**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 (≥0.5%) were injection site reactions, increased hepatic enzymes, 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](http://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. (6.4)

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

11/2016
NovoEight®, Antihemophilic Factor (Recombinant)

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.
- If the patient uses more than one vial of NovoEight® per injection, reconstitute each vial according to the following instructions.

Overview of NovoEight® Package

Vial with NovoEight® powder

<table>
<thead>
<tr>
<th>Vial adapter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plastic cap</td>
</tr>
<tr>
<td>Rubber stopper</td>
</tr>
<tr>
<td>Protective cap</td>
</tr>
</tbody>
</table>

Pre-filled syringe with diluent

<table>
<thead>
<tr>
<th>Syringe cap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spike (under protective paper)</td>
</tr>
<tr>
<td>Thread</td>
</tr>
<tr>
<td>Protective paper</td>
</tr>
</tbody>
</table>

Syringe cap

| The instructions below serve as a general guideline for preparation and reconstitution of NovoEight®. For full instructions, refer to the FDA-approved patient information and Instructions for Use. |

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. Do not remove the vial adapter from the protective cap.
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 down firmly on the protective cap until the vial adapter spike penetrates the rubber stopper.
6. 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. The reconstituted solution should be inspected visually for particulate matter before administration. Do not use if particulate matter or discoloration is observed.

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>20-40</td>
<td>Every other day</td>
</tr>
<tr>
<td>Adults and adolescents (≥12 years)</td>
<td>25-60</td>
<td>Every other day</td>
</tr>
<tr>
<td>Children (≥12 years)</td>
<td>25-50</td>
<td>Every other day</td>
</tr>
</tbody>
</table>

2.3 Administration

For intravenous injection only.

- 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.
- 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.
6.2 Immunogenicity

Subjects were monitored for neutralizing antibodies to factor VIII and binding antibodies to CHO and murine protein. No subjects developed confirmed neutralizing antibodies to factor VIII. One twenty-two month old child had a positive neutralizing antibody to factor VIII of 1.3 (IU) in the Bethesda assay after 15 exposure days that was not confirmed when checked after 20 exposure days. In vivo recovery was normal for this child and no clinical adverse findings were noted.

No patients developed de novo anti-murine antibodies. Nineteen subjects were positive for anti-Chinese hamster ovary (CHO) cell protein antibodies. Two of these subjects changed from anti-CHO negative to anti-CHO positive and 6 subjects changed from anti-CHO positive to anti-CHO negative. The remaining 11 subjects were either positive prior to the start of the trials (n=6), negative at baseline and end-of trial but with transient positive samples (n=2), or positive at baseline and end-of trial but with negative samples in between (n=3). No clinical adverse findings were observed in any of these subjects.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. As a result, the overall 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

As hemophilia mainly affects males, there are no adequate and well-controlled studies using Novoeight® in pregnant women to determine whether there is a drug-associated risk. Animal reproduction studies have not been conducted with Novoeight®.

In the U.S. general population, the estimated background risk of major congenital anomalies is 2-4% and of minor anomalies is 6%. In U.S. clinical trials of Novoeight®, the incidence of major anomalies was 0.025 (0.006) and of minor anomalies was 0.020 (0.004).

The most frequently reported adverse reactions (≥5%) were injection site reactions, increased hepatic enzymes, and pyrexia. The most frequently reported adverse reactions (≥0.5%) were injection site reactions or the chromatographic assay. The most frequently reported adverse reactions (≥0.5%) were injection site reactions, increased hepatic enzymes, and pyrexia.

4 CONTRAINDICATIONS

Novoeight® is contraindicated in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components (including traces of hamster proteins).

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, are possible with Novoeight®. Novoeight® contains trace amounts of hamster proteins. Patients treated with this product may develop hypersensitivity to these non-human mammalian proteins. Early signs of hypersensitivity reactions that can progress to anaphylaxis include angioedema, chest tightness, dyspnea, wheezing, urticaria, and pruritus. Immediately discontinue administration and initiate appropriate treatment in allergic- or anaphylactictype reactions occur.

