



## 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

**From:** Jing Lin, Ph.D.  
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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

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- 3.1 (b) (4)

3.2 (b) (4)

### Summary of Review

The original Biologics License Application (BLA) STN# 125671/0 for turoctocog alfa pegol, a purified recombinant human antihemophilic factor VIII (rFVIII) with a glycoPEGylation, was submitted by Novo Nordisk Inc. on Feb 27, 2018 for approval to use in adults and children with hemophilia A. This is Primary Review Memo, covering the following analytical methods and their validations:

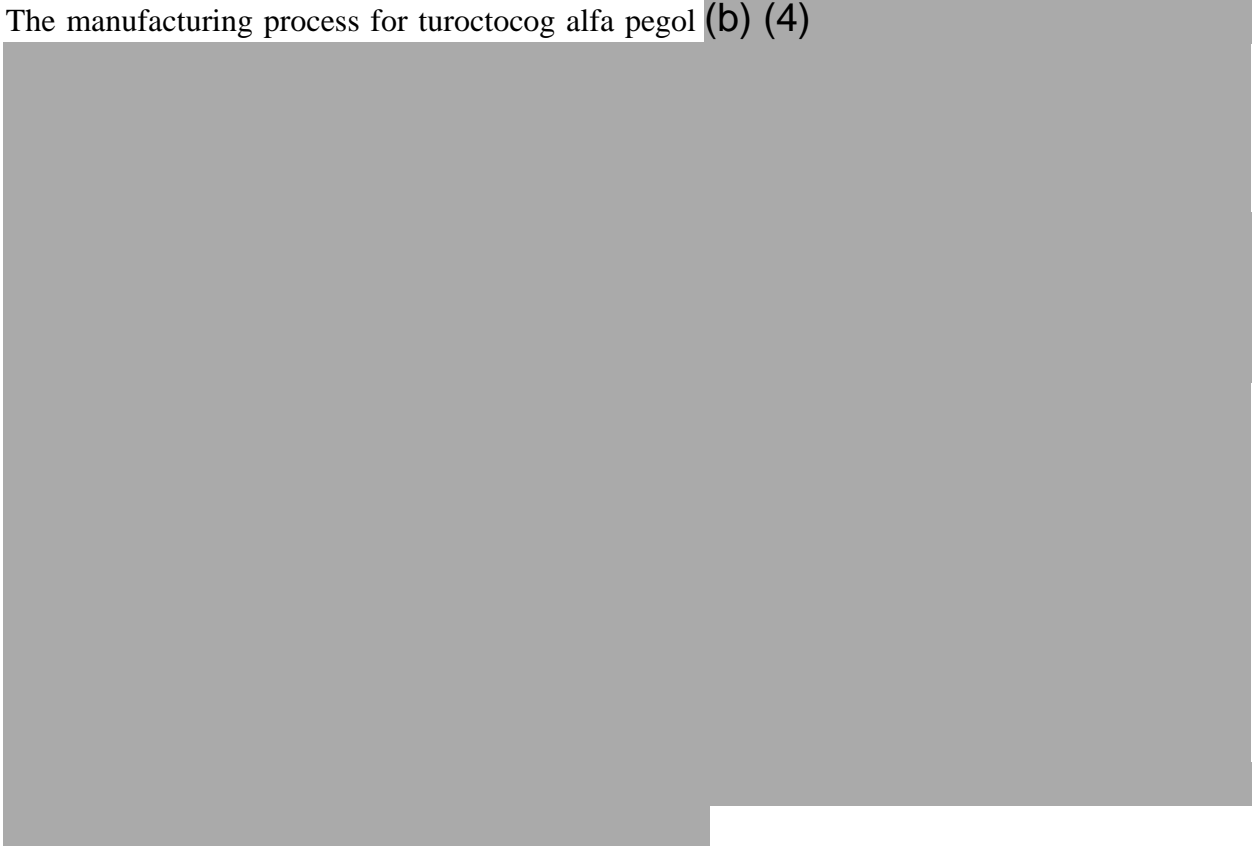
(b) (4)

Based on the review of the original submissions and amendments, the assays listed above are approvable for use in quality control testing for turoctocog alfa pegol (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]

