Late-cycle internal meeting summary

Application type and number: BLA 125606/0
Product name: C1 Esterase Inhibitor Subcutaneous (Human)
Proposed Indication: For routine prophylaxis against Hereditary Angioedema (HAE) attacks in adolescent and adult patients with HAE.
Applicant: CSL Behring GmbH
Meeting date & time: February 21, 2017, 1:00 PM – 2:00 PM
Date of LCM with applicant: March 13, 2017
Committee Chair: Felice D'Agnillo/Ewa Marszal
RPM: Nannette Cagungun

Attendees:

Discipline	Name	Attended meeting?
Regulatory Project Manager (RPM)	Nannette Cagungun	Yes
Chair	Felice D'Agnillo, PhD Ewa Marszal, PhD	Yes No
Clinical Reviewer	Ilan Irony, MD Laurence Landow, MD	Yes No
CMC Reviewer	Matthew Williams, MSc Yiping Jia, PhD Tigist Kassa, PhD	No No No
Clinical Pharmacology Reviewer	Mahmood Iftekhar, PhD	
Pharmacology/Toxicology Reviewers	Jin Hyen Baek, PhD Mercedes Serabian, MS Theresa Chen, PhD	No Yes Yes
OCBQ/DMPQ Reviewer	Donald Ertel, MS, MT(ASCP)	Yes
OCBQ/DMPQ/PRB Reviewer	Cheryl Hulme	No
Statistical Reviewer of clinical data	Lin Huo, PhD	Yes
Postmarketing Safety Epidemiological Reviewer	Jaspal Ahluwalia, MD	Yes
OCBQ/APLB Reviewer	Alpita Popat, PharmD, MBA	Yes
OCBQ/BIMO Reviewer	Dennis Cato	Yes
OCBQ/DBSQC or OVRR/LIB Reviewer	Marie Anderson, MS, PhD Hyesuk Kong, PhD	No Yes
Other Attendees		
OTAT	Wilson Bryan, MD	Yes
OTAT/DPPT	Mahmood Farshid, PhD	Yes
OTAT/DPPT/PDB	Dorothy Scott, MD	Yes
OTAT/DPPT/PDB	Michael Kennedy, PhD	Yes

Discipline	Name	Attended meeting?
OCBQ/DMPQ/B1	Deborah Trout	Yes
OCBQ/DCM/APLB	Lisa Stockbridge, PhD	Yes
OBE/DE/AEB	Deepa Arya, PhD, MPH, MBA	Yes
OBE/DB/TEB	Renee Rees, PhD	Yes

Discussion:

Dr. Felice D'Agnillo presented a summary of the CMC review to the meeting attendees. OTAT will now chair the review of this submission but Dr. D'Agnillo will continue to provide support to this BLA as a consult reviewer.

Dr. D'Agnillo indicated the original CMC reviewers would update their mid-cycle memos to include their assessment of CSLB's responses to the CMC information requests sent to CSLB on January 5, 2017. These memos would represent the final memos from the original CMC team. Dr. D'Agnillo also indicated that he should be consulted regarding any CMC issue or questions related to the original CMC team reviews.

Each of the reviewers then gave a brief update on the status of their review. The reviewers have not identified any substantive issues with this BLA to date.

The following upcoming timelines were discussed next.

- The Late-Cycle Meeting (LCM) is currently scheduled for March 13, 2017. The LCM materials will be sent to the applicant by March 1, 2017.
- Discipline Executive Summary to Chair: May 8, 2017
- Draft Approval Letter: May 15, 2017
- SBRA to Product Division Director: May 22, 2017
- Labeling Target Date: May 31, 2017
- PMC Target Date: May 31, 2017

The Plasma Derivative Branch will evaluate the need for a press release. Some attendees at the meeting expressed the idea that a press release may be helpful given the subcutaneous route of administration for this product as well as the ongoing uncertainties regarding the potential availability of the only other C1 inhibitor product approved for prophylaxis.

Several information requests (IR) were sent to CSLB recently. These include the following:

- DMPQ IR sent 2/17/17*
- Clinical Pharmacology IR sent 2/13/17*
- Request for samples of the product (Lots (b) (4) were sent on 2/21/17

The asterisked IRs above will not be included in the LCM agenda because we requested CSLB to respond by February 28.

Dr. D'Agnillo recommended the following actions:

1. The incoming review team should decide on the suitability of the post-approval stability protocol and whether CSLB should submit these proposed studies as part of a PMC.

2. Discuss the need for CSLB to further explain the issue about the process parameter (b) (4) . The incoming review team should decide on whether CSLB needs to provide additional data to support the acceptance criteria for this process parameter.

3. CSLB should provide updated SOPs for the virus filtration step for review as soon as they are available.

4. Discuss the need for CSLB to address the storage temperature discrepancy for CSL830. CSLB proposed storage at 30°C but the labeling information states 2 - 30°C.

5. The incoming review team should evaluate the need for further discussions regarding the assessment of (b) (4) .

With respect to the product shelf-life, CSLB has only provided (b) (4) stability data. They indicated that the (b) (4) data will be submitted in April 2017.

Dr. Ewa Marszal is assuming the role of Chairperson of this BLA. She will meet with the RPM to finalize items to be included on the agenda for the LCM with the applicant**.**

The meeting ended.