5.2 Neutralizing Antibodies

Formation of neutralizing antibodies (inhibitors) to factor VIII can occur following administration of Novoeight®. Monitor all patients for the development of inhibitors by appropriate clinical observation and laboratory testing. If the expected plasma levels of factor VIII activity are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with the expected dose of Novoeight®. Determine inhibitor levels in Bethesda Units.

6 ADVERSE REACTIONS

The most frequently reported adverse reactions (≥0.5%) were injection site reactions, increased hepatic enzymes, and pyrexia.

6.1 Clinical Trials Experience

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

During the clinical development of Novoeight®, 214 male previously treated patients were treated with Novoeight® (range 1-442) per subject, and had a total of 32,929 exposure days during prevention and treatment of bleeds.

The most frequently reported adverse reactions in previously treated patients was injection site reactions (2.3%), increased hepatic enzymes (1.4%), and pyrexia (0.9%).

7.1 Pharmacokinetics

The pre-filled diluent syringe is made of glass with an internal plastic, 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 Novoeight® through incompatible needless connectors, withdraw the reconstituted product into a standard 10 mL sterile Luer-lock plastic syringe.

If you encounter any problems with attaching the pre-filled sodium chloride diluent syringe to any Luer-lock compatible device, please contact Novo Nordisk at (844) 360-4448.

9.2 Vaccines

The active partial thromboplastin time (aPTT) is prolonged in patients with hemophilia A. Determination of aPTT is a conventional in vitro assay for the biological activity of FVIII. Treatment with Novoeight® normalizes aPTT over the effective dosing period.

12.2 Pharmacodynamics

The activated partial thromboplastin time (aPTT) is prolonged in patients with hemophilia A. Determination of aPTT is a conventional in vitro assay for the biological activity of FVIII. Treatment with Novoeight® normalizes aPTT over the effective dosing period.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.

5.3 Monitoring Laboratory Tests

• Monitor plasma factor VIII activity levels by the one-stage clotting assay or the chromogenic substrate assay to confirm that adequate factor VIII levels have been achieved and maintained, when clinically indicated. (See Dosage and Administration (2.1))

• Perform assay for factor VIII inhibitor if present. If expected plasma factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform testing for factor VIII inhibitors.
The pharmacokinetic parameters were comparable between younger (0 to < 6 years) and older (6 to < 12 years) children. The mean clearance of NovoEight® in younger and older children was 67% and 34% higher (based on kg body weight) than in adults (3.74 mL/h/kg) when using the clotting assay, and 60% and 29% higher in adults (2.87 mL/h/kg) when using the chromogenic assay. The mean half-life of NovoEight® in younger and older children was 29% and 26% shorter than in adults (10.8 hours) when using the clotting assay, and 16% and 21% shorter than in adults (12 hours) when using the chromogenic assay.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

14 CLINICAL STUDIES

Three multi-center, open-label, non-controlled trials have been conducted to evaluate the safety and efficacy of NovoEight® in the control and prevention of breakthrough bleeds; routine prophylaxis and perioperative management in previously treated patients with hemophilia A. The analysis included 213 exposed subjects: 150 adolescents or adult subjects from the age of 12 years (≥150 exposure days) and 63 pediatric subjects below the age of 12 years (≥250 exposure days). Immune-competent patients with severe hemophilia A (factor VIII activity ≤1%) and no history of FVIII inhibitors were eligible for the trials. A total of 187 out of 213 subjects continued in the safety extension trial. All subjects received preventive treatment every other day or three times weekly at the dose levels described in Table 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.

Control and Prevention of Bleeding Episodes

A total of 991 bleeds in 158 subjects were treated with NovoEight®. The majority of the bleeds (86%) were of mild/moderate severity, 62% of the bleeds were spontaneous and 72% 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 991 bleeds, 838 (84%) were rated excellent or good in their response to treatment with NovoEight® and 17 (1.7%) were rated as having no response. A total of 898 (91%) of the bleeds were resolved with one or two injections of NovoEight®.

