



Our STN: BL 125641/0

BLA APPROVAL
April 1, 2020

Laboratoire Francais du Fractionnement
et des Biotechnologies SA (LFB S.A.)
Attention: Fernanda Giupponi
LFB USA, Inc.
175 Crossing Boulevard
Framingham, MA 01702

Dear Ms. Giupponi:

Please refer to your Biologics License Application (BLA) submitted and received October 13, 2016, under section 351(a) of the Public Health Service Act (PHS Act) for coagulation factor VIIa (recombinant)-jncw.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2061 to Laboratoire Francais du Fractionnement et des Biotechnologies S.A. (LFB S.A.), France, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product coagulation factor VIIa (recombinant)-jncw, which is indicated for treatment and control of bleeding episodes occurring in adults and adolescents (12 years of age and older) with hemophilia A or B with inhibitors.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT01708564, NCT02020369, NCT02448680, and NCT02548143.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture coagulation factor VIIa (recombinant)-jncw drug substance at (b) (4)

The final formulated product will be manufactured and filled at (b) (4), labeled and packaged at (b) (4)

(b) (4) . The diluent Water for Injection will be manufactured at (b) (4)

You may label your product with the proprietary name SEVENFACT and market it in single-dose vials containing 1 or 5 mg coagulation factor VIIa (recombinant)-jncw.

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 coagulation factor VIIa (recombinant)-jncw shall be 48 months from the date of manufacture when stored at 2°C to 30°C. 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). The expiration date for the packaged product, coagulation factor VIIa (recombinant)-jncw plus diluent, water, 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 coagulation factor VIIa (recombinant)-jncw 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 coagulation factor VIIa (recombinant)-jncw, 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, and the draft carton and container labeling, submitted on March 31, 2020.

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 package and container labels that are identical to the package and container labels submitted on March 31, 2020, 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 125641/0 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 are deferring submission of your pediatric study until July 10, 2020, because the product is ready for approval for use in adults and adolescents, and the pediatric study has not been completed.

Your deferred pediatric study required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) is a required postmarketing study. The status of this postmarketing study must be reported according to 21 CFR 601.28 and section 505B(a)(4)(C) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. This required study is listed below:

1. Deferred pediatric study under PREA for “A phase III Study on the Safety, Pharmacokinetics, and Efficacy of Coagulation Factor VIIa (Recombinant) in Congenital Hemophilia A or B Patients from birth to <12 years old with Inhibitors to Factor VIII or IX.”

Final Protocol Submission: Completed

Study Completion Date: Completed

Final Report Submission: July 10, 2020

Submit final study reports to this BLA, STN BL 125641/0. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated as:

- **Required Pediatric Assessment**

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your commitment as described in your amendment, submitted and received March 23, 2020, as outlined below:

2. Laboratoire Francais du Fractionnement et des Biotechnologies SA (LFB S.A.) commits to complete Performance Qualification (PQ) (b) (4) studies for the following:

(b) (4)

(b) (4)

The PQ final study reports will be submitted for CBER review as a PMC-Final Study Report by October 10, 2020.

Final Report Submission: October 10, 2020

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN BL 125641/0. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

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,

Mary A. Malarkey
Director
Office of Compliance and
Biologics Quality
Center for Biologics
Evaluation and Research

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