur, discontinue Novoeight® and administer appropriate treatment. (5.1)

• Development of activity-neutralizing antibodies (inhibitors) may occur. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform an assay that measures factor VIII inhibitor concentration. (5.2, 5.3)

ADVERSE REACTIONS

The most frequently reported adverse reactions (≥ 1%) were inhibitors in Previously Untreated Patients (PUPs), injection site reactions, and pyrexia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-844-303-4448 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

• Pediatric Use: Clearance (based on per kg body weight) is higher in children. Higher or more frequent dosing may be needed. (8.4)

• Obesity: The area under the curve (AUC) is higher and clearance lower in adult patients with body mass index (BMI) ≥ 30 kg/m² than in patients with BMI < 30 kg/m². Adjust dose as necessary. (8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Novoeight®, Antihemophilic Factor (Recombinant), is a human antihemophilic factor (human blood coagulation factor VIII (FVIII)) indicated for use in adults and children with hemophilia A for:

- On-demand treatment and control of bleeding episodes
- Perioperative management
- Routine prophylaxis to reduce the frequency of bleeding episodes

Novoeight® is not indicated for the treatment of von Willebrand disease.

2. DOSAGE AND ADMINISTRATION

For intravenous injection after reconstitution only.

2.1 Dose

- Dosage and duration of treatment depend on the severity of the factor VIII deficiency, on the location and extent of bleeding, and the patient’s clinical condition. Careful monitoring of replacement therapy is necessary in cases of major surgery or life-threatening bleeding episodes.

- Each vial of Novoeight® contains the labeled amount of recombinant factor VIII in international units (IU). One IU of factor VIII activity corresponds to the quantity of factor VIII in one milliliter of normal human plasma. The calculation of the required dosage of factor VIII is based on the empirical finding that one IU of factor VIII per kg body weight raises the plasma factor VIII activity by two IU/dL. This relationship causes a factor of 0.5 to be present in the dose calculation formula shown below.

- The required dosage can be determined using the following formula:

\[
\text{Dosage (IU) = Body Weight (kg) \times Desired Factor VIII} \times 0.5
\]

2.2 Preparation and Reconstitution

- Always wash hands and ensure that the area is clean before performing the procedures.

- Use aseptic technique during the reconstitution procedures.

Overview of Novoeight® Package

Vial with NovoEight® powder        Vial adapter
Plastic cap                        Rubber stopper (under plastic cap)
Syringe tip (under vial adapter cap)  Protective cap
Spike (under protective paper)  Protective paper
Pre-filled syringe with diluent

Reconstitution

1. Bring the Novoeight® vial and the pre-filled diluent syringe to room temperature.

2. Remove the plastic cap from the Novoeight® vial.

3. Wipe the rubber stopper on the vial with a sterile alcohol swab and allow it to dry prior to use.

4. Remove the protective paper from the vial adapter.

5. Place the vial on a flat and solid surface. While holding the protective cap, place the vial adapter over the Novoeight® vial and press firmly on the protective cap until the vial adapter spike penetrates the rubber stopper.

6. Carefully remove the protective cap from the vial adapter.

7. Grasp the plunger rod as shown in the diagram. Attach the plunger rod to the syringe by holding the plunger rod by the wide top end. Turn the plunger rod clockwise into the rubber plunger inside the pre-filled diluent syringe until resistance is felt.

8. Break off the syringe cap from the pre-filled diluent syringe by snapping the perforation of the cap.

9. Connect the pre-filled diluent syringe to the vial adapter by turning it clockwise until it is secured.

10. Push the plunger rod to slowly inject all the diluent into the vial.

11. Without removing the syringe, gently swirl the Novoeight® vial until all of the powder is dissolved.

12. Use the Novoeight® solution immediately. If not, store the solution in the vial with the vial adapter and the syringe attached. Use Novoeight® within 4 hours after reconstitution when stored at <86°F (30°C) or within 2 hours when stored between 86°F (30°C) to 104°F (40°C).

