



U.S. FOOD & DRUG
ADMINISTRATION

Memorandum

DATE July 06, 2023

FROM Triet M. Tran, PharmD, Consumer Safety Officer
Bioresearch Monitoring Branch (BMB)
Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)
Telephone: 240-425-3201

THROUGH Dennis T. Cato, Branch Chief, BMB

THROUGH Carrie Mampilly, MPH, Division Director, DIS

TO Ze Peng, PhD, Chair, STN 125776/0
Karl Kasamon, MD, Clinical Reviewer
Eden Chane, MS, RPM

SUBJECT Bioresearch Monitoring Final Review Memo
SPONSOR Octapharma Pharmazeutika Produktionsges.m.b.H
PRODUCT OCTAPLEX (Prothrombin Complex Concentrate (Human))
BLA STN 125776/0

Final Summary Statement

A Bioresearch Monitoring (BIMO) inspection was performed for one foreign clinical study site, and a Remote Regulatory Assessment (RRA) was performed for another foreign clinical study site that participated in the conduct of study LEX-209. The inspection and RRA did not reveal significant problems impacting the data submitted in support of this original Biologics License Application (BLA).

Background

Two foreign clinical investigator (CI) sites were selected, one for inspection and the other for a RRA, in support of this BLA. The clinical study sites were selected based on subject enrollment, previous inspection history, as well as the data and information submitted in BLA 125776/0. The inspection and RRA were issued for the following study protocol:

Protocol LEX-209: Phase III, randomized, double-blind, multicenter study to assess the efficacy and safety of OCTAPLEX, a four-factor prothrombin complex concentrate (4F-PCC), compared to the 4F-PCC Beriplex® P/N (Kcentra), for the reversal of vitamin K

antagonist (VKA) induced anticoagulation in patients needing urgent surgery with significant bleeding risk.

The inspection and RRA were conducted in accordance with FDA's Compliance Program (CP) 7348.811, Inspection Program for CIs. The inspection and RRA included specific questions related to the study protocol, and information submitted in the BLA was compared to source documents at each site.

The sponsor reported that this study was conducted at 27 sites globally: Belarus (1), Georgia (5), Romania (2), Russia (6), Ukraine (9), and the United States (4). As of the data cutoff date (July 8, 2022), 214 subjects were screened, and 208 subjects were enrolled. In our review, we selected two CI sites, which accounted for a total enrollment of 46 subjects, representing 27% of the study population.

Inspection and RRA Outcome

No significant objectionable inspectional findings were observed during the inspection and RRA. The table below summarizes the BIMO inspection and RRA:

Type	Site ID	Number of subjects randomized	Location	483 Issued	Final Inspection Classification
Inspection	1405	10	Dr. Jano Vashadze JSC - EVEX Hospitals 21 Lubliana str., 0159 Tbilisi, Georgia	No	No Action Indicated (NAI)
RRA	4002	46	Dr. Anca-Ileana Ruxanda JSC Jerarsi Clinic 2a Mukhiani str, 0167 Tbilisi, Georgia	No	NAI

The inspection and RRA verified the data reported in the BLA, including but not limited to: subject eligibility, protocol deviations, study drug administration, primary efficacy endpoint, and adverse events for all subjects enrolled at the inspected clinical sites. No Form FDA 483 was issued.

Noteworthy inspectional findings

The inspection and RRA did not reveal substantive issues that impact the data submitted in the BLA.

Sponsor Issues

No significant sponsor issues were noted.

Financial Disclosure

The CI CP directs the FDA investigators to ask the CI if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouses and dependent children, and if and when the information was last

updated. The information submitted to the BLA was verified at the inspected/assessed clinical sites no deviations were found in the submitted data.

Administrative follow-up

No administrative follow-up is warranted at this time from BIMO. Should you have any questions about the contents of this memo or any aspect of BIMO, please contact me at 240-425-3201.

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Consumer Safety Officer

Electronic Copies

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Draft Triet: 06/23/2023

Reviewed: Cato: 07/06/2023