



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](mailto: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) (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.