2.3 Administration

For intravenous injection only.

- Inspect the reconstituted Novoeight® solution 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 administer Novoeight® in the same tubing or container with other medicinal products.

1. Invert the Novoeight® vial and slowly draw the solution into the syringe.

2. Detach the syringe from the vial adapter by turning the syringe counterclockwise.

3. Attach the syringe to the luer end of an infusion needle set.

4. Inject the reconstituted Novoeight® intravenously slowly over 2 to 5 minutes.

5. After injection, safely dispose of the syringe with the infusion set, the vial with the vial adapter, any unused Novoeight® and other waste materials. Accidental needle stick with a needle contaminated with blood can transmit infectious viruses including HIV (AIDS) and hepatitis. Obtain immediate medical attention if injury occurs. Place needles in a sharps container after single-use.

Routine Prophylaxis

A guide for dosing Novoeight® for routine prophylaxis is included below in Table 3.

Table 3: Dosing for Routine Prophylaxis

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Factor VIII Dose Required (IU/kg)</th>
<th>Frequency of Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents (&lt;12 years)</td>
<td>20-50</td>
<td>3 times weekly</td>
</tr>
<tr>
<td>Children (&lt;12 years)</td>
<td>25-60</td>
<td>3 times weekly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Perioperative Management

A guide for dosing Novoeight® during surgery (perioperative management) is provided in Table 2. Consider maintaining a plasma factor VIII activity level at or above the plasma levels (in % of normal or in IU/dL) outlined in Table 2.

Table 2: Dosing for Perioperative Management

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Factor VIII Level Required (IU/dL or % of normal)</th>
<th>Frequency of Doses (hours)</th>
<th>Duration of Therapy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor, including tooth extraction</td>
<td>30-60</td>
<td>24</td>
<td>7-10</td>
</tr>
<tr>
<td>Major, including intra-abdominal, intrathoracic, or joint replacement surgery</td>
<td>80-100 (pre-and post-operative)</td>
<td>8-24</td>
<td>7-10</td>
</tr>
</tbody>
</table>

Table of Dosing for On-demand Treatment and Control of Bleeding Episodes

<table>
<thead>
<tr>
<th>Type of Bleeding Episodes</th>
<th>Factor VIII Level Required (IU/dL or % of normal)</th>
<th>Frequency of Doses (hours)</th>
<th>Duration of Therapy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor, early hemarthrosis, minor muscle or oral bleeding</td>
<td>20-60</td>
<td>12-24</td>
<td>At least 1 day until bleeding resolution is achieved</td>
</tr>
<tr>
<td>Moderate, muscle bleeding, bleeding into the oral cavity or mild head trauma</td>
<td>30-60</td>
<td>12-24</td>
<td>Until pain and acute disability are resolved (approximately 3-4 days)</td>
</tr>
<tr>
<td>Major, life or limb-threatening hemorrhage, Gastrointestinal bleeding, intracranial, intra-abdominal or intrathoracic bleeding, fractures</td>
<td>50-100</td>
<td>8-24</td>
<td>Until resolution of bleeding (approximately 7-10 days)</td>
</tr>
</tbody>
</table>

Base the dose and frequency of Novoeight® on the individual clinical response. Patients may vary in their pharmacokinetic and clinical responses (see Clinical Pharmacology).
Novoeight®, Antihemophilic Factor (Recombinant)

8.5 Geriatric Use
Clinical studies of Novoeight® did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

8.6 Obesity
In the extension trial, in six adult patients with body mass index (BMI) ≥ 30 kg/m², the AUC was higher and clearance lower than in patients with BMI < 30 kg/m². There is insufficient data to recommend specific dose adjustments for patients with BMI ≥ 30 kg/m². Adjust dose as necessary and per prescriber’s discretion for patients with BMI ≥ 30 kg/m². [See Clinical Pharmacology (12.3)].

