**Indications and Usage**

- Novoeight® (antihemophilic factor, recombinant) is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes.
- Novoeight® is not indicated for the treatment of von Willebrand disease.

**Important Safety Information**

**Contraindications**

- Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components, including hamster proteins.

Please see Prescribing Information for complete storage conditions.

Dylan lives with hemophilia A.
“I’m planning on working as a camp counselor this summer. Having a factor I can store and take with me is a huge relief.”

—Patient with hemophilia A

**Important Safety Information**

**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.
Novoeight®—A higher degree of stability

Novoeight® is the only standard half-life (SHL) factor VIII with stability up to 104°F for up to 3 months.\(^{1-11}\)

**Important Safety Information**

**Warnings and Precautions (cont’d)**

- Development of activity-neutralizing antibodies (inhibitors) may occur. Previously untreated patients (PUPs) are at greatest risk for inhibitor development with all factor VIII products. Inhibitors have been reported following administration of Novoeight® in PUPs. 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.

---

Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Help your patients explore life up to 104°F—with the ability to store factor out of the fridge

The SHL with the highest storage temperature for the longest duration

**Novoeight® can be stored**:

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Storage Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 104°F</td>
<td>For up to 3 months</td>
</tr>
<tr>
<td>Up to 86°F</td>
<td>For up to 12 months</td>
</tr>
</tbody>
</table>

**Highest storage temperature after reconstitution**\(^1\,\text{a}\):

- Up to 2-hour storage time at 104°F

**Longest room temperature storage time after reconstitution**\(^1\,\text{a}\):

- Up to 4-hour storage time at 86°F

\(^1\,\text{a}\) Compared with other SHL recombinant FVIII products. Please see Prescribing Information for complete storage conditions.

**Important Safety Information**

**Adverse Reactions**

- The most frequently reported adverse reactions (≥1%) were inhibitors in previously untreated patients (PUPs), injection site reactions, and pyrexia
Portability that fits into your patients’ lifestyle

Indications and Usage

- Novoeight® (antihemophilic factor, recombinant) is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes.
- Novoeight® is not indicated for the treatment of von Willebrand disease.

Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Novoeight® offers quick reconstitution and multiple dose strengths

With MixPro®, preparing a dose of Novoeight® is as quick as ATTACH, TWIST, MIX

**PREFILLED DILUENT SYRINGE**
Contains 4 mL of diluent—works with any dose strength

**ADAPTER**
Connects the syringe and vial with a 25-µm inline particle filter

**VIAL WITH COLORED CAP**
Easy recognition of different dose strengths by color-coded vial caps

Multiple dose strengths help more patients infuse with fewer vials

Important Safety Information

**Contraindications**
• Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components, including hamster proteins
NOVOEIGHT® FITS INTO AN active lifestyle

“When I’m out and doing physical activity, it’s helpful that Novoeight® is easy to take with me and use.”

—Vaughn, Novoeight® user

Important Safety Information

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.
Novoeight® PK profile achieves the needed peak levels of factor activity\textsuperscript{1,12,13,a,b}

Dosing and appropriate level of activity may be different from person to person. Appropriate dosing regimen and level of activity should be determined individually for each patient.

Novoeight® is approved for routine prophylaxis every other day or 3 times weekly. Please see Prescribing Information for complete dosing information.\textsuperscript{1}

Important Safety Information

**Warnings and Precautions (cont’d)**

- Development of activity-neutralizing antibodies (inhibitors) may occur. Previously untreated patients (PUPs) are at greatest risk for inhibitor development with all factor VIII products. Inhibitors have been reported following administration of Novoeight® in PUPs. 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.
WITH NOVOEIGHT®
YOUR PATIENTS CAN
take control
of their bleeds

“We’ve found Novoeight® to be the right therapy that fits with his life and effectively controls his bleeds.”
—Caregiver of patient with hemophilia A

Important Safety Information
Adverse Reactions
• The most frequently reported adverse reactions (≥1%) were inhibitors in previously untreated patients (PUPs), injection site reactions, and pyrexia

Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Proven effective across age groups

Novoeight® continued to reduce frequency of bleeds, demonstrating effective, long-term prophylaxis\textsuperscript{15,\textit{a}}

