Esperoct (antihemophilic factor [recombinant], glycopegylated-exei)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Esperoct
- **Generic name:** Antihemophilic Factor VIII (recombinant), glycopegylated-exei
- **Pharmacologic class:** Clotting factor
- **Strength and Formulation:** 500 IU, 1000 IU, 1500 IU, 2000 IU, 3000 IU; per vial; lyophilized powder for IV inj after reconstitution; preservative-free
- **Manufacturer:** Novo Nordisk
- **How supplied:** Single-dose vial—1(w. diluent + vial adapter)
- **Legal Classification:** Rx

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Esperoct

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Indication

- In adults and children with **hemophilia A** for:
  - On-demand treatment and control of bleeding episodes
  - Perioperative management of bleeding
  - Routine prophylaxis to reduce the frequency of bleeding episodes

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Limitation of Use

- Not for treatment of von Willebrand disease

Dosage and Administration

- Individualize; infuse slowly over 2mins
- **To control bleeding episodes:**
  - **<12yrs:** 65 IU/kg; (Minor): one dose is sufficient; (Moderate): an additional dose may be given after 24hrs; (Major): additional dose(s) may be given every 24hrs
  - **≥12yrs:** (Minor): 40 IU/kg; one dose should be sufficient; (Moderate): 40 IU/kg; an additional dose may be given after 24hrs; (Major): 50 IU/kg; additional dose(s) may be given every 24hrs

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Dosage and Administration

- **Perioperative:**
  - **<12yrs:** 65 IU/kg; (Minor): additional dose(s) can be given after 24hrs; (Major): additional dose(s) can be given approx. every 24hrs for the first week, then approx. every 48hrs until wound has healed
  - **≥12yrs:** 50 IU/kg; (Minor): additional dose(s) can be given after 24hrs; (Major): additional dose(s) can be given approx. every 24hrs for the first week, then approx. every 48hrs until wound has healed

Dosage and Administration

- **Routine prophylaxis:**
  - **<12yrs:** 65 IU/kg twice weekly; then may adjust individually based on bleeding episodes
  - **≥12yrs:** initially 50 IU/kg every 4 days; then may adjust individually based on bleeding episodes

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Dosage and Administration

- To achieve a specific target Factor VIII activity level, calculate dose using:

Dosage Required (IU) = Body Weight (kg) × Desired Factor VIII Increase (IU/dL or % of Normal) × 0.5

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Considerations for Special Populations

- **Pregnancy:** no data to determine drug-associated risk
- **Nursing mothers**: no information regarding presence in human milk
- **Pediatric**: because clearance (per kg body weight) is higher in children (<12 years), a higher dose and more frequent dosing may be needed in this population
- **Geriatric:** studies did not include sufficient numbers to determine whether response different from younger patients

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Contraindications

- Hamster protein sensitivity

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Warnings/Precautions

- Discontinue if hypersensitivity reactions occur
- Monitor for development of Factor VIII inhibitors
- Perform a Bethesda assay if expected plasma FVIII levels not attained or if bleeding uncontrolled with recommended dose

Adverse Reactions

- **Most frequent (incidence >1%)**: rash, redness, itching, injection site reactions
- **Others**: antibody formation

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Mechanism of Action

- Esperoct, a glycopegylated form of recombinant antihemophilic factor, temporarily replaces the missing coagulation Factor VIII needed for effective hemostasis in congenital hemophilia A patients
- The Factor VIII in Esperoct is conjugated to a 40-kDa polyethylene glycol molecule which increases the half-life and decreases the clearance compared to the non-pegylated molecule

Pharmacokinetics

- Half-life following single dose of 50 IU/kg
  - 1 to <6 years old: 14.7 hours
  - 6 to <12 years old: 13.8 hours
  - 12 to <18 years old: 17.4 hours
  - ≥18 years old: 21.7 hours

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Clinical Trials

- Safety and efficacy evaluated in 5 open-label trials in male patients with severe hemophilia A (<1% endogenous Factor VIII activity)
- All patients were previously treated, defined as having received other Factor VIII products for ≥150 exposure days for adolescents and adults, and ≥50 exposure days for pediatric subjects

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Clinical Trials

On-demand Treatment and Control of Bleeding Episodes

- 1506 bleeds reported in 171 of 254 patients across the completed clinical trials
- Of the 1407 mild and moderate bleeding episodes in all patients in the adolescent/adult study, median dose used was 42 IU/kg
- For patients who were on the on-demand arm, median initial dose was 28 IU/kg and 88.4% of the bleeds were treated successfully with a single dose

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Clinical Trials

- In patients receiving routine prophylaxis, median initial dose was 52 IU/kg, and 76.4% of the bleeds were successfully treated with a single dose
- Of the 15 severe bleeds, 12 (80%) required more than 1 dose with total median dose of 111 IU/kg
- In the pediatric study, 70 mild/moderate bleeds in children <12 years receiving routine prophylaxis were treated with median initial dose of 64 IU/kg per injection, with 63% treated with a single injection
- When needed, additional median doses of 62 IU/kg were used at approximately 24 hour intervals
- Median total dose was 70 IU/kg per bleed

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Clinical Trials

Perioperative Management

- Included 45 major surgical procedures performed in 33 adolescent and adult patients
- Clinical evaluation of hemostatic response during major surgery was assessed using a 4-point scale of excellent, good, moderate, or none
- Hemostatic effect was rated as “excellent” or “good” in 43 of 45 surgeries (95.6%), while the effect was rated as “moderate” in 2 surgeries (4.4%)
- No surgery had an outcome rated as “none” or “missing”

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Clinical Trials

- Median preoperative dose for adults and adolescents undergoing major surgeries was 52 IU/kg, and median total dose was 702 IU/kg
- During postop days 1-6, median dose was 32 IU/kg at approximately 24 hour intervals
- During postop days 7-14, median dose was 36 IU/kg at approximately 28 hour intervals
- Number of doses and duration of treatment varied by procedure

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Clinical Trials

Routine Prophylaxis in Adolescents/Adults

- Routine prophylaxis with every 4 day dosing was demonstrated for the adult/adolescent population
- During Main Phase of adolescent/adult trial, 186 patients had a total of 159 exposure years
- Median annualized bleeding rate (ABR) for treated bleeds in adults and adolescents treated every 4 days was 1.2 (IQR: 0.0:4.3), and mean ABR was 3.0 (SD: 4.7)
- When including all bleeds (treated and non-treated), median ABR was 1.2 (IQR: 0.0; 4.7) and mean ABR was 3.3 (SD: 4.9)

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Clinical Trials

Routine Prophylaxis in Children <12 Years Old

- 68 children received prophylactic treatment at an average dose of approximately 65 IU/kg twice weekly
- The prophylactic effect was demonstrated with a median ABR rate of 2.0 (IQR: 0.0; 2.8) and 2.0 (IQR: 0.0; 4.2) for treated bleeds and all bleeds, respectively
- Mean ABR (SD) for treated bleeds and all bleeds were 3.1 (7.1) and 4.4 (8.7), respectively
- Of the 68 children, 22 (32%) did not experience any bleeding episodes and 29 (43%) did not experience any bleeding episodes that required treatment during the Main Phase of the trial
- Of the 13 patients with 17 documented target joints at baseline, 10 patients (77%) and 14 target joints (82%) did not have any bleeds during the Main Phase of the trial

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New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/esperoct/