EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Esperoct 500 I.U
Esperoct 1000 I.U

Date: August 2024

Assessment report

Unit: Technical Assessment Unit

Esperoct

Administrative information:

Trade name of the medicinal product:	Esperoct
INN (or common name) of the active substance(s):	Turoctocog alfa pegol 500 I.U. and 1000 I.U
Manufacturer of the finished product	Novo Nordik A/S, Hagedornsvej 1, DK-2820 Gentofte-Denmark
Marketing Authorization holder	Novo Nordisk A/S, Novo Alle, DK-2880 Bagsvaerd- Denmark
Applied Indication(s):	treatment and prophylaxis of haemorrhages in previously treated patients with haemophilia A (congenital factor VIII deficiency)
Pharmaceutical form(s) and strength(s):	Powder and Solvent for Solution for I.V. injection **Strengths:** 500IU and 1000 IU
Route of administration	I.V
Approved pack	Each carton box contains: - Powder vial: 5 ml clear colorless glass vial (Eur,JP, USP type I) closed with a grey chlorobutyl B2coated rubber stopper, an aluminum seal with a plastic snap-off cap - Sterile vial adaptor: the vial adapter is a sterile,disposable device packed in a blister package. - Solvent pre-filled syringe: Clear colorless borosilicate glass syringe (Eur, JP, USP Type I) of 4 ml with a threaded bromobutyl rubber plunger, a tip cap made of bromobutyl rubber and plunger rod made of polypropylene.

List of abbreviations

DS	Drug substance
FP	Frug Product
FVIII	Factor VIII

I.U	international unit
PEG	polyethylene glycol
rFVIII	recombinant factor VIII

Dossier initial submission and evaluation process.

- The product was submitted for registration via reliance model level 2
- The dossier evaluation by the registration administration units was started on 9.10.2022 after providing all the required documents according to the "Checklist for documents of new biological products registration file".

1. **'General introduction about the product including brief description of the AI, its mode of action and indications:**

- FP is presented as a lyophilized powder to be reconstituted with the supplied solvent (sodium chloride 9 mg/mL (0.9%) solution for injection) before administration. The finished product is presented in a 5 mL type I glass vial in two different strengths: 500 IU/vial, 1000 IU/vial.

-Turoctocog alfa pegol is a recombinant human factor VIII (FVIII) product, produced In Chinese Hamster Ovary (CHO) cells, with a specific glycoPEGylation on the O-linked glycan (primarily on Ser750 in the 21 amino acid B-domain). The turoctocog alfa pegol molecule consists of a heavy chain of 87 kDa (excluding post-translational modifications and PEG moiety) and a light chain of 79 kDa (excluding post-translational modifications) held together by noncovalent interactions. Post-translational modifications of turoctocog alfa intermediate include disulphide bridges, tyrosine sulphations and glycosylations.

-Turoctocog alfa pegol is produced by glycoPEGylation of turoctocog alfa intermediate (truncated recombinant human FVIII containing 21 amino acids of the native B- domain). The size of the polyethylene glycol (PEG) attached to the O-linked glycan is 40kDa.

- Esperoct is used in treatment and prophylaxis of haemorrhages in previously treated patients with haemophilia A (congenital factor VIII disorder).

- Esperoct does not contain any pharmacologically active quantities of the von Willebrand factor and is therefore not suitable for the treatment of von willebrand's disease.

2. Quality aspects:

Manufacturer(s)

Active substance:

- Turoctocog alfa pegol drug substance (DS) is manufactured, at Novo Nordisk USBio Production Inc. 9 Technology Drive West Lebanon NH 03784 USA.

The finished product is manufactured at: Novo Nordik A/S, Hagedornsvej 1, DK-2820 Gentofte-Denmark

-All manufacturers are authorized according to current GMP regulations.

Stability

Active substance:

- **Storage Conditions of the active substance**: -80°C
- **shelf life of the active substance** is 36 months.

Drug product:

- **Storage Conditions of the finished product** (2 - 8 °C). Do not freeze
- **Shelf life of the finished product is** 36 months if stored in the refrigerator (2-8°C)

-During its shelf life, it can be stored for no longer than 12 months at room temp (≤ 30°C) or no longer than 3 months above room temp (> 30 °C- 40 °C).

• **Adventitious agents:**

-Overall, the risk of contamination of turoctocog alfa pegol with adventitious agents is considered very low.

-No animal- or human-derived raw materials are used for manufacture of turoctocog alfa pegol and raw materials and hence the viral and risk for TSE is deemed negligible.

3. Non-clinical and clinical aspects:

The submitted non clinical and clinical program adequately characterizes the efficacy and safety of turoctocog alfa pegol to support chronic use in patients with hemophilia A.

- **General Conclusion and Recommendations if any:**

  Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/esperoct-epar-public-assessment-report_en.pdf