This Abbreviated Prescribing Information (API) reflects SmPC version valid since EMA approval in June 2019 updated in October 2022

Were changes done to this API versus previous version as a result of any SmPC change?

YES ☒ NO ☐

Prepared and updated by Global Medical Affairs based on EU SmPC
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Abbreviated prescribing information Esperoct®

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the full Summary of Product Characteristics for how to report adverse reactions. Consult Summary of Product Characteristics before prescribing.

Presentation: Esperoct® 500 IU powder and solvent for solution for injection, Esperoct® 1000 IU powder and solvent for solution for injection, Esperoct®1500 IU powder and solvent for solution for injection, Esperoct® 2000 IU powder and solvent for solution for injection, Esperoct® 3000 IU powder and solvent for solution for injection. **Composition:** Esperoct® is a recombinant human factor VIII, produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology, covalently conjugated to a 40 kDa polyethylene-glycol (PEG). No additives of human or animal origin are used in the cell culture, purification, conjugation or formulation of Esperoct®.

500 IU turoctocog alfa pegol (After reconstitution, approximately 125 IU /1 mL), 1000 IU turoctocog alfa pegol (after reconstitution approximately 250 IU /1 mL). 1500 IU turoctocog alfa pegol (after reconstitution approximately 375 IU /1 mL). 2000 IU turoctocog alfa pegol (after reconstitution approximately 500 IU /1 mL).

3000 IU turoctocog alfa pegol (after reconstitution approximately 750 IU /1 mL).

The medicinal product contains 30.5 mg sodium per reconstituted vial, equivalent to 1.5% of the WHO recommended maximum daily intake for an adult.

List of excipients: Powder: Sodium chloride, L-Histidine, Sucrose, Polysorbate 80, L-Methionine, Calcium chloride dihydrate, Sodium hydroxide (for pH adjustment), Hydrochloric acid (for pH adjustment)

Solvent: Sodium chloride, Water for injections

Indications: Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia A (congenital factor VIII deficiency).

Posology and mode of administration:

Previously untreated patients: The safety and efficacy of Esperoct® in previously untreated patients have not yet been established.

Paediatric population: The dose in adolescents (12 years and above) is the same as for adults. In children below 12 years long-term safety has not been established.

Treatment monitoring :

The factor VIII activity of Esperoct® can be measured using the conventional factor VIII assays, the chromogenic assay and the one-stage assay.

When using a one-stage clotting assays some silica-based reagents should be avoided as they cause underestimation.

Posology: The dose, dosing interval and duration of the substitution therapy depend on the severity of the factor VIII deficiency, on the location and extent of the bleeding, on the targeted factor VIII activity level and the patient's clinical condition.

Prophylaxis: The recommended dose is 50 IU of Esperoct® per kg body weight every 4 days. Adjustments of doses and administration intervals may be considered based on achieved factor VIII levels and individual bleeding tendency.

On-demand treatment and treatment of bleeding episodes:

The required dose is determined using the following formula:

Required units (IU) = body weight (kg) x desired factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL).

Guidance for the dosing of Esperoct®, according to degree of haemorrhage

Mild: Early haemarthrosis, mild muscle bleeding or mild oral bleeding: Factor VIII level required (IU/dL or % of normal): 20-40, every 12-24 hours until the bleeding is resolved

Moderate: More extensive haemarthrosis, muscle bleeding, haematoma: Factor VIII level required (IU/dL or % of normal): 30-60, every 12-24 hours until the bleeding is resolved

Severe or life-threatening haemorrhages: Factor VIII level required (IU/dL or % of normal): 60-100, every 8-24 hours until the threat is resolved.

Perioperative management
The dose level and dosing intervals for surgery depend on the procedure and local practice. A maximum single dose of Esperoct at 75 IU/kg and a maximum total dose of 200 IU/kg/24 hours may be administered.
Minor surgery, Including tooth extraction. Factor VIII level required (IU/dL or % of normal): 30-60 IU/kg, dose within 1 hour before surgery, single dose or repeat injection /24 hours until healing achieved.
Major surgery: 80-100 IU/kg (pre- and post-operative), dose within 1 hour before surgery to achieve factor VIII activity within the target range, repeat every 8 to 24 hours to maintain factor VIII activity within the target range and as necessary until adequate wound healing is achieved. Consider continuing therapy for another 7 days to maintain a factor VIII activity of 30% to 60% (IU/dL).
The frequency of doses and duration of therapy should always be individually adjusted based on individual clinical response.

Contraindications: Hypersensitivity to the active substance, or to any of the excipients or to hamster protein.

Interaction with other medicinal products and other forms of interaction

No interactions of human coagulation factor VIII (rDNA) with other medicinal products have been reported.

Special warnings and precautions for use
Traceability
The name and the batch number of the administered product should be clearly recorded.
Hypersensitivity
Allergic type hypersensitivity reactions are possible with Esperoct®. If symptoms of hypersensitivity occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician.
Inhibitors
If the expected factor VIII activity plasma levels are not attained, or if bleeding is not controlled with an appropriate dose, testing for factor VIII inhibitor presence should be performed. In patients with high levels of inhibitor, factor VIII therapy may not be effective and other therapeutic options should be considered.
Decreased factor VIII activity in previously treated patients
From post marketing reports, a decreased factor VIII activity in the absence of detectable factor VIII inhibitors has been reported in previously treated patients. The decreased factor VIII activity was observed at time of switching to Esperoct and may, in some cases, have been associated with anti-PEG antibodies. Appropriate determination of factor VIII activity upon switching should be considered.

Undesirable effects Common (≥ 1/100 to < 1/10): Rash, Erythema, Pruritus, Injection site reactions; Uncommon (≥ 1/1,000 to < 1/100): Factor VIII inhibition (in previously treated patients (PTPs)), hypersensitivity; Unknown (based on post marketing reports): coagulation factor VIII level decreased
Factor VIII inhibitors: One confirmed case of factor VIII inhibitor occurred in an 18-year-old previously treated patient on prophylactic treatment with Esperoct® factor VIII products.

Anti-PEG antibodies: During the clinical trial programme, thirty-two patients had pre-existing anti-PEG antibodies before administration of Esperoct. No correlation with adverse events could be established.

From post-marketing reporting, occurrence of anti-PEG-antibodies has also been observed at time of switching to Esperoct. In some patients anti-PEG antibodies may have been associated with lower than expected level of FVIII activity.

Overdose
No symptoms of overdose with recombinant coagulation factor VIII have been reported.

Shelf life:
Unopened vial(before reconstitution): 30 months when stored in a refrigerator (2°C – 8°C)
During the shelf life which the product may be kept:

- at room temperature (≤ 30°C) for a single period no longer than 12 months
- Or, above room temperature (>30°C up to 40°C) for a single period no longer than 3 months

  Once the product has been stored outside of the refrigerator, the product must not be returned for storage in the refrigerator. Record the beginning of storage outside refrigerator and the storage temperature in the space provided in the carton.

After reconstitution: Chemical and physical in-use stability have been demonstrated for 24 hours when stored in a refrigerator (2°C - 8°C) or 4 hours at ≤ 30°C, or 1 hour between >30°C up to 40°C, only if the product was stored above room temperature (>30°C up to 40°C) before reconstitution for no longer than 3 months.

Method of Administration:
Esperoct® should be administered by intravenous injection (over approximately 2 minutes) after reconstitution of the powder with 4 mL supplied solvent (sodium chloride 9 mg/mL (0.9%) solution for injection).

Legal category: Prescription-only medicine (POM). **Authorisation holder:** Novo Nordisk A/S, Novo Alle, Bagsvaerd, Denmark.
Date of last revision: December 2022
For more detailed information please consult the EMEA product information.

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