11 DESCRIPTION
Novoeight® is formulated as a sterile, non-pyrogenic, lyophilized powder for intravenous reconstitution with the diluent (0.9% sodium chloride). Novoeight® is available in single-dose vials that contain nominally 250, 500, 1000, 1500, 2000 or 3000 international units (IU) per vial. When reconstituted with the appropriate volume of diluent, the product contains the following components per mL: 18 mg sodium chloride, 1.5 mg L-histidine, 3 mg succrose, 0.1 mg polysorbate 80, 0.055 mg L-methionine and 0.25 mg calcium chloride dihydrate. The product contains no preservative. Each vial of Novoeight® is labeled with the actual rFVIII activity expressed in IU determined by the one-stage clotting assay, using a reference material calibrated against a World Health Organization (WHO) International Standard for FVIII Concentrates. One IU, as defined by the WHO standard for human FVIII, is approximately equal to the level of FVIII activity in 1 mL of fresh pooled human plasma. The specific activity of Novoeight® is expressed as the number of WHO International Units per milligram of protein.

The active ingredient in Novoeight® is a recombinant (r) analogue of human coagulation factor VIII (FVIII) with a molecular mass of 166 kDa, calculated excluding post-translational modifications. The rFVIII molecule in Novoeight® is a glycoprotein containing a heavy chain and a light chain, with 21 of the 908 amino acids of the B-domain of endogenous FVIII connected to the C-terminus of the heavy chain. Once activated, the resulting rFVIIIa has a comparable structure to the endogenous FVIIa.

Novoeight® is synthesized by a genetically engineered Chinese hamster ovary (CHO) cell line cell which secretes rFVIII into the cell culture medium. The rFVIII protein is purified using a series of chromatography steps, one of which is the use of an immunosaffinity column in which a monoclonal antibody, produced in CHO cells and directed against FVIII, is employed to selectively isolate the rFVIII from the medium. The production process includes two dedicated viral clearance steps – a detergent treatment step for inactivation and a 20-nm filtration step for removal of viruses. No additives of human or animal origin are used in the cell culture, purification and formulation of Novoeight®.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Novoeight® transiently replaces the missing clotting factor VIII that is needed for effective hemostasis.

12.2 Pharmacodynamics
The activated partial thromboplastin time (aPTT) is prolonged in patients with hemophilia A. Determination of aPTT is a conventional test used to determine the presence of an inhibitor. A prolonged aPTT is consistent with an inhibitor.

In vivo and in vitro studies have shown that Novoeight® prolongs the aPTT in subjects with hemophilia A [See Clinical Pharmacology (12.3)]. The aPTT is prolonged in patients with hemophilia A compared to normal subjects. The aPTT is prolonged in patients with hemophilia A compared to normal subjects. The aPTT is prolonged in patients with hemophilia A compared to normal subjects. The aPTT is prolonged in patients with hemophilia A compared to normal subjects.
NovoSeven®, Antihemophilic Factor (Recombinant)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate the carcinogenic potential of NovoSeven®, or studies to determine the effects of NovoSeven® on genetic toxicity or fertility have not been performed. An assessment of the carcinogenic potential of NovoSeven® was completed, and no carcinogenic risk from product use has been identified.

14 CLINICAL STUDIES

Four multi-center, open-label, non-controlled trials have been conducted to evaluate the safety and efficacy of NovoSeven® in the on-demand treatment and control of breakthrough bleeds, routine prophylaxis and perioperative management in patients with hemophilia A. Three of these trials were performed in PTPs (two trials and one extension trial) and the fourth in PUPs. The analysis included 297 exposed subjects: 175 previously treated adolescents or adult subjects above 12 years of age (≤150 exposure days), 63 previously treated pediatric subjects below the age of 12 years (≤50 exposure days) and 59 PUPs below 6 years of age. Immunocompetent patients with severe hemophilia A (factor VIII activity ≤ 1%) and no history of FVIII inhibitors were eligible for the trials. Subjects undergoing routine prophylaxis and treatment of bleeds received NovoSeven® at the dose levels described in Tables 1 and 3. Breakthrough bleeds were treated at the investigator’s discretion aiming for a FVIII activity level above 0.5 IU/mL. Treatment during surgery was at the investigator’s discretion aiming for a FVIII trough activity level above 0.5 IU/mL.

15 ON-DEMAND TREATMENT AND CONTROL OF BREAKTHROUGH BLEEDING

A total of 3153 bleeds in 260 subjects were treated with NovoSeven®. The majority of the bleeds (90%) were of mild/moderate severity. 54% of the bleeds were spontaneous and 67% of the bleeds were localized in joints. An overall assessment of efficacy was performed by the subject (for home treatment) or study site investigator (for treatment under medical supervision) using a four-point scale of excellent, good, moderate, or none. If the hemostatic response was rated as “excellent” or “good”, the treatment of the bleed was considered a success. If the hemostatic response was rated as “moderate or none” the treatment was considered a failure. Of these 3,153 bleeds, 2,209 (89%) were rated excellent or good in their response to treatment with NovoSeven®, 274 (9%) were rated as moderate, 20 (0.8%) were rated as having no response and for 45 (1%) the response to treatment was unknown. A total of 2,794 (89%) of the bleeds were resolved with one or two injections of NovoSeven®.

Of the 238 PTPs, 206 patients experienced 2,793 bleeds of which 2,492 (89%) were rated excellent or good in their response to treatment with NovoSeven®, 244 (9%) were moderate, 23 (0.8%) were rated as having no response, and for 34 (1%) the response to treatment was unknown. Of the 2,793 reported bleeds observed in 206 of the patients, 2,504 (90%) of the bleeds were resolved with 1–2 injections of NovoSeven®. The majority of the bleeds were of mild/moderate severity.

Of the 59 PUPs, 54 patients experienced 360 bleeds of which 317 (88%) were rated excellent or good in their response to treatment with NovoSeven®, 30 (8%) were moderate, 2 (0.6%) were rated as having no response, and for 11 (3%) the response to treatment was unknown. Of the 360 reported bleeds observed in 54 of the patients, 290 (81%) of the bleeds were resolved with 1–2 injections of NovoSeven®. The majority of the bleeds were of mild/moderate severity and the most frequent bleeds were subcutaneous.

Routine Prophylaxis

In the two trials, one trial including 150 adult/adolescent subjects (6 months duration) and the other trial including 63 pediatric subjects (4 months duration) received NovoSeven® for routine prophylaxis (Table 8). These previously treated patients received prophylaxis treatment every other day or three times weekly at the dose levels described in Table 3.

Table 8: Annualized Bleeding Rate (ABR) for previously treated patients from the two trials

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Clotting Assay</th>
<th>Chromogenic Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Incremental Recovery (IU/mL)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>0.018 (0.007)</td>
<td>0.020 (0.004)</td>
<td>0.022 (0.006)</td>
</tr>
<tr>
<td>AUC (IU/mL)</td>
<td>9.9 (4.1)</td>
<td>11.1 (4.3)</td>
</tr>
<tr>
<td>CL (mL/h)</td>
<td>6.26 (7.23)</td>
<td>5.02 (1.67)</td>
</tr>
<tr>
<td>t½ (h)</td>
<td>7.7 (1.8)</td>
<td>8.0 (1.9)</td>
</tr>
<tr>
<td>CI (mL/kg)</td>
<td>1.0 (0.56)</td>
<td>1.0 (0.56)</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>9.7 (2.5)</td>
<td>9.9 (2.6)</td>
</tr>
</tbody>
</table>

Presentation (Nominal Product Strength) | Carbon Number | Components |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>250 International Units</td>
<td>NDC 0169-7821-01</td>
<td>NovoSeven® in single-dose vial (NDC 0169-7820-91)</td>
</tr>
<tr>
<td>Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
<td></td>
<td>Vial adapter</td>
</tr>
<tr>
<td>500 International Units</td>
<td>NDC 0169-7850-01</td>
<td>NovoSeven® in single-dose vial (NDC 0169-7811-11)</td>
</tr>
<tr>
<td>Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
<td></td>
<td>Vial adapter</td>
</tr>
<tr>
<td>1000 International Units</td>
<td>NDC 0169-7820-11</td>
<td>NovoSeven® in single-dose vial (NDC 0169-7811-11)</td>
</tr>
<tr>
<td>Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
<td></td>
<td>Vial adapter</td>
</tr>
<tr>
<td>1500 International Units</td>
<td>NDC 0169-7820-14</td>
<td>NovoSeven® in single-dose vial (NDC 0169-7811-11)</td>
</tr>
<tr>
<td>Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
<td></td>
<td>Vial adapter</td>
</tr>
<tr>
<td>2000 International Units</td>
<td>NDC 0169-7820-14</td>
<td>NovoSeven® in single-dose vial (NDC 0169-7811-11)</td>
</tr>
<tr>
<td>Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
<td></td>
<td>Vial adapter</td>
</tr>
<tr>
<td>3000 International Units</td>
<td>NDC 0169-7820-14</td>
<td>NovoSeven® in single-dose vial (NDC 0169-7811-11)</td>
</tr>
<tr>
<td>Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
<td></td>
<td>Vial adapter</td>
</tr>
</tbody>
</table>

The NovoSeven® vials are made of glass, closed with a chlorobutyl rubber stopper not made with natural rubber latex, and sealed 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.

Abbreviations: N: number of patients, IQR: interquartile range defined as the difference between the 75th percentile and the 25th percentile; CI: confidence interval.
Storage and Handling

- The closed vials and pre-filled diluent syringes are equipped with a tamper-evident snap-off cap which is made of polypropylene.

Storage and Handling

- Store Novoeight® in the original package in order to protect from light.
- Store Novoeight® under refrigeration at a temperature of 36°F to 46°F (2°C to 8°C) for up to 30 months from the date of manufacture until the expiration date stated on the carton. During the 30-month shelf life, Novoeight® may be kept at room temperature:
  - up to 86°F (≤30°C) for no longer than 12 months
  - up to 104°F (≤40°C) for no longer than 3 months
- Clearly record the date when the product was removed from the refrigerator in the space provided on the outer carton. Do not return the product to the refrigerator. Do not freeze Novoeight®.
- Use Novoeight® within 4 hours after reconstitution when stored at ≤86°F (30°C) or within 2 hours when stored between 86°F (30°C) to 104°F (40°C). Store the reconstituted product in the vial.
- Discard any unused reconstituted product.

17 PATIENT COUNSELING INFORMATION

- Advise patients to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Allergic-type hypersensitivity reactions or anaphylaxis are possible with use of Novoeight®. Inform patients of the early signs of hypersensitivity reactions including rash, hives, itching, facial swelling, tightness of the chest and wheezing. Advise patients to discontinue use of Novoeight® immediately and contact their physician, and go to the emergency department if these symptoms occur.
- Advise patients to contact their physician or treatment facility for further treatment and/or assessment if they experience a lack of a clinical response to factor VIII replacement therapy, as this may be a manifestation of an inhibitor.
- Advise patients to consult with their healthcare provider prior to traveling. While traveling, patients should be advised to bring an adequate supply of Novoeight® based on their current treatment regimen.
What is the most important information I need to know about Novoeight®?

Do not attempt to do an infusion yourself unless you have been taught how by your healthcare provider or hemophilia center. You must carefully follow your healthcare provider's instructions regarding the dose and schedule for infusing Novoeight® so that your treatment will work best for you.

What is Novoeight®?

Novoeight® is an injectable medicine used to replace clotting factor VIII that is missing in patients with hemophilia A. Hemophilia A is an inherited bleeding disorder that prevents your body from clotting normally.

Your healthcare provider will calculate the dose of Novoeight® (in international units, IU) depending on your condition and body weight. Call your healthcare provider right away if your bleeding does not stop after taking Novoeight®.

Development of factor VIII inhibitors

Your body can also make antibodies called “inhibitors” against Novoeight®, which may stop Novoeight® from working properly. If your bleeding is not adequately controlled, it could be due to the development of factor VIII inhibitors. This should be checked by your healthcare provider. You might need a higher dose of Novoeight® or even a different product to control bleeding.

Do not increase the total dose of Novoeight® to control your bleeding without consulting your healthcare provider.

Use in children

Novoeight® can be used in children. Your healthcare provider will decide the dose of Novoeight® you will receive.

If you forget to use Novoeight®

Do not inject a double dose to make up for a forgotten dose. Proceed with the next injections as scheduled and continue as advised by your healthcare provider.

If you stop using Novoeight®

If you stop using Novoeight® you are not protected against bleeding. Do not stop using Novoeight® without consulting your healthcare provider.

What if I take too much Novoeight®?

Always take Novoeight® exactly as your healthcare provider has told you. You should check with your healthcare provider if you are not sure. If you inject more Novoeight® than recommended, tell your healthcare provider as soon as possible.

What are the possible side effects of Novoeight®?

Common Side Effects Include:

• Inhibitors in patients who were not previously treated with Factor VIII products
• Swelling or itching at the location of injection
• Fever

Other Possible Side Effects:

You could have an allergic reaction to coagulation factor VIII products. Call your healthcare provider right away and stop treatment if you get any of the following signs of an allergic reaction:

• rashes including hives
• difficulty breathing, shortness of breath or wheezing
• tightness of the chest or throat, difficulty swallowing
• swelling of the lips and tongue
• light-headedness, dizziness or loss of consciousness
• pale and cold skin, fast heart beat which may be signs of low blood pressure
• red or swollen face or hands

These are not all of the possible side effects from Novoeight®. Ask your healthcare provider for more information. You are encouraged to report side effects to FDA at 1-800-FDA-1088. Tell your healthcare provider about any side effect that bothers you or that does not go away.

What are the Novoeight® dosage strengths?

Novoeight® comes in six different dosage strengths. The actual number of international units (IU) of factor VIII in the vial will be imprinted on the label and on the box. The six different strengths are as follows:

- Dosage strength of approximately 3000 IU per vial
- Dosage strength of approximately 1500 IU per vial
- Dosage strength of approximately 500 IU per vial
- Dosage strength of approximately 250 IU per vial
- Dosage strength of approximately 100 IU per vial
- Dosage strength of approximately 50 IU per vial

Always check the actual dosage strength printed on the label to make sure you are using the strength prescribed by your doctor.

How should I store Novoeight®?

Prior to Reconstitution:

Store in original package in order to protect from light. Do not freeze Novoeight®.

Novoeight® vials can be stored in the refrigerator (36°F to 46°F [2°C to 8°C]) for up to 30 months or up to the expiration date. During the 30 month shelf life, the product may be kept at room temperature up to 86°F (30°C) for no longer than 12 months, or up to 104°F (40°C) for no longer than 3 months.

If you choose to store Novoeight® at room temperature:

• Note the date that the product is removed from refrigeration on the box.
• Do not return the product to the refrigerator.
• Do not use after 12 months if stored up to 86°F (30°C) or after 3 months if stored up to 104°F (40°C) or the expiration date listed on the vial, whichever is earlier.

Do not use this medication after the expiration date which is on the outer carton and the vial. The expiration date refers to the last day of that month.

