

Request for Information, 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 17, 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 request for additional information to continue our review:

1. –b(4)----- is essential for the increased circulatory lifetime of the rFVIII Fc product *in vivo*, and should be monitored in stability studies. Please include the parameter, --b(4)----- in on-going stability studies and in future stability protocols on rFVIII Fc final product.
2. In your stability protocols for drug substance, under the heading Attributes, you provide rFVIII Fc –b(4)----- assay results in terms of –b(4)----- . Please list –b(4)----- separately from the Attribute *rFVIII Fc* ---b(4)----- in the stability protocols. Please make similar changes for the stability protocols for rFVIII Fc drug product.
3. Please provide updated stability data on rFVIII Fc drug substance batches –b(4)----- , and perform trend analyses on stability-indicating parameters.
4. Please provide updated stability data for the rFVIII Fc final product lots manufactured at the –b(4)-- facility including process validation lots and clinical lots,

and perform trend analyses on stability-indicating parameters.

5. Please provide updated stability data on lot –b(4)-- stored in the –b(4)----- final container, --b(4)----- