



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993-0002

MEMORANDUM

Date: February 20, 2019

To: Biologics License Application: STN# BLA 125671/0

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Through: Muhammad Shahabuddin, Ph.D.
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Applicant: Novo Nordisk

Product: Antihemophilic Factor (Recombinant), GlycoPEGylated

Submitted: February 27, 2018

Subject: Review of Analytical Methods used for determining the process-related impurities in turoctocog alfa pegol (b) (4)

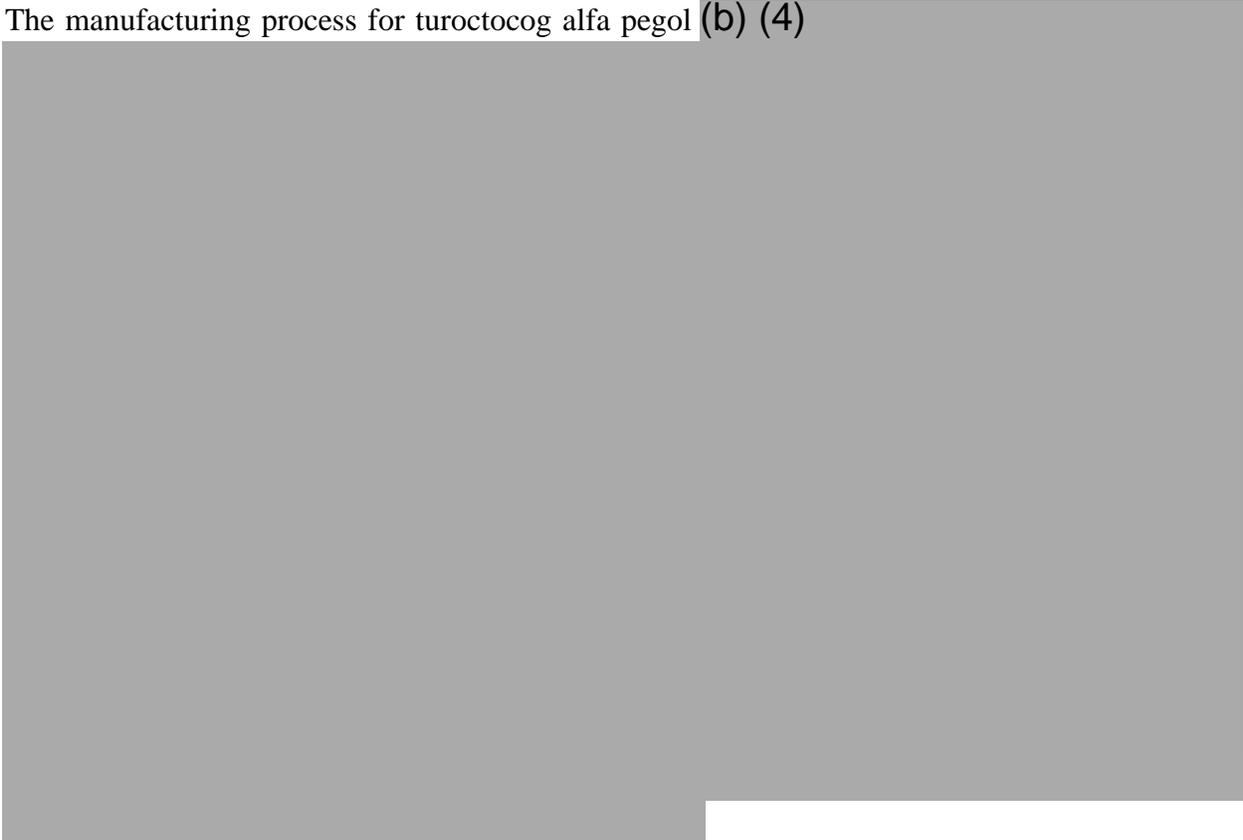
Recommendation: Approval

1. [Summary of Review](#)
2. [Background](#)
3. [Submitted Information Reviewed](#)
 - 3.1 (b) (4)

Background

Hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. The human Factor VIII consists of 2332 amino acids forming six domains described as A1-A2-B-A3-C1-C2. During secretion, the single chain form is cleaved by furin (a transmembrane protease) into a heavy chain and a light chain held together by metal ions. FVIII is converted into FVIIIa by thrombin cleavage at three sites, resulting in a three-chain molecule without the B-domain. Intensive investigations have shown that the B-domain may not be needed for FVIII biological function. Turoctocog alfa is a recombinant factor VIII (rFVIII) with a (b) (4) truncated B-domain ((b) (4) of the naturally occurring B-domain linked to (b) (4) of the B-domain) that has been approved for hemophilia A treatment. Turoctocog alfa pegol is a glycoPEGylated form of turoctocog alfa that has an extended half-life allowing for less frequent dosing to reduce treatment burden.

The manufacturing process for turoctocog alfa pegol (b) (4)



Submitted Information Reviewed

This is an electronic submission. Information submitted and reviewed includes:

- (1). 125671/0

3.2.S.4.2 – Analytical Procedures

- (b) (4) [Redacted]

(2). 125671/0

3.2.S.4.3 – Validation of Analytical Procedures

- (b) (4) [Redacted]

(3). 125671/0.22

1.11.1. Quality Information Amendment

- Response to FDA CMC IR dated August 1, 2018
- SOP Y9-442 turotocog alfa HCP (b) (4)

Review

1. (b) (4) [Redacted]

[Redacted]

14 pages determined to be not releasable: (b)(4)