MOVE BEYOND THE THRESHOLD[a]

Esperoct®, an EHL rFVIII, provides[1]

- **High trough levels**
- **Low ABR**
- **Proven starting dose and ability to individualize to meet patient's needs**

ABR=annualized bleed rate; EHL=extended half-life.
[a]Of 1% trough levels for standard half-life (SHL) products in adults and adolescents.[1,2]
[b]For up to 3 months.[1]

INDICATIONS AND USAGE

Esperoct® [antihemophilic factor (recombinant), glycopegylated-exei] is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes

- Esperoct® is not indicated for the treatment of von Willebrand disease

novo nordisk®

Please see Important Safety Information throughout.
Please see accompanying Prescribing Information.

esperoct®
antihemophilic factor (recombinant), glycopegylated-exei

KEEP THEM PROTECTED WITH ONE PROVEN DOSE

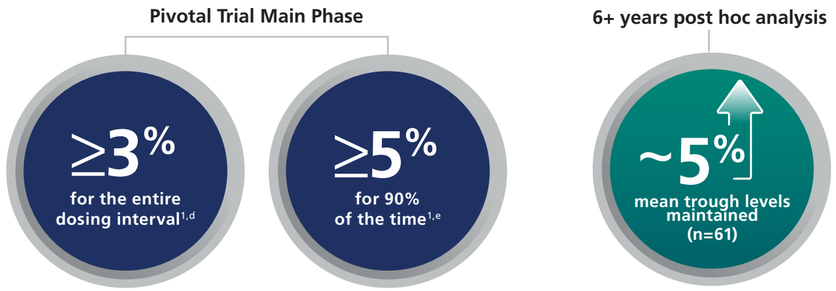
In a post hoc analysis, long-term prophylaxis (≥6 years) showed a stabilization in mean FVIII trough levels and decrease in ABR over time.[3,a]

Routine prophylaxis:

50 IU/kg every 4 days
- No dose adjustment needed and related pharmacokinetic (PK) testing required[1,2]

- Regimen can be individually tailored to less or more frequent dosing[1,b]
- Up to 50% fewer infusions[c] per year compared to SHL[4]

Trough levels stabilized in the range of moderate/mild hemophilia for the majority of the time



Benefits of higher factor trough levels, according to WFH, include

- More effective prophylaxis—higher level of prevention of bleeds (both clinically evident and subclinical microbleeds) while maintaining similar dosing schedules[5]
- Potentially greater level of sports participation (possibly including sports that have traditionally been discouraged) without incurring a substantially increased risk of bleeding[5]

WFH=World Federation of Hemophilia.

[a]Post hoc analyses were performed on data from the pathfinder 2 trial of patients aged (>12) with severe hemophilia A. Exploratory descriptive analyses of the data were used to evaluate long-term annual bleed rates and mean factor VIII trough levels which were assessed over time in 61 patients who received ≥6 years of prophylaxis, every 4 days.[3] Limitations of the analyses include the lack of baseline joint status data, which is clinically relevant for phenotypic assessment prior to treatment initiation. The absence limits the ability to draw conclusions regarding improvement in joint status over time. Several trough-level data were excluded if it was believed that they were elevated due to dosing to treat a recent bleed.

[b]Based on bleeding episodes.

[c]50% fewer if previously dosed every other day; 40% fewer if previously dosed 3x/week.

[d]In a phase 3, open-label study, safety, efficacy, and PK of Esperoct® were evaluated in previously treated patients (PTPs) aged >12 years with severe hemophilia A. Single-dose PK studies were performed in 42 adults after receiving Esperoct® 50 IU/kg; 175 PTPs received routine prophylaxis (50 IU/kg Q4D) for 76 weeks. Mean trough levels for adolescents (12-<18 years) were 2.7 IU/dL.[1,2]

[e]Steady-state FVIII activity profiles were estimated in 143 patients using a one-compartment model with first-order elimination with PK parameters of clearance and volume of distribution.[1]

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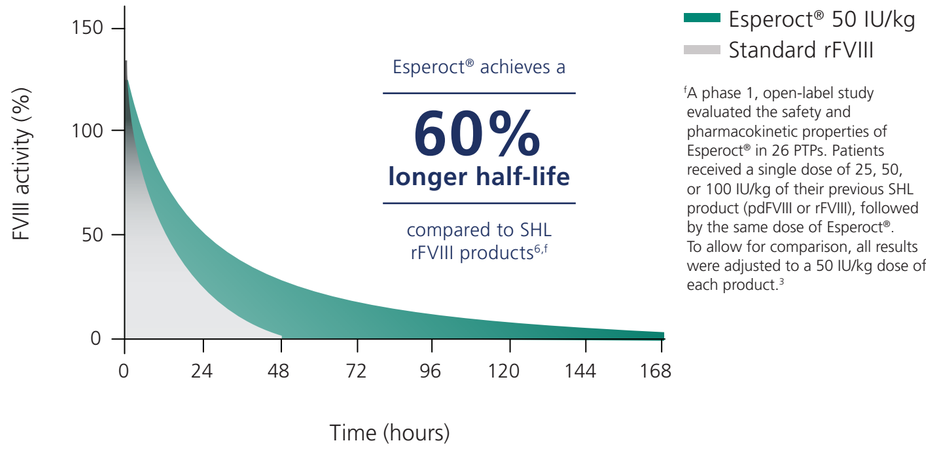
EXTEND HALF-LIFE BEYOND THE STANDARD



[f]A phase 1, open-label study evaluated the safety and pharmacokinetic properties of Esperoct® in 26 PTPs. Patients received a single dose of 25, 50, or 100 IU/kg of their previous SHL product (pdFVIII or rFVIII), followed by the same dose of Esperoct®. To allow for comparison, all results were adjusted to a 50 IU/kg dose of each product.[3]

Achieved an unprecedented half-life[d,g]

22 hours in adults with site-directed glycoPEGylation[1,d,g]

[g]Mean half-life in adults and adolescents, compared with other EHL FVIII products; the mean half-life in adults is 19.7 hours for Eloctate®, 14.7 for Adynovate®, and 17.9-18.6 for Jivi® (values obtained using chromogenic assay).[7-9]

IMPORTANT SAFETY INFORMATION

Contraindications

- Do not use in patients who have known hypersensitivity to Esperoct® or its components, including hamster proteins

esperoct®
antihemophilic factor (recombinant), glycopegylated-exei

KEEP THEM PROTECTED FROM BLEEDS

Long-term trial results confirm effective prophylaxis in adults and adolescents—for up to 6.6 years[10]

A lower overall median ABR in patients (aged 12 to 70 years) compared with the main phase was achieved[10,a]

0.8

Overall bleeds per year[b]
N=177

Based on a post-hoc analysis, the majority of adults/adolescents who completed the entire trial experienced no annual bleeds after year 1[10,c]

[a]In a phase 3, open-label study, safety, PK, and efficacy of Esperoct® were evaluated in PTPs aged ≥12 years with severe hemophilia A; 175 received routine prophylaxis (50 IU/kg every 4 days) and 12 adults elected to be treated on-demand during the main phase. After the main phase, a subset of patients continued on in extension phase part 1. After 24 weeks, patients from extension phase part 1 continued into the non-randomized extension phase part 2 until the end of trial.[2,10]
[b]Median annualized bleeding rate shown is from the main and extension phases of the pivotal clinical trial of previously treated people aged ≥12 years with severe hemophilia A who received Esperoct® 50 IU/kg every 4 days, for up to 6.6 years.[10]
[c]Based on a post hoc analysis of patients who completed the entire pathfinder™ 2 trial (n=110) who took Esperoct® 50 IU/kg every 4 days for up to 6.6 years. Patients evaluated at year 2 (n=103), year 3 (n=66), year 4 (n=62), year 5 (n=62), year 6 (n=59).[10]

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Hypersensitivity reactions, including anaphylaxis, may occur. Should hypersensitivity reactions occur, discontinue Esperoct® and administer appropriate treatment
- Development of neutralizing antibodies (inhibitors) has occurred. Perform an assay that measures Factor VIII inhibitor concentration if bleeding is not controlled with the recommended dose of Esperoct® or if the expected plasma Factor VIII activity levels are not attained

Please see additional Important Safety Information throughout.
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PREPARE THEM FOR THE UNEXPECTED

Effective bleed control on-demand

97%

of 532 bleeds controlled with 1-2 infusions[2,d]

On-demand dosing[1]:

Minor/moderate bleeds: 40 IU/kg
Major bleeds: 50 IU/kg[e]

Effective perioperative control

96%

efficacy shown in 45 major surgical procedures[1,f]

Perioperative dosing[1]:

50 IU/kg for all surgeries[g,h]

[d]In a phase 3, open-label study, safety, PK, and efficacy of Esperoct® were evaluated in PTPs aged ≥12 years with severe hemophilia A; 175 received routine prophylaxis (50 IU/kg every 4 days) and 12 adults elected to be treated on-demand during the main phase. Treatment-requiring bleeds were reported by patients through diaries.[2]
[e]Additional dose can be administered every 24 hours for major or life-threatening bleeding.[1]
[f]A phase 3, open-label, nonrandomized trial to assess the hemostatic efficacy of Esperoct® during major surgery in 33 patients with hemophilia A who underwent 45 major surgeries, 41 of which were orthopedic (15 joint replacements, 9 arthroscopic orthopedic interventions, and 17 classified as "other" orthopedic interventions). The success rate in bleed control during surgery was evaluated on a 4-point scale of excellent, good, moderate, or poor. Treatment success was defined as excellent or good bleed control.[1,11]
[g]Perioperative dosing recommendation for pediatric patients is 65 IU/kg.[1]
[h]For minor surgeries, additional dose(s) can be administered after 24 hours; for major surgeries, additional doses can be administered every 24 hours in the first week and then every 48 hours in the second week.[1]

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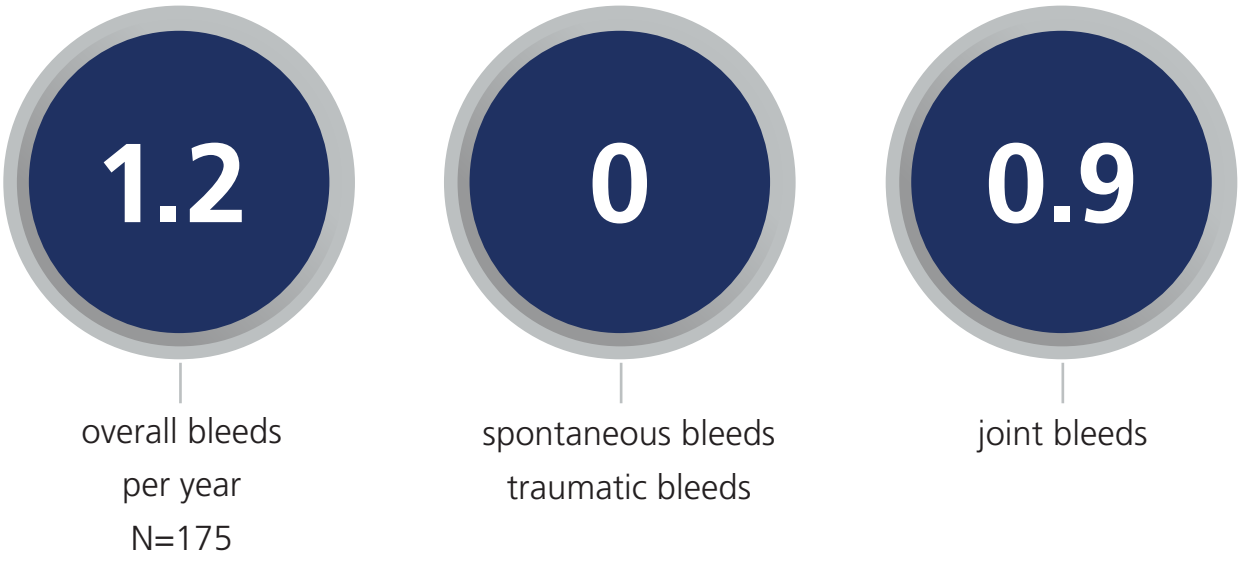
PIVOTAL TRIAL MAIN PHASE DATA

Effective prophylaxis with a low median ABR in all patients (aged 12 to 70 years)[1,a]



ABR=annualized bleed rate.