**Median ABR**

<table>
<thead>
<tr>
<th>All patients (0–65 years old)</th>
<th>Children (≤11 years old)</th>
<th>Long-term safety trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.7 median bleeds per year\textsuperscript{:\textit{a}}</td>
<td>3.0 median bleeds per year\textsuperscript{16,\textit{b}}</td>
<td>1.4 median bleeds per year\textsuperscript{1,\textit{a}}</td>
</tr>
</tbody>
</table>

*guardian™2: a phase 3b, non-randomized, open-label extension trial investigating the long-term safety and efficacy of turoctocog alfa in 213 previously treated males of all ages with severe hemophilia A. Of the 207 patients on prophylaxis, accumulated patient-years on prophylaxis was 730.8.\textsuperscript{15}
*guardian™3: a multicenter, multinational, noncontrolled, open-label safety, efficacy, and pharmacokinetic trial in 63 previously treated pediatric patients (aged 0 to 11 years) with hemophilia A in which patients were exposed to turoctocog alfa for a mean of 60 exposure days (ranging from 20 to 104 exposure days).\textsuperscript{16}

ABR=annualized bleed rate.

**Indications and Usage**

- Novoeight® (antihemophilic factor, recombinant) is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes
- Novoeight® is not indicated for the treatment of von Willebrand disease

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\textsuperscript{1} guardian™2: a phase 3b, non-randomized, open-label extension trial investigating the long-term safety and efficacy of turoctocog alfa in 213 previously treated males of all ages with severe hemophilia A. Of the 207 patients on prophylaxis, accumulated patient-years on prophylaxis was 730.8.\textsuperscript{15}
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ABR=annualized bleed rate.
Novoeight®—proven reliability for the treatment of bleeds

Results from guardian™1 and guardian™3 pivotal trials16-18,a,b,c

Bleeds controlled with 1 or 2 infusions

Adolescents and adults
aged 12–65 | N=150

Children
aged 0–11 | N=63

Hemostatic success rate in major and minor surgeriesc

All patients

89%

95%

100%

*guardian™3: a multicenter, multinational, noncontrolled, open-label safety, efficacy, and pharmacokinetic trial in 63 previously treated pediatric patients (aged 0 to 11 years) with hemophilia A in which patients were exposed to turoctocog alfa for a mean of 60 exposure days (ranging from 20 to 104 exposure days).16

*guardian™1: a multicenter, multinational, open-label, single-arm efficacy and safety trial in 150 patients (aged 12 to 65 years) with severe hemophilia A on a prophylactic treatment regimen who were exposed to turoctocog alfa for a mean of 85 exposure days (ranging from 11 to 172 exposure days).17

A hemostatic response rated as "excellent" or "good" was considered treatment success. If hemostatic response was rated as "moderate" or "none," the treatment was considered treatment failure. Missing data were included in the treatment failure category.18

Important Safety Information

Contraindications
• Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components, including hamster proteins

Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Proven reliable in PTPs who switched to Novoeight®

0 inhibitors were confirmed in one of the largest clinical trials with\(^1\)

\[\text{238 previously treated patients}^{a} \quad \text{over} \quad >130,000 \text{ exposure days}^{a}\]

\(^{a}\) In a clinical trial of PUPs, 42.9% developed inhibitors\(^{1,4}\)

PUP=previously untreated patient; PTP=previously treated patient.

\(^{1}\)PTPs who participated in the guardian 1, 2 and 3 clinical trials.\(^{16,17,18}\)

\(^{4}\)59 PUPs with severe hemophilia A (factor VIII level ≤1%) received at least one dose of Novoeight® as part of either routine prophylaxis or on-demand treatment of bleeding episodes. Patients developed inhibitors with a mean of 14.1 exposure days at the time of the first positive inhibitor test. High-risk genetic mutations were identified in 91.7% of the overall inhibitors and 93.3% of the high titer inhibitors.\(^1\)

Important Safety Information

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.

Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Established safety profile of Novoeight®

Novoeight® was shown to be safe in pivotal trials\(^1,16,17\)

- Safety results consistent among adults, adolescents, and children\(^1\)
- The most frequently reported adverse reactions in PTPs were injection site reactions (1.0%), and pyrexia (1.0%)\(^1\)
- Adverse reactions reported during postmarketing period were similar to those observed during clinical trials\(^1\)

Designed with purity in mind

- A rigorous 5-step purification process, including immunoaffinity chromatography, ensures a refined product\(^20,21\)

Important Safety Information

**Warnings and Precautions (cont’d)**

- Development of activity-neutralizing antibodies (inhibitors) may occur. Previously untreated patients (PUPs) are at greatest risk for inhibitor development with all factor VIII products. Inhibitors have been reported following administration of Novoeight® in PUPs. 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

Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Consider the features of Novoeight® for your patients who are on the go

Is it time to reconsider your patients’ treatment?

rFVIII SHL and EHL Comparison Guide\(^a,b\)

<table>
<thead>
<tr>
<th>Choosing an rFVIII Product</th>
<th>Novoeight(^b)</th>
<th>Adynovate(^a)</th>
<th>Advate(^a)</th>
<th>Afstyla(^a)</th>
<th>Eloctate(^a)</th>
<th>Jivi(^a)</th>
<th>Kogenate® FS(^a)</th>
<th>Kovaltry(^a)</th>
<th>Nuwiq(^a)</th>
<th>Recombinate(^b)</th>
<th>Xyntha(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Storage temperature up to 104°F for 3 months</td>
<td>✓</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Storage temperature up to 86°F for 12 months</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Greater than 4 hours of room temperature stability after reconstitution (at 86°F)</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mixing device includes prefilled diluent syringe</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>6 or more vial sizes</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Diluent volume consistent across all vial sizes</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>Lowest available diluent volume</td>
<td>4 mL</td>
<td>2 mL</td>
<td>2 mL</td>
<td>2.5 mL</td>
<td>3 mL</td>
<td>2.5 mL</td>
<td>2.5 mL</td>
<td>2.5 mL</td>
<td>2.5 mL</td>
<td>5 mL</td>
<td>4 mL</td>
</tr>
</tbody>
</table>

The above table is not intended to compare the safety or efficacy of any of the products.

\(^a\)Does not include the EHL Esperoct (antihemophilic factor [recombinant], glycopegylated-exei).

\(^b\)Data current as of December 2, 2020.

**Important Safety Information**

**Adverse Reactions**
- The most frequently reported adverse reactions (≥1%) were inhibitors in previously untreated patients (PUPs), injection site reactions, and pyrexia

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Please tap the ISI tab for additional Important Safety Information and tap the PI tab for Prescribing Information.
Ready to prescribe Novoeight®?

We can help your patients

Free trial program
• Talk to a [NovoSecure™] Specialist to find out if you’re eligible

Product Assistance Program
• Apply for the Product Assistance Program by calling 1-844-NOVOSEC (1-844-668-6732) for more information

Co-pay assistance program
• Get help with co-pay costs for Novoeight®, if eligible

Visit [MYNOVOSECURE.COM] or call 1-844-NOVOSEC (1-844-668-6732) to speak with a [NovoSecure™] Specialist

Indications and Usage
• Novoeight® (antihemophilic factor, recombinant) is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes
• Novoeight® is not indicated for the treatment of von Willebrand disease

Patients who have been prescribed a Novo Nordisk hemophilia and rare bleeding disorder product for an FDA-approved indication, and who have commercial insurance, may be eligible to receive a limited supply of free product. Patient is not eligible if he/she participates in or seeks reimbursement or submits a claim for reimbursement to any federal or state healthcare program with prescription drug coverage, such as Medicaid, Medicare, Medigap, VA, DOD, TRICARE, or any similar federal or state health care program. Product is provided at no cost to the patient and is not contingent on any product purchase. Physician and patient shall not: (1) bill any third-party for the free product, or (2) resell the free product. The Novo Nordisk Hemophilia & Rare Bleeding Disorders Product Assistance Program (PAP) is administered by [NovoSecure™]. To qualify for the PAP, patients must demonstrate financial need and be prescribed a Novo Nordisk factor product for an FDA indicated condition. Several factors are considered in evaluating financial need, including cost of living, size of household, and burden of total medical expenses. If the applicant qualifies under the PAP guidelines, a limited supply of the requested medication(s) will be shipped to the patient. Patients who qualify for the PAP may be eligible to receive the prescribed Novo Nordisk product, for up to 1 year from the approval date. Product limits vary.

