Our STN: BL 125671/0

BLA APPROVAL
February 19, 2019

Novo Nordisk, Inc.
Attention: Barbara Davies
P.O. Box 846
Plainsboro, NJ 08536

Dear Ms. Davies:

Please refer to your Biologics License Application (BLA) submitted February 27, 2018, received February 27, 2018, under section 351(a) of the Public Health Service Act (PHS Act) for Antihemophilic Factor (Recombinant), GlycoPEGylated-exei.

LICENSING

We have approved your BLA for Antihemophilic Factor (Recombinant), GlycoPEGylated-exei effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Antihemophilic Factor (Recombinant), GlycoPEGylated-exei under your existing Department of Health and Human Services U.S. License No. 1261. Antihemophilic Factor (Recombinant), GlycoPEGylated-exei is indicated for use in adults and children with hemophilia A for: (1) on-demand treatment and control of bleeding episodes, (2) perioperative management of bleeding, and (3) routine prophylaxis to reduce the frequency of bleeding episodes.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT01205724, NCT01480180, NCT01489111, NCT01731600, NCT02137850, and NCT02920398.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Antihemophilic Factor (Recombinant), GlycoPEGylated-exei drug substance at your Novo Nordisk (b) (4) , facility in (b) (4) The final lyophilized drug product will be manufactured at your Novo Nordisk A/S facility in (b) (4) , and labeled and packaged at your Novo Nordisk A/S facility in (b) (4) The diluent, 0.9% sodium chloride solution, will be manufactured at (b) (4)

You may label your product with the proprietary name ESPEROCT and market it in single-dose vials containing nominally 500 international units (IU), 1000 IU, 1500 IU, 2000 IU, or 3000 IU of Factor VIII potency per vial.

We did not refer your application to the Blood Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for Antihemophilic Factor (Recombinant), GlycoPEGylated-exei shall be 30 months from the date of manufacture when stored at +5 °C ± 3 °C. During the dating period, the drug product may be stored at temperatures at or below +30 °C for a single period of up to 12 months. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) when stored at -(b) (4) The expiration date for the packaged product, Antihemophilic Factor (Recombinant), GlycoPEGylated-exei plus diluent, 0.9% sodium chloride solution (supplied in a pre-filled syringe), shall be dependent on the shortest expiration date of any component.

FDA LOT RELEASE

You are not currently required to submit samples or protocols of future lots of Antihemophilic Factor (Recombinant), GlycoPEGylated-exei to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2(a). We will continue to monitor compliance with 21 CFR 610.1 requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of Antihemophilic Factor (Recombinant), GlycoPEGylated-exei, or in the manufacturing facilities.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft package insert labeling submitted under amendment 62, dated February 11, 2019; the draft package labeling submitted under amendment 58, dated January 17, 2019; and draft container labeling submitted under amendment 38, dated November 12, 2018.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed container labels that are identical to the container labels submitted on November 12, 2018, and package labels that are identical to the package labels submitted on January 17, 2019, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD*

Specifications at https://www.fda.gov/downloads/drugs/guidancecompliance regulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA 125671/0 at the time of use (prior to marketing) and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports* at https://www.fda.gov/ downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm458559.pdf and FDA's Adverse Event reporting System website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have fulfilled the pediatric study requirement for all relevant pediatric age groups for this application.

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biological products qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST-APPROVAL FEEDBACK MEETING

New biological products qualify for a post-approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Wilson W. Bryan, MD
Director
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research