[a]In a phase 3, open-label study, safety, pharmacokinetics, and efficacy of Esperoct® were evaluated in PTPs aged ≥12 years with severe hemophilia A; 175 received routine prophylaxis (50 IU/kg every 4 days) and 12 adults elected to be treated on-demand during the main phase.[2]

PROTECTION THAT KEEPS UP WITH THEM

Approved for prophylactic, on-demand, and perioperative management in children aged 0-<12 years[1]

One proven dose:	**65 IU/kg twice weekly** • No dose adjustment needed and related PK testing required[1,2]

- Because the clearance of FVIII products may be higher in children <12 years compared to adolescents/adults, higher and more frequent dosing may be required.[1]

Higher factor levels for your pediatric patients[a,b]

14.3
-hour mean half-life[1,12,c]

85% longer half-life compared with SHL rFVIII products[13]

~4%
mean trough levels maintained (n=54)[3,d]

Over 5 years of treatment

In a post hoc analysis, long-term prophylaxis (≥5 years) showed a stabilization in mean FVIII trough levels.[3,d]

[a]Compared with SHL products.[12]
[b]In a phase 3 study of children (aged <12 years) a single-dose PK comparison was performed in 27 children between previous SHL products and Esperoct® at the same administered dose prior to the start of routine prophylaxis. Half-life comparison is based upon the estimated half-life derived from a population-based model. During the main phase, 68 children received prophylaxis at an average dose of approximately 65 IU/kg twice weekly for 26 weeks.[12,13]
[c]Geometric mean terminal half-life in 23 children. The subjects were 12 children aged 0-5 years and 10 children aged 6-11 years. Estimated geometric terminal mean half-life was 14.7 hours in the younger cohort and 13.8 hours in the older cohort.[12,13]
[d]Post hoc analyses were performed on data from the pathfinder™ 5 trial of patients (aged <12) with severe hemophilia A. Exploratory descriptive analyses of the data were used to evaluate mean factor VIII trough levels which were assessed over time in 54 patients who received ≥5 years of twice-weekly prophylaxis. Limitations of the analyses include the exclusion of several trough-level data if believed that they were elevated due to dosing to treat a recent bleed.[3]

IMPORTANT SAFETY INFORMATION

Adverse Reactions

- The most frequently reported adverse reactions in clinical trials (≥1%) were rash, redness, itching (pruritus), and injection site reactions

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Long-term trial results confirm effective prophylaxis in children —for up to 5.4 years[14]

A lower overall median ABR in patients (aged 0 to <12 years) compared with the main phase was achieved[14,e]

ABR

0.8

Overall bleeds per year[f]
N=68

100% resolution of target joints[14,g]

Based on a post hoc analysis of patients who completed the entire trial, the proportion of patients who experienced no annual bleeding episodes more than doubled from year 1 to year 5[14,h]

