

From: Cagungun, Nannette
Sent: Monday, February 13, 2017 2:19 PM
To: Michele.Walsh@csllab.com
Subject: Information Request_C1INH/CSL830

Our Reference: BL 125606/0

Dear Ms. Walsh:

We are reviewing your June 30, 2016, biologics license application for C1 Esterase Inhibitor Subcutaneous (Human) for routine prophylaxis to prevent Hereditary Angioedema attacks in adult and adolescent patients. We have the following comments and request for additional information:

Study # CSL 830-1001

1. Please explain the reason for not calculating AUC(0-inf) for most of the subjects. Please calculate clearance based on AUC(0-last) for all subjects (only for CSL-830) by functional activity.

Study # CSL 830-2001

In Table 9.3, you mentioned that C1-INH functional activity was measured at several time points. However, you also mentioned in section 9.5.4 that Plasma concentrations of CSL830 were not measured in this study. Functional activity can also be interpreted as concentrations.

2. From Table 9.3 it appears that you have several functional activities of CSL830 over time. From these time points, please calculate the PK parameters for all subjects (3 subjects rescued can be omitted from the study) using non-compartmental analysis.

3. In a Tabulated form (in a single Table) please provide subject ID, body weight, age and gender along with PK parameters of CSL 830 (Cmax, AUC, Clearance, Volume of distribution, and half-life) estimated by non-compartmental analysis.

4. In a separate Table, please provide the functional activities at time points you measured these activities in each subject for studies CSL830-2001 and CSL830-3001.

Please submit the requested information in an amendment to the file by Tuesday, February 28, 2017, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact me immediately so a new response date can be identified.

If you have any questions, please contact me at (240) 402-8267.

Sincerely,
Nannette Cagungun, MS, PD, RAC
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Center for Biologics Evaluation and Research
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