FILING MEETING SUMMARY

Application type and number: BL 125606/0
Product name: C1 Esterase Inhibitor Subcutaneous (Human)
Proposed indication: Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients
Applicant: CSL Behring GmbH
Meeting date & time: August 15, 2016, 1:30 PM – 2:30 PM
Meeting Chair: Felice D'Agnillo, PhD
Meeting Recorder: Nannette Cagungun, MS, PD, RAC
Background: CSL 830 is a plasma-derived C1 Esterase Inhibitor (Human) concentrate (b) (4) for subcutaneous administration as a (b) (4)

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Manager (RPM)	Nannette Cagungun	Yes	X		
Chair	Felice D'Agnillo	Yes	X		
DHRR Division Director/Deputy	Basil Golding Mahmood Farshid				
Clinical Reviewer	Laurence Landow	Yes	X		
Clinical Pharmacology Reviewer	Iftekhar Mahmood	No	X		
PharmTox Reviewer	Jin Hyen Baek	Yes	X		
CMC Reviewers	Yiping Jia Matthew Williams Tigist Kassa	Yes Yes Yes	X X X		
OCBQ/DMPQ Reviewer	Donald Ertel	Yes	X		
OCBQ/DMPQ/PRB Reviewer	Jacqueline Glen	No	-		
OCBQ/APLB Reviewer	Alpita Popat	No	X		
OCBQ/BIMO Reviewer	Dennis Cato	Yes	X		
OCBQ/DBSQC Reviewers	Marie Anderson Hyesuk Kong Leslyn Aaron Hsiaoling Wang	Yes Yes No Yes	X X X X		
Statistical Reviewer of clinical data	Lin Huo	Yes	X		
Postmarketing Safety Epidemiological/Pharmacologovigilance Reviewer	Jaspal Ahluwalia	Yes	X		
Consult Reviewer(s)	None				

Discipline/Organization	Name	Attended meeting	Fileable	RTF	Deficiencies Identified
Other Attendees	Renee Rees Deborah Trout Howard Chazin	Yes Yes Yes			

REGULATORY CONCLUSIONS / DEFICIENCIES

1. **Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and will require a RTF letter?**

   Fileable

2. **If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application**:

   None identified

3. **If RTF, list any issues that would make this application unsuitable for filing? NA**

FILING MEETING DISCUSSION, IF FILED:

4. **Indicate any comments on the status of the proprietary name review.**

   The proprietary name review has been completed. The proprietary name, HAEGARDA, is acceptable.

5. **Indicate whether the product would be subject to lot release, surveillance, or exempt from lot release.**

   This product is subject to lot release.

6. **What is the review classification of this application?**

   Standard Review

7. **Indicate the decision regarding the need for an Advisory Committee.**

   The review committee felt that there is no need to present this BLA to the advisory committee because there is already a licensed plasma-derived C1 esterase inhibitor (Cinryze) on the market for this indication. Moreover, CSL 830 is a subcutaneously administered (b) (4)

8. Indicate whether the submission triggers PREA; if yes, a PeRC meeting is needed.

This product is an orphan product and therefore does not trigger PREA.

9. Is a comprehensive and readily located list of all clinical sites included or referenced in the application?

Yes. The Pivotal Study (Study CSL830_3001) was conducted at 38 sites in 10 different countries. The BIMO reviewer has selected 3 clinical sites for inspection: Bethesda, MD (Dr. Lee); Cincinnati, OH (Dr. Bernstein); and a clinical site in Canada. BIMO inspection is expected to be completed by December 16, 2016. A recent BIMO inspection was conducted at a clinical site overseen by Dr. James Baker. As such, this site will not be considered for a new BIMO inspection at this time, but the inspection report from this recent inspection will be reviewed for information relevant to this submission.

10. Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?

Yes. There is only one manufacturing site for (b) (4) **drug product (Marburg, Germany). According to DMPQ (LCDR Donald Ertel), it appears that the Pre-license inspection may be able to be waived per CBER SOPP 8410 "Determining When Pre-Licensing/Pre-Approval Inspections (PLI/PAI) are necessary." LCDR Ertel submitted an information request to the Firm to verify information to support a pre-license inspection waiver. The drafting of the Inspection Waiver memorandum** (b) (4) **.**

11. Indicate any updates since the first committee meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is the establishment(s) ready for inspection?)

Please see above.

12. If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

This BLA is not affected by the Application Integrity Policy (AIP).

13. Is the product an Original Biological Product or a New Molecular Entity (NME), for NDAs only?

This product is an Original Biological Product.

FOR APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs), IF FILED

14. Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.

This BLA does not have late submission components.

15. Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?

Yes, the submission was complete on submission.

ADMINISTRATIVE DETAILS, IF FILED:

16. Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the first committee meeting.

There are no issues with the review schedule.

17. Enter the date of the Mid-cycle Meeting, if appropriate (required for NME NDAs/BLAs in "the Program" PDUFA V):

The Mid-Cycle review committee meeting is scheduled for December 12, 2016.