Our STN: BL 125612/67

SUPPLEMENT APPROVAL
POSTMARKETING REQUIREMENT
FULFILLED
December 23, 2020

Octapharma Pharmazeutika Produktionsges.m.b.H.
Attention: Stanley Ammons
Octapharma USA, Inc.
117 West Century Road
Paramus, NJ 07652

Dear Mr. Ammons:

We have approved your request submitted and received on June 26, 2020, to supplement your Biologics License Application (BLA) under section 351(a) of the Public Health Service Act for Fibrinogen (Human) [Fibryga®] for the following:

1. to submit the final study report for Postmarketing Requirement (PMR) #1 noted in the approval letter for STN BL 125612/0 dated June 7, 2017 and

2. to expand the indication for on-demand treatment of acute bleeding episodes to pediatric patients <12 years of age with congenital fibrinogen deficiency.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: 02267226 and 02408484.

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 21, dated December 23, 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.

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)).

Please submit an amendment to all pending supplemental applications for this BLA that include revised labeling incorporating a revised content of labeling that includes these changes.

FULFILLED POSTMARKETING PEDIATRIC REQUIREMENT

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.

This submission fulfills your PMR #1 identified in the June 7, 2017, approval letter for BLA STN BL 125612/0 for Fibrinogen (Human) [Fibryga®]. The requirement addressed in this submission is as follows:

PMR #1: Deferred pediatric study under PREA for the treatment of acute bleeding in pediatric patients ages < 12 years of age with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Final Protocol Submission: September 28, 2015

Study Completion Date: December 31, 2020

Final Report Submission: June 30, 2021

We note that you have fulfilled the pediatric study requirement for all relevant pediatric age groups to include children <12 years of age for this application.

RELEASE FROM POSTMARKETING REQUIREMENT UNDER SECTION 505(o)

We have received your submission on June 26, 2020, reporting on the following postmarketing requirement (PMR) identified in the June 7, 2017, approval letter:

STN: BL 125612/0

PMR #2: A prospective observational study of patients ≥12 years of age with congenital afibrinogenemia and hypofibrinogenemia treated with FIBRYNA for at least 10 major bleeding events to further characterize the risk of thromboembolic events following FIBRYNA treatment.

Final Protocol Submission: September 30, 2017

Study Completion Date: March 31, 2024

Final Report Submission: June 30, 2024

We have completed the review of your submission and conclude that you are released from the above PMR because you will instead conduct a study in children and adults with congenital afibrinogenemia and hypofibrinogenemia treated with FIBRYGA. The above PMR is now considered closed and will be replaced by the new PMR described below.

NEW POSTMARKETING REQUIREMENT UNDER SECTION 505(o)

Section 505(o) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of thromboembolic events in children and adults following Fibryga treatment.

Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following study:

1. A prospective observational study in children and adults with congenital afibrinogenemia and hypofibrinogenemia treated with FIBRYGA for at least 10 major bleeding events to further characterize the risk of thromboembolic events following FIBRYGA treatment.

We acknowledge the timetable you submitted on December 4, 2020, which states that you will conduct this study, according to the following schedule:

Final Protocol Submission: January 15, 2021

Study Completion Date: December 31, 2027

Final Report Submission: June 30, 2028

Please submit the protocol to your IND 14777, with a cross-reference letter to BLA STN BL 125612/0 explaining that this protocol was submitted to the IND. Please refer to the sequential number for each study trial and the submission number as shown in this letter.

Please submit final study reports to the BLA. If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement to BLA STN BL 125612/0. For administrative purposes, all submissions related to this postmarketing study required under section 505(o) must be submitted to this BLA and be clearly designated as:

- **Required Postmarketing Correspondence under Section 505(o)**
- **Required Postmarketing Final Report under Section 505(o)**

- **Supplement contains Required Postmarketing Final Report under Section 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. 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.

You must describe the status in an annual report on postmarketing studies for this product. 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 the approval of BLA 125612/0 until all requirements and commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will consider the submission of your annual report under section 506B of the FDCA and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in section 505(o) and 21 CFR 601.70. We remind you that to comply with section 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

Tejashri Purohit-Sheth, MD
Director
Division of Clinical Evaluation and
Pharmacology/Toxicology
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research