Eligibility and Restrictions:
In order to redeem this offer patient must have a valid prescription for the brand being filled. A valid Prescriber ID# is required on the prescription. Patient is not eligible if he/she participates in or seeks reimbursement or submits a claim for reimbursement to any federal or state healthcare program with prescription drug coverage, such as Medicaid, Medicare, Medigap, VA, DOD, TRICARE, or any similar federal or state health care program (each a Government Program), or where prohibited by law. Patient must be enrolled in, and must seek reimbursement from or submit a claim for reimbursement to, a commercial insurance plan. The brand and the prescription being filled must be covered by the patient’s commercial insurance plan. Offer excludes all cash-paying patients. This offer may not be redeemed for cash. By using this offer, you are certifying that you meet the eligibility criteria and will comply with the terms and conditions described herein and will not seek reimbursement for any benefit received through this card. Novo Nordisk’s Eligibility and Restrictions, and Offer Details may change from time to time, and for the most recent version, please visit [https://www.mynovosecure.com/copayassistant/copay-form.html#/register-copay]. Re-confirmation of information may be requested periodically to ensure accuracy of data and compliance with terms.
This offer is valid in the United States and may be redeemed at participating retail pharmacies. Absent a change in Massachusetts law, effective July 1, 2019, the Savings Card will no longer be valid for residents of Massachusetts. Void where taxed, restricted, or prohibited by law. This offer is not transferrable and is limited to one offer per person. Not valid if reproduced.
Cash Discount Cards and other non-insurance plans are not valid as primary insurance under this offer. If the patient is eligible for drug benefits under any such program, the patient cannot use this offer. This Savings Card cannot be combined with any coupon, certificate, voucher, or similar offer.
This program is managed by ConnectiveRx on behalf of Novo Nordisk. The parties reserve the right to rescind, revoke or amend this offer without notice at any time.
References


Clyde lives with hemophilia A.
Novoeight®—designed to keep your patients on the go

**READY TO GO**

The SHL with

- Highest storage temperature for the longest duration:
  - up to 104°F for up to 3 months
  - up to 86°F for up to 12 months
- Longest room temperature storage time after reconstitution—up to 4 hours at up to 86°F and up to 2 hours at up to 104°F
- PK profile that allows tailored dosing to achieve the needed peak levels of factor activity

*a* Refer to Prescribing Information for recommended prophylaxis dosing.

Please see Prescribing Information for complete storage conditions.

**Important Safety Information**

**Contraindications**

- Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components, including hamster proteins
Indications and Usage

- Novoeight® (antihemophilic factor, recombinant) is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes
- Novoeight® is not indicated for the treatment of von Willebrand disease

Important Safety Information

Contraindications

- Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components, including hamster proteins

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
- Development of activity-neutralizing antibodies (inhibitors) may occur. Previously untreated patients (PUPs) are at greatest risk for inhibitor development with all factor VIII products. Inhibitors have been reported following administration of Novoeight® in PUPs. 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

Adverse Reactions

- The most frequently reported adverse reactions (≥1%) were inhibitors in previously untreated patients (PUPs), injection site reactions, and pyrexia

Please tap the PI tab for Prescribing Information.
Tap here for Prescribing Information

novoeight®
Antihemophilic Factor (Recombinant)

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NOVOEIGHT® safely and effectively. See full prescribing information for NOVOEIGHT®. DO NOT USE FOR FALLBACK ITEMS: 1. See full prescribing information for NOVOEIGHT®. 2. Novoeight® (Antihemophilic Factor [Recombinant]) is 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. (1)

—- INDICATIONS AND USAGE —-
Novoeight® is an Antihemophilic Factor (Recombinant) 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. (1)

—- DOSAGE AND ADMINISTRATION —-
For intravenous injection only (2)
- Each vial of Novoeight® contains the labeled amount of Antihemophilic Factor VIII in international units (IU). (2)
- The required dosage is determined using the following formula:

\[
\text{Dosage Required (IU)} = \text{Body Weight (kg)} \times \text{Desired Factor VIII Increase (IU/dL or % normal)} \times 0.5 \text{ (IU/kg per IU/dL)}
\]
- Frequency of Novoeight® administration is determined by the type of bleeding episode and the recommendation of the treating physician. (2.1)