After Reconstitution (mixing the dry powder in the vial with the diluent):

The reconstituted Novoeight® should appear clear to slightly unclear without particles. The reconstituted Novoeight® should be used immediately.

If you cannot use the Novoeight® immediately after it is mixed, it must be used within 4 hours when stored at <86°F (30°C) or within 2 hours when stored between 86°F (30°C) to 104°F (40°C). Store the reconstituted product in the vial.

Keep this medicine out of the sight and out of reach of children.

What else should I know about Novoeight® and hemophilia A?

Medicines are sometimes prescribed for purposes other than those listed here. Do not use Novoeight® for a condition for which it is not prescribed. Do not share Novoeight® with other people, even if they have the same symptoms that you have.

Instructions on how to use Novoeight® MixPro®

READ THESE INSTRUCTIONS CAREFULLY BEFORE USING NOVOEIGHT®.

Novoeight® 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 sodium chloride solution. The mixed Novoeight® must be injected into your vein (intravenous injection). The equipment in this package is designed to mix and inject Novoeight®. 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 wash your hands and ensure that the area around you is clean. When you prepare and inject medication directly into the veins, it is important to use a clean and germ free (aseptic) technique. Improper technique can introduce germs that can infect the blood.

Don't open the equipment until you are ready to use 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 use the equipment if you suspect it is contaminated. Use a new package instead.

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

The equipment is for single use only. Single-dose vial. Discard unused portion.

Content

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

Overview

Vial with Novoeight® powder

Plastic cap
Rubber stopper
Pre-filled syringe with diluent
Syringe cap
Scale
Thread
Wide top end
Spike (under protective paper)
Protective cap
Plunger rod

1. Prepare the vial and the syringe
   - Take out the number of Novoeight® 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 dryer.
   - 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. You can do this by holding them in your hands until they feel as warm as your hands.

2. Attach the vial adapter
   - Remove the plastic cap from the vial. If the plastic cap is loose or missing, don’t use the vial.
   - Wrap the rubber stopper with a sterile alcohol swab and allow it to air dry for a few seconds before use to ensure that it is as germ free as possible.
   - Don’t touch the rubber stopper with your fingers as this can transfer germs.

3. Attach the plunger rod and the syringe
   - Grasp the plunger rod by the wide top end and take it out of the carton. Don’t touch the sides or the thread of the plunger rod. If you touch the sides or the thread germs from your fingers can be transferred.
   - Immediately connect the plunger rod to the 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 to slightly opalescent (slightly unclear). If you notice visible particles or discoloration, don’t use it. Use a new package instead.

Novoeight® is recommended to be used immediately after it is mixed. This is because if left, the medicine may no longer be sterile and could cause infections.

If you cannot use the mixed Novoeight® solution immediately, it must be used within 4 hours when stored at <36°F (30°C) or within 2 hours when stored between 86°F (30°C) to 104°F (40°C). Store the reconstituted product in the vial.

Do not freeze mixed Novoeight® solution or store it in syringes.

Keep mixed Novoeight® 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.
Disposal

- After injection, safely dispose of all unused Novoeight® solution, the syringe with the infusion set, the vial with the vial adapter, and other waste materials in an appropriate container for throwing away medical waste.
- 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.

Important information
Contact your healthcare provider or local hemophilia treatment center if you experience any problems.
For full Prescribing Information please read the other insert included in this package.

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

Some needleless connectors for intravenous catheters are incompatible with the glass diluent syringes (for example, certain connectors with an internal spike, such as Clave®/MicroClave®, InVision-Plus®, InVision-Plus CS®, Invision-Plus Junior®, Bionector®).

The use of these needleless connectors can damage the connector and affect administration.
To administer Novoeight® 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 sodium chloride diluent syringe to any Luer-lock compatible device, please contact Novo Nordisk at (844) 303-4448.

5. Inject the mixed solution
Novoeight® is now ready to inject into your vein.
- Do not mix Novoeight® 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 line before or after Novoeight® injection.

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