Clinical trials of NovoEight® included 79 previously treated patients between one to 16 years of age. The hemostatic efficacy in treatment of bleeds was rated as either "excellent" or "good" on a pre-specified rating scale for 86% of the 244 bleeds reported in 54 subjects.

Routine Prophylaxis

All 213 subjects received NovoEight® for routine prophylaxis. The prophylactic regimen for the 150 adolescent and adult subjects consisted of 20-40 IU/kg every other day or 20-50 IU/kg three times per week. The prophylactic regimen for the 63 pediatric subjects consisted of 25-50 IU/kg every other day or 25-60 IU/kg three times per week. The majority of the subjects (>80%) were treated with the three times per week regimen.

The median annualized bleeding rates are provided in Table 6.

Table 6: Annualized Bleeding Rate in All Patients

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Small children 0 – &lt;6 years</th>
<th>Older children 6 – &lt;12 years</th>
<th>Adolescents 12 – &lt;18 years</th>
<th>Adults ≥18 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized bleeding rate (median) (QR)</td>
<td>2.9 (6.3)</td>
<td>4.1 (6.8)</td>
<td>4.4 (6.9)</td>
<td>3.1 (5.6)</td>
<td>3.1 (7.3)</td>
</tr>
</tbody>
</table>

A total of 68 subjects were treated with NovoEight® for at least 12 months, including seven subjects <12 years. The ABR was similar for the subjects treated for 12 months when compared to the ABR for the total trial population.

Perioperative Management

A total of 11 surgeries were performed in 11 previously treated subjects between 14 and 55 years of age, of which 10 were major surgeries (five synovectomies, two total hip arthroplasties, one knee replacement, arthroscopy, and circumcision), and one was minor (forth extraction).

The investigator’s ratings of intra- and post-operative quality of hemostasis for these subjects were “excellent” or “good” for all cases.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

- NovoEight® is supplied in packages comprised of a single-use vial containing nominally 250, 500, 1000, 1500, 2000, or 3000 international units (IU) of FVIII potency, a MixPro® pre-filled diluent syringe containing 0.9% sodium chloride solution, and sterile vial adapter with 25 micrometer filter, which serves as a needless reconstitution device.

- The actual amount of FVIII potency in IU is stated on each carton and vial.

Table 7: Annualized Bleeding Rate in All Patients

<table>
<thead>
<tr>
<th>Presentation (Nominal Product Strength)</th>
<th>Carton NDC Number</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 International Units</td>
<td>NDC 0169 7825 01</td>
<td>• NovoEight® in single-use vial (NDC 0169-7829-11)</td>
</tr>
<tr>
<td>1000 International Units</td>
<td>NDC 0169 7801 01</td>
<td>• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
</tr>
<tr>
<td>1500 International Units</td>
<td>NDC 0169 7815 01</td>
<td>• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
</tr>
<tr>
<td>3000 International Units</td>
<td>NDC 0169 7803 01</td>
<td>• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7008-98)</td>
</tr>
</tbody>
</table>

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 expiry date shown on the label. Within the 30-month period, NovoEight® may also be stored at room temperature not to exceed 86°F (30°C) for up to twelve (12) months.
- If you choose to store NovoEight® at room temperature, clearly record the date when the product was removed from the refrigerator and the date shown on the vial. The total time of storage at room temperature should not exceed 12 months. Do not remove the product to the refrigerator.
- Do not use NovoEight® after the end of the 12-month period at room temperature storage, or after the expiration date shown on the vial, whichever occurs earlier.
- Do not freeze NovoEight®.

Use NovoEight® within 4 hours after reconstitution when stored at room temperature. Store the reconstituted product in the vial.

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 contact 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.
- Advise patients to follow the recommendations regarding proper sharps disposal provided in the FDA-approved Instructions for Use.

Version: 5
License Number: 1261
NovoEight® and MixPro® are registered trademarks of Novo Nordisk Health Care AG.
Clave® and MicroClave® are registered trademarks of ICU Medical Inc.
InVision-Plus®, InVision-Plus CSP®, Invision-Plus® Junior® are registered trademarks of RyMed Technologies, Inc.
Bionectro® is a registered trademark of VYGON.
For information contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536, USA
1-844-30-EIGHT

Manufactured by:
Novo Nordisk A/S
Novo Allé, DK-2880 Bagsvaerd
© 2016 Novo Nordisk
USA16HDM05031 12/2016
Patient Product Information
Novoeight® (N̄ō-vō-eyt)
Antihemophilic Factor (Recombinant)

Read the Patient Product Information and the Instructions For Use that come with Novoeight® before you start taking this medicine and each time you get a refill. There may be new information. This Patient Product Information does not take the place of talking with your healthcare provider about your medical condition or treatment. If you have questions about Novoeight® after reading this information, ask your healthcare provider.

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 blood from clotting normally. Novoeight® is used to control and prevent bleeding in people with hemophilia A.
Your healthcare provider may give you Novoeight® when you have surgery.
Novoeight® is not used to treat von Willebrand Disease.

Who should not use Novoeight®?
You should not use Novoeight® if you
• are allergic to factor VIII or any of the other ingredients of Novoeight®
• if you are allergic to hamster proteins
Tell your healthcare provider if you are pregnant or nursing because Novoeight® might not be right for you.

What should I tell my healthcare provider before I use Novoeight®?
You should tell your healthcare provider if you
• Have or have had any medical conditions.
• Take any medicines, including non-prescription medicines and dietary supplements.
• Are nursing.
• Are pregnant or planning to become pregnant.
• Have been told that you have inhibitors to factor VIII.

How should I use Novoeight®?
Treatment with Novoeight® should be started by a healthcare provider who is experienced in the care of patients with hemophilia A.
Novoeight® is given as an injection into the vein. You may infuse Novoeight® at a hemophilia treatment center, at your healthcare provider’s office or in your home. You should be trained on how to do infusions by your hemophilia treatment center or healthcare provider. Many people with hemophilia A learn to infuse the medicine by themselves or with the help of a family member.
Your healthcare provider will tell you how much Novoeight® to use based on your weight, the severity of your hemophilia A, and where you are bleeding.
You may need to have blood tests done after getting Novoeight® to be sure that your blood level of factor VIII is high enough to clot your blood. This is particularly important if you are having major surgery.
Your healthcare provider will calculate your 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.
If you have any further questions on the use of this product, ask 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:
• swelling or itching at the location of injection
• changes in liver tests
• 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 250 IU per vial
Dosage strength of approximately 500 IU per vial
Dosage strength of approximately 1000 IU per vial
Dosage strength of approximately 1500 IU per vial
Dosage strength of approximately 2000 IU per vial
Dosage strength of approximately 3000 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, or at room temperature (up to 86°F [30°C]) for a single period not exceeding 12 months.
If you choose to store Novoeight® at room temperature:
• Note the date that the product is removed from refrigeration on the box.
• The total time of storage at room temperature should not exceed 12 months. Do not return the product to the refrigerator.
• Do not use after 12 months from this date or the expiration date listed on the vial, whichever is earlier.
Do not use this medicine 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 should be used within 4 hours when stored at ≤ 86°F (30°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.

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 (under plastic cap)
- Spike (under protective paper)
- Protective paper

Pre-filled syringe with diluent
- Syringe tip (under syringe cap)
- Rubber plunger
- Thread
- Plunger rod
- Wide top end
- Scale

Syringe cap

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 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. 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.
   - Remove the protective paper from the vial adapter. If the protective paper is not fully sealed or if it is broken, don’t use the vial adapter.
   - Do not 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 should be used within 4 hours when stored at ≤ 86ºF (30°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.

---

**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 sterile Luer-lock plastic syringe.
- 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.