—- DOSAGE FORMS AND STRENGTHS —-
Novoeight® is available as a lyophilized powder in single-dose vials of 250, 500, 1000, 1500, 2000 and 3000 international units. (3)

—- CONTRAINDICATIONS —-
Do not use in patients who have had an anaphylactic or severe hypersensitivity reaction to Novoeight® or its components, including hamster proteins. (4)

—- ADVERSE REACTIONS —-
Hypersensitivity and severe hypersensitivity reactions are possible. Following any adverse reactions leading to hospitalization, patients are tested for plasma factor VIII activity. (5.1)
- Development of activity-neutralizing antibodies (inhibitors) may occur. Frequent monitoring of factor VIII activity levels is recommended. (5.2, 5.3)

—- EFFECTIVENESS —-
The most frequently reported adverse reactions are injection site reactions, injection site hemorrhage, injection site pain, hematoma, and rash. (6)

—- USE IN SPECIFIC POPULATIONS —-
- Pregnancy (8.1)
- Lactation (8.2)
- 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.

07/2020

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2 DOSAGE AND ADMINISTRATION
2.1 Dose
2.2 Preparation and Reconstitution
2.3 Administration
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Hypersensitivity Reactions
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6.1 Clinical Experience
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7 USE IN SPECIFIC POPULATIONS
8 CLINICAL PHARMACOLOGY
8.1 Mechanism of Action
8.2 Pharmacodynamics
8.3 Pharmacokinetics
9 NONCLINICAL TOXICOLOGY
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11 DESCRIPTION
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14 HOW SUPPLIED/STORAGE AND HANDLING
15 PATIENT COUNSELING INFORMATION
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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NOVOEIGHT® safely and effectively. See full prescribing information for NOVOEIGHT®.
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NOVOEIGHT® safely and effectively. See full prescribing information for NOVOEIGHT®.

NOVOEIGHT® (antihemophilic factor, recombinant)
yyophilized powder for solution, for intravenous use
Initial U.S. Approval: 2013

INDICATIONS AND USAGE
Novoeight® is an Antihemophilic Factor (Recombinant) 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. (1)

DOSAGE AND ADMINISTRATION
For intravenous injection after reconstitution only (2)
• Each vial of Novoeight® contains the labeled amount of recombinant Factor VIII in international units (IU). (2)
• The required dosage is determined using the following formula:
Dosage Required (IU) = Body Weight (kg) × Desired Factor VIII Increase (IU/dL or % normal) × 0.5 (IU/kg per IU/dL)
• Frequency of Novoeight® administration is determined by the type of bleeding episode and the recommendation of the treating physician. (2.1)

DOSAGE FORMS AND STRENGTHS
Novoeight® is available as a lyophilized powder in single-dose vials of 250, 500, 1000, 1500, 2000 and 3000 international units. (3)

CONTRAINDICATIONS
Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight® or its components, including hamster proteins. (4)

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.

07/2020
FULL PRESCRIBING INFORMATION
1 INDICATIONS AND USAGE
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:
  \[
  \text{Dosage (IU)} = \text{Body Weight (kg)} \times \text{Desired Factor VIII Increase (IU/dL or % normal)} \times 0.5
  \]
  The final dose calculated is expressed as IU
• Base the dose and frequency of Novoeight® on the individual clinical response. Patients may vary in their pharmacokinetic and clinical responses (See Clinical Pharmacology (12.3)).

On-demand Treatment and Control of Bleeding Episodes
A guide for dosing Novoeight® for on-demand treatment and control of bleeding episodes is provided in Table 1. Dose to maintain a plasma factor VIII activity level at or above the plasma levels (in % of normal or in IU/dL) outlined in Table 1.

