

Information Request, August 17, 2013- Eloctate

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

Our Reference: BL 125487/0

Biogen Idec Inc.
Attention: Ms. Debra Segal
August 26, 2013
Sent by email

Dear Ms. Segal:

We are reviewing your March 7, 2013 biologics license application (BLA) for Antihemophilic Factor (Recombinant), Fc Fusion protein. We are providing this request for additional information to continue our review:

1. It is stated in the section 4.4 of your SOP –b(4)--22895 that a -----
b(4)----- as a sequence listed in the Table 1.

[b(4)]

If the system suitability did not meet the acceptance criteria, the same sequence should be repeated. It is also stated in the section 4.6 of the same SOP that a run sequence as described in Table 2 should be used for a –b(4)----- to run samples.

[b(4)]

Please clarify if a –b(4)----- is used to run sample, it is necessary to run both sequences in their entirety, even if the system suitability met acceptance criteria during the -b(4)----- run. Or there is option to –b(4)----- in Table 1 and –b(4)---- of Table 2 plus a –b(4)----- run in the end as a single sequence.

2. Safety extension study 9HB01EXT is listed in the Pharmacovigilance Plan (PVP) on page 25 of the Risk Management Plan (RMP). Please clarify if this study is part of the PVP for this product. If so, please provide a copy of the study protocol and

interim study report if applicable.

3. The following Important Potential Risks were identified on review of prelicensure clinical trial data:
 - a. Development of anti-Drug (Eloctate) Antibodies (ADA)
 - b. Thrombotic Events
 - c. Dosage errors

The following Important Missing Information was identified on review of prelicensure clinical trial data:

- a. Use in pregnancy and lactation
- b. Use in previously untreated patients

Please add the five safety concerns listed above to the PVP and include planned action(s) to address each safety concern. If the planned action includes a clinical study, please provide a copy of the study protocol and interim study report if applicable

4. The Extension study 8HA01EXT is listed in the PVP as part of the long-term evaluation of the safety of Eloctate. However, the planned duration of the trial is \leq 4 years or until the product is commercially available in the applicable participating country. Because the study duration is dependent upon the date of licensure, the study may last significantly less than 4 years, in which case the study would fail to meet the primary objective to evaluate the long-term safety of this product. Please clarify the exact duration of the study regardless of licensure or marketing in participating countries and explain how the duration of the study will meet the stated primary objective.
5. Please provide a schedule of milestones for the two studies listed in the PVP – Pediatric study 8HA02PED and Extension study 8HA01EXT. Please include target dates to reach goal enrollment as well as dates for submission of interim and final study reports.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

Please submit your response to question #1 (-b(4)----- assay) by September 3, 2013 and questions #2 - #5 (Epidemiology) by September 9, 2013, referencing the date of this request.

The action due date for this file is March 8, 2014.

If you have any questions, please contact me at (301) 827-6116.

Sincerely,

Leigh Pracht
Regulatory Project Manager
FDA/CBER/OBRR/DBA/RPMB