[e]In a phase 3 multinational, open-label, single-arm, non-randomized, non-controlled trial of 68 previously treated male patients aged <12 years old with severe congenital hemophilia A, comprising a main phase and an extension phase.[13,14]
[f]Median annualized bleeding rate shown is from the main and extension phases of previously treated children with severe hemophilia A, who took Esperoct® 60 IU/kg (50-75 IU/kg) twice weekly for a median of 5 years.[14]
[g]A target joint was defined as a single joint with ≥3 bleeding episodes in 6 consecutive months. All baseline target joints reached the per-protocol definition of target joint resolution in slightly over 2 years of treatment with Esperoct®. Per protocol, a target joint was no longer considered a target joint if there were no bleeding episodes for 12 consecutive months. Twelve patients with 16 documented target joints at the baseline participated in main and extension phase of pathfinder™ 5 clinical trial.[14]
[h]Based on a post-hoc analysis of patients who completed the entire pathfinder™ 5 trial who took Esperoct® 60 IU/kg (50 IU/kg - 75 IU/kg) twice weekly for up to 5 years (n=63). Approximately 32% of the patients that participated in both the main and extension phases experienced no bleeding episodes during year 1, ~50% during year 2, <50% during year 3, 56% during year 4, and ~70% during year 5 had no annual bleeding episodes.[14]

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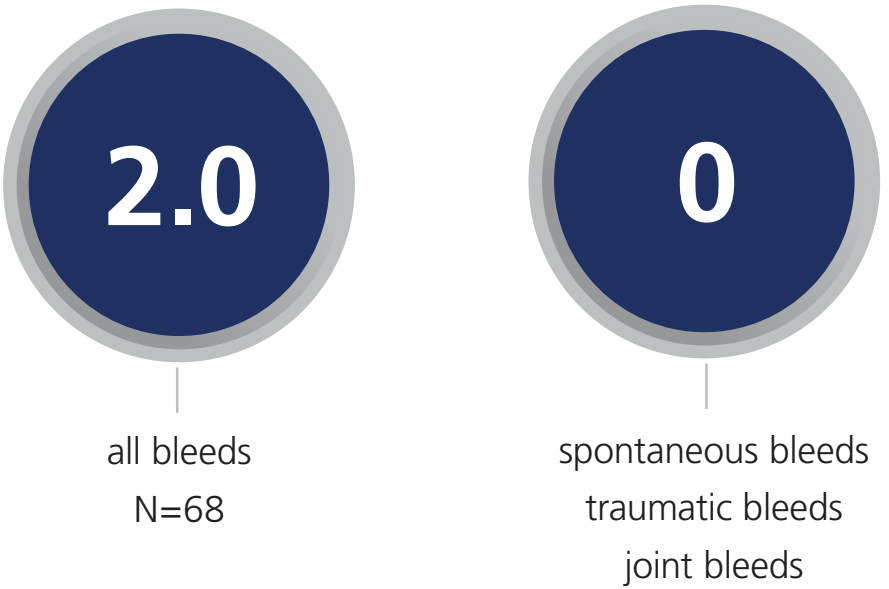
Keep them covered with a low median ABR in all children (aged 0 - <12 years)[1,a]



[a]In a phase 3 study of children (aged <12 years) a single-dose PK comparison was performed in 27 children between previous SHL products and Esperoct® at the same administered dose prior to the start of routine prophylaxis. Half-life comparison is based upon the estimated half-life derived from a population-based model. During the main phase, 68 children received prophylaxis at an average dose of approximately 65 IU/kg twice weekly for 26 weeks.[12,13]

PIVOTAL TRIAL MAIN PHASE DATA

COUNT ON A **PROVEN SAFETY PROFILE**

0 thrombotic events across 5 clinical trials in[1]

270 previously treated patients (PTPs) — over — **80,000** exposure days[1]

- Observed inhibitor development is consistent with the rate reported in epidemiologic studies (0.15 per 100 patient years)[15]
  - One PTP with an intron 22 inversion developed a FVIII inhibitor[1,2,a]
- No development of neutralizing anti-PEG antibodies nor hypersensitivity to PEG[1,b]

[a]An 18-year-old African-American male with an intron 22 inversion developed a low titer inhibitor after 93 Esperoct® exposure days that subsequently rose to 13.5 Bethesda units, prompting withdrawal from the study. There was no change in efficacy, and the inhibitor eventually went away on its own (without use of ITI).[2]
[b]Anti-PEG antibodies of no clinical consequence were detected in 45 subjects, 32 of whom had preexisting anti-PEG antibodies.[1]