Table 1: 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</td>
<td>20-40</td>
<td>At least 1 day until bleeding resolution is achieved</td>
<td>At least 1 day</td>
</tr>
<tr>
<td>Moderate</td>
<td>30-60</td>
<td>Until pain and acute disability are resolved (approximately 3-4 days)</td>
<td>12-24</td>
</tr>
<tr>
<td>Major</td>
<td>60-100</td>
<td>Until resolution of bleed (approximately 7-10 days)</td>
<td>7-12-24</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</td>
<td>30-60</td>
<td>At least 1 day until healing is achieved</td>
<td>24</td>
</tr>
<tr>
<td>Major</td>
<td>80-100 (pre-and post-operative)</td>
<td>Until adequate wound healing, then continue therapy for at least 7 days to maintain a factor VIII activity of 80% to 90% (IU/dL)</td>
<td>8-24</td>
</tr>
</tbody>
</table>

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 (≥ 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>
</tbody>
</table>

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 dose requires more than one vial of Novoeight® per injection, reconstitute each vial according to the following instructions:

Overview of Novoeight® Package
Vial with NovoEight® powder in pre-filled diluent syringe

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. 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.

Preparation of Novoeight® for On-demand treatment and control of bleeding episodes

2 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.
Novoeight® is a recombinant (r) analogue of human coagulation factor VIII (FVIII) with a molecular mass of approximately 14.1 exposure days at the time of the first positive inhibitor test; 15 (26.8%) PUPs developed high titer (≥ 5 BU) inhibitors. High risk of inhibitors was normal for this child and no clinical adverse findings that was not confirmed when checked after 20 exposure days. In vivo recovery was normal for this child and no clinical adverse findings were observed. In the completed main phase of the clinical trial in PUPs, 241 of 563 (42.9%) patients developed inhibitors with a mean of 14.1 exposure days at the time of the first positive inhibitor test. 15 (26.8%) PUPs developed high titer (≥ 5 BU) inhibitors. High risk genetic mutations were identified in 91.7% of the overall inhibitors and 93.3% of the high titer inhibitors.

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 throughout 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. 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, it may be misleading to compare the incidence of antibodies to Novoeight® with the incidence of antibodies to other products.

6.2 Postmarketing Experience

Adverse reactions reported during post marketing period were similar in nature to those observed during clinical trials. Clinical pharmacology.
In a single dose PK assessment in adult patients with BMI ≥ 30 kg/m² in the extension trial (See Clinical Studies), the AUC was 59% higher and clearance was 33% lower in 6 subjects with BMI ≥ 30 kg/m² compared to subjects with normal BMI, see Table 6.

Table 6: Pharmacokinetics of Novoeight® in 6 adult patients with BMI ≥ 30 kg/m²

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Clotting Assay</th>
<th>Chromogenic Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Incremental Recovery (IU/mL/kg)</td>
<td>0.029 (0.002)</td>
<td>0.032 (0.005)</td>
</tr>
<tr>
<td>AUC (IU/mL)</td>
<td>14.2 (3.8)</td>
<td>12.8 (5.1)</td>
</tr>
<tr>
<td>CL (mL/kg)</td>
<td>2.43 (0.80)</td>
<td>2.57 (0.80)</td>
</tr>
<tr>
<td>Tr (h)</td>
<td>10.0 (4.9)</td>
<td>12.0 (5.3)</td>
</tr>
<tr>
<td>Vis (mL/kg)</td>
<td>53.4 (10.9)</td>
<td>44.3 (8.2)</td>
</tr>
<tr>
<td>Exa (IU/mL)</td>
<td>1.07 (0.16)</td>
<td>1.54 (0.29)</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>15.4 (4.6)</td>
<td>16.4 (10.1)</td>
</tr>
</tbody>
</table>

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 per kg body weight) than in adults (3.47 mL/h/kg) when using the clotting assay, and 60% and 29% higher than 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 genetic toxicity 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

Four multi-center, open-label, non-controlled trials have been conducted to evaluate the safety and efficacy of Novoeight® 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 patients above 12 years of age, 84 previously treated pediatric subjects below the age of 12 years (±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. Immuno-resistant patients with severe hemophilia A (factor VIII activity ≤ 1%) and no history of FVIII inhibitors were eligible for the trials. Subjects conducted during routine prophylaxis and treatment of bleeds received Novoeight® 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.

On-demand Treatment and Control of Bleeding Episodes

A total of 3153 bleeds in 260 subjects were treated with Novoeight®. 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” then the treatment was considered a failure. Of these 3,153 bleeds, 2,089 (89%) were rated excellent or good in their response to treatment with Novoeight®, 274 (9%) were rated as moderate, 25 (0.8%) were rated as having no response and for 45 (1%) the response to treatment was unknown. A total of 2,794 (88%) of the bleeds were resolved with one or two injections of Novoeight®.

