



Our STN: BL 125776/0

**MID-CYCLE COMMUNICATION
SUMMARY**

February 16, 2023

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

Dear Mr. Ammons:

Attached is a copy of the summary of your January 26, 2023, Mid-Cycle Communication Teleconference with CBER. This memorandum constitutes the official record of the teleconference. If your understanding of the teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER as soon as possible.

Please include a reference to STN BL 125776/0 in your future submissions related to your Prothrombin Complex Concentrate (Human).

If you have any questions, please contact Eden Chane at eden.chane@fda.hhs.gov.

Sincerely,

Basil Golding, MD
Director
Division of Plasma Protein Therapeutics
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

Mid-Cycle Communication Teleconference Summary

Application type and number: BLA 125776/0
Product name: BALFAXAR/Prothrombin Complex Concentrate (Human)
Proposed Indication: Urgent reversal of acquired coagulation factor deficiency induced by Vitamin K antagonist (VKA, e.g., warfarin) therapy in adult patients with (b) (4) need for an urgent surgery/invasive procedure
Applicant: OCTAPHARMA Pharmazeutika Produktionsges.m.b.H.
Meeting date & time: January 26, 2023, 11:00-12:00 ET
Committee Chair: Ze Peng, PhD
RPM: Eden Chane, MS

FDA Attendees:

Meghna Alimchandani, MD, CBER/OBPV/DPV
Rondine Allen, PhD, CBER/OTAT/DCEPT
Wilson W. Bryan, MD, CBER/OTAT
Eden Chane, MS, CBER/OTAT/DRPM
Jiang Hu, PhD, CBER/OBPV
Christopher Jason, MD, CBER/OBPV/DVP
Margarita M Gomez Lorenzo, MD, CBER/OBPV/DVP
Christopher Saeui, PhD, CBER/OTAT/DCEPT
Karl Kasamon, MD, CBER/OTAT/DCEPT
Julia Wright, MHA, RN, CBER/OTAT/DRPM
Nadia Whitt, MS, CBER/OTAT/DRPM
Wei Liang, PhD, CBER/OTAT
Parmesh Dutt, PhD, CBER/OCBQ/DBSQC
Ramani Sista, PhD, CBER/OTAT/DRPM
Lori Tull, CBER/OTAT/DRPM
Xiaofei Wang, PhD, CBER/OTAT/DCEPT
Emnet Yitbarek, PhD, CBER/OCBQ/DBSQC
Tyree Newman, MDiv, CBER/OTAT/DRPM
Zuben Sauna, PhD, CBER/OTAT/DPPT/HB

Applicant Attendees:

Barbara Rangetiner, Director Int. Drug Regulatory Affairs, General Manager OPG
Simone Meindl-Wilhelm, Deputy Director Int. Drug Regulatory Affairs
Xenia Serro, Int. Drug Regulatory Affairs Manager
Victoria Welch, Int. Drug Regulatory Affairs Manager
Harald Mayer, Head of Operations Support
(b) (6) Team Leader Innovation and Evaluation Unit, R&D Plasma
Andreas Volk, Head of Virus & Prion Validation
Oliver Hegener, Vice President, Head of IBU Critical Care

(b) (6), Project Manager IBU

Silvio Wuschko, Senior Director Pharmacology & Toxicology

Josef Weinberger, Board Member, Corporate Quality and Compliance Officer

Stanley Ammons, Local Agent / Senior Director Government Policy & Corporate Compliance

Dmitrii Matveev, Vice President, Head of CR&D Immunology and Critical Care

Doris Hinterberger, Senior Global Clinical Project Manager

Bernhard Rohrbacher, Vice President Global Medical & Scientific Affairs

Michelle Gareis, Senior Global Medical Advisor Critical Care

Barbara Malkowsky, Team Manager corporate QC method validation

Martina Schwarz, Head of Quality Control

(b) (6) Medical Device Expert

Balazs Toth, Head of corporate Drug Safety Unit

Sigurd Knaub, Senior Vice President clinical R&D Haematology

Werner Giefing, Head of Quality Assurance & Quality in Operations

Flemming Nielsen, President Octapharma USA, Inc. & Board Member

Octapharma Group

Agenda:

To provide a review update that includes any issues of concern that requires a discussion.

Discussion Summary:

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.
 - a. Chemistry, Manufacturing, and Controls (CMC):
No significant issues/major deficiencies have been identified at this time.
 - b. Clinical:
Preliminary review of BLA submission reveals insufficient data to support the (b) (4) indication. An information request was sent on January 19, 2023, regarding this matter. The efficacy data for the perioperative indication are currently being reviewed, and no significant issues have been identified. IRs will be sent as warranted as the review is ongoing.
2. Information regarding major safety concerns.
 - a. Clinical: There are safety concerns related to excess deaths and TEEs reported in Octaplex recipients, and an IR was sent on January 17, 2023.
3. Preliminary Review Committee thinking regarding risk management.

- a. At this time, the review teams have not identified a need for a Risk Evaluation Mitigation Strategy (REMS).
4. Any information requests (IRs) sent, and responses not received.
 - a. A DBSQC IR was submitted on December 30, 2022, for analytical method validations & response was received on January 17, 2023; the response is under review.
 - b. An IR from CMC-product was sent on January 9, 2023, and the responses are expected to be received by January 23, 2023.
 - c. OBPV/DPV sent an IR on January 23, 2023, with recommendations for the pharmacovigilance plan and to request sponsor proposal for a postmarketing study to assess TEEs following administration of BALFAXAR and submit a protocol synopsis. The responses are expected to be received by February 3, 2023.
5. Any new information requests to be communicated.
 - a. As review continues, new IRs will be conveyed as warranted.
6. Proposed date for the Late-Cycle meeting (LCM).
 - a. Late cycle meeting is scheduled for April 13, 2023, 11:00 AM-12:00 PM.
 - b. The meeting material will be provided by April 3, 2023.
7. Updates regarding plans for the AC meeting.
 - a. AC meeting is not anticipated.
8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.
 - a. There are no planned inspections of manufacturing facilities.
 - b. Tentative Labeling Target Date: June 28, 2023.
 - c. BIMO Target Date: May 20, 2023.