IMPORTANT SAFETY INFORMATION

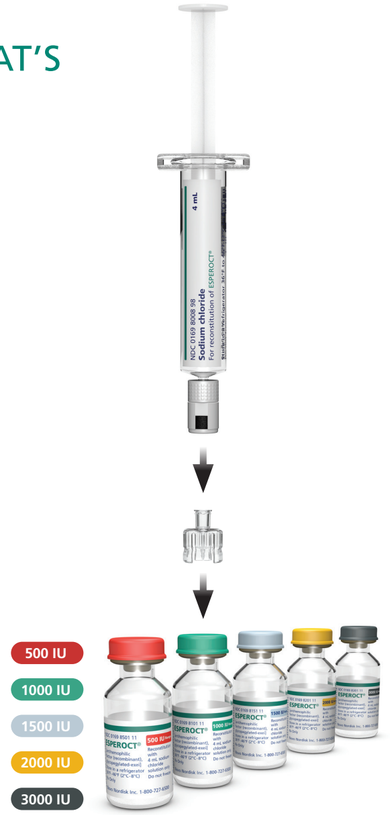
Contraindications

- Do not use in patients who have known hypersensitivity to Esperoct® or its components, including hamster proteins

Please see additional Important Safety Information throughout.
Please see accompanying Prescribing Information.

CHOOSE A PRODUCT THAT'S **READY WHEN THEY ARE**

Your patients can infuse in 2 minutes with MixPro®[1]



ATTACH

Prefilled diluent syringe contains 4 mL of diluent—works with any dose strength[1]

TWIST

Adapter connects the syringe and vial with a 25 µm inline particle filter[1]

MIX

After mixing, the reconstituted solution can be administered[1]

The **EHL** product with the **highest** storage temperature for the **longest** time[1,7-9]

Can be stored up to **86˚F** up to **12 months**

Can be stored from **86˚F - 104˚F** up to **3 months**

After reconstitution: Can be used up to **4 hours** at up to **86˚F**

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OUR **COMMITMENT TO THE ENVIRONMENT**

We not only aspire to be a respected leader in the healthcare industry, we also continuously strive to minimize the environmental impact of our activities.

As of 2020, all production facilities for Esperoct® will source 100% renewable power[16]

MEASURING **FACTOR VIII ACTIVITY**

Factor VIII activity assay results may be significantly affected by the type of aPTT reagent, which can result in over- or under-estimation of FVIII activity.

Esperoct® FVIII activity levels and inhibitor testing is available through the Novo Nordisk Lab Program, using validated assays in compliance with CAP/CLIA regulations.

To activate your Labcorp account and participate in the program, download and complete the form, then email it to **fixsupport@labcorp.com**.

Please see Prescribing Information for complete monitoring information.

Scan to start

IMPORTANT SAFETY INFORMATION

Adverse Reactions

- The most frequently reported adverse reactions in clinical trials (≥1%) were rash, redness, itching (pruritus), and injection site reactions

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HAVE A **QUESTION?**

Our Hemophilia Treatment Managers (HTMs) are ready to answer your questions and provide you with resources to help your practice and patients.