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 Novoeight®, 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, 2,204 (99%) of the bleeds were resolved with 1–2 injections of Novoeight®. The majority of the bleeds were of mild/moderate severity.

The median annualized bleeding rate in the previously untreated patients was 2.9 (IQR 5.4) and the mean (95%CI) was 4.3 (3.5, 5.8).

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

• Novoeight® is supplied in packages comprised of a single-dose vial containing nominally 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 investigator’s ratings of intra- and post-operative quality of hemostasis for these subjects were “excellent” or “good” for all cases.

Presentation (Nominal Product Strength) | Carton Number | NDC Number | Components
---|---|---|---
250 International Units | 0169 7826 01 | 0169-7826-11 | • Novoeight® in single-dose vial (NDC 0169-7826-11)
• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7808-98)
• Vial adapter

500 International Units | 0169 7860 01 | 0169-7861-11 | • Novoeight® in single-dose vial (NDC 0169-7861-11)
• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7808-98)
• Vial adapter

1000 International Units | 0169 7870 01 | 0169-7871-11 | • Novoeight® in single-dose vial (NDC 0169-7871-11)
• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7808-98)
• Vial adapter

2000 International Units | 0169 7870 01 | 0169-7871-11 | • Novoeight® in single-dose vial (NDC 0169-7871-11)
• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7808-98)
• Vial adapter

3000 International Units | 0169 7870 01 | 0169-7871-11 | • Novoeight® in single-dose vial (NDC 0169-7871-11)
• Pre-filled sodium chloride diluent in syringe, 4 mL (NDC 0169-7808-98)
• Vial adapter

• The Novoeight® vials are made of glass, closed with a chromiumyl 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.

Table 5: Pharmacokinetics of Novoeight® in 20 adult and adolescent patients with hemophilia A

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Clotting Assay</th>
<th>Chromogenic Assay</th>
</tr>
</thead>
<tbody>
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<td>BMI (kg/m²)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Incremental Recovery (IU/mL/kg)</td>
<td>0.020 (0.002)</td>
<td>0.028 (0.006)</td>
</tr>
<tr>
<td>AUC (IU/mL)</td>
<td>14.2 (3.8)</td>
<td>12.8 (5.1)</td>
</tr>
<tr>
<td>CL (mL/kg)</td>
<td>2.43 (0.80)</td>
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<td>1.07 (0.16)</td>
<td>1.54 (0.29)</td>
</tr>
<tr>
<td>MRT (h)</td>
<td>15.4 (4.6)</td>
<td>16.4 (10.1)</td>
</tr>
</tbody>
</table>

a: Dose: 50 IU/kg turoctocog alfa (single i.v. dose)

b: Patients dosed every other day or three times weekly

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

In the trial with previously untreated patients, 56 subjects below 6 years of age received Novoeight® for routine prophylaxis. The median annualized bleeding rate in the previously untreated patients was 2.9 (IQR 5.4) and the mean (95%CI) was 4.3 (3.5, 5.8).

Perioperative Management

A total of 30 surgeries were performed in 25 previously treated subjects between 6 and 58 years of age, of which 26 were major surgeries (20 orthopaedic, 5 non-orthopaedic and a circumcision), and 4 were minor (2 dental, 1 circumcision and 1 insertion of port-a-cath).

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

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Bionector® is a registered trademark of Vygon.
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Manufactured by:
Novo Nordisk A/S
Novo Allé, DK-2880 Bagsvaerd
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NovoEight®, 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.

If your bleeding does not stop after taking NovoEight®, 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:

- 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 printed 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. 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 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 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.

For more information about NovoEight®, please call Novo Nordisk at 1-844-30-EIGHT.

Revised: 07/2020

Novo Eight® is a registered trademark of Novo Nordisk Health Care AG.


For information about NovoEight® contact:

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Plainboro, NJ 08536, USA

Manufactured by:

Novo Nordisk A/S

DK-2880 Bagsvaerd, Denmark

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6
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
Vial adapter
Protective cap
Plunger rod

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

Syringe cap
Scale

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.
- Wipe 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.