Scan to connect

Area for business card

REFERENCES: 1. Esperoct® [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; 2019. **2.** Giangrande P, Andreeva T, Chowdary P, et al. Clinical evaluation of glycoPEGylated recombinant FVIII: efficacy and safety in severe haemophilia A. *Thromb Haemost.* 2017;117(2):252-261. **3.** Tiede A, Hampton K, Jiménez-Yuste V, Young G, Benchikh El Fegoun S, Chowdry P. Post-hoc analysis on the long-term response to fixed-dose prophylaxis with N8-GP in patients with haemophilia A. *Haemophilia.* 2021;10.1111/hae.14409. **4.** Cafuir LA, Kempton CL. Current and emerging factor VIII replacement products for hemophilia A. *Ther Adv Hematol.* 2017;8(10):303-313. **5.** Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia.* 2020;26(suppl 6):1-158. **6.** Tiede A, Brand B, Fischer R, et al. Enhancing the pharmacokinetic properties of recombinant factor VIII: first-in-human trial of glycoPEGylated recombinant factor VIII in patients with hemophilia A. *J Thromb Haemost.* 2013;11(4):670-678. **7.** Eloctate® [package insert]. Bioverativ Therapeutics Inc.; 2020. **8.** Adynovate® [package insert]. Lexington, MA: Baxalta US Inc.; 2020. **9.** Jivi® [package insert]. Whippany, NJ: Bayer HealthCare LLC; 2018. **10.** Giangrande P, Abdul Karim F, Nemes L, et al. Long-term safety and efficacy of N8-GP in previously treated adults and adolescents with hemophilia A: final results from pathfinder2. *J Thromb Haemost.* 2020;18(suppl 1):5-14. **11.** Hampton K, Chowdary P, Dunkley S, et al. First report on the safety and efficacy of an extended half-life glycoPEGylated recombinant FVIII for major surgery in severe haemophilia A. *Haemophilia.* 2017;23(5):689-696. **12.** Data on file. Novo Nordisk Inc; Plainsboro, NJ. **13.** Meunier S, Alamelu J, Ehrenforth S, et al. Safety and efficacy of a glycoPEGylated rFVIII (turoctocog alpha pegol, N8-GP) in paediatric patients with severe haemophilia A. *Thromb Haemost.* 2017;117(9):1705-1713. **14.** Šaulytė Trakymiene S, Economou M, Kenet G, Landorph A, Shen C, Kearney S. Long-term safety and efficacy of N8-GP in previously treated pediatric patients with hemophilia A: final results from pathfinder5. *J Thromb Haemost.* 2020;18(suppl 1):15-25. **15.** Fischer K, Lassila R, Peyvandi F, et al. Inhibitor development in haemophilia according to concentrate four-year results from the European HAemophilia Safety Surveillance (EUHASS) project. *Thromb Haemost.* 2015;113(5):968-975. **16.** Novo Nordisk Annual Report, 2019. **17.** Data on file. Novo Nordisk Inc.; Plainsboro, NJ.

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FOR ADULT AND ADOLESCENT PATIENTS

MOVE BEYOND THE THRESHOLD[a]

Among EHL products, fewer Esperoct® prescriptions were switched to another product[17,b]

One proven starting dose:

50 IU/kg every 4 days[1]

- Ability to individualize to meet patient's needs[1]

High trough levels:

- ≥3% for the entire dosing interval[1,c]
- ≥5% for 90% of the dosing interval[1,d]
- ~5%, based on post hoc analysis of 6+ years treatment data[3,e]

Low median ABR:

- Pivotal trial main phase: 1.2 across all bleeds[2,f]
- Long-term trial: 0.8 across all bleeds[10,g]

[a]Of 1% trough levels for SHL products in adults and adolescents.[1,6]
[b]Based on data for Q2 2020-Q2 2021; accounts for net gains and losses of patients switching to and from extended half-life rFVIII available for at least one year.[17]
[c]In a phase 3, open-label study, safety, efficacy, and PK of Esperoct® were evaluated in PTPs aged >12 years with severe hemophilia A. Single-dose PK studies were performed in 42 adults after receiving Esperoct® 50 IU/kg; 175 PTPs received routine prophylaxis (50 IU/kg Q4D) for 76 weeks and 12 adults elected to be treated on-demand during the main phase. Mean trough levels for adolescents (12-<18 years) were 2.7 IU/dL.[1,2]
[d]Steady-state FVIII activity profiles were estimated using a one-compartment model with first-order elimination with PK parameters of clearance and volume of distribution.[1]
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[g]Median annualized bleeding rate shown is from the main and extension phases of the pivotal clinical trial of previously treated people aged ≥12 years with severe hemophilia A who received Esperoct® 50 IU/kg every 4 days, for up to 6.6 years.[10]

INDICATIONS AND USAGE

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IMPORTANT SAFETY INFORMATION

Contraindications

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Please see accompanying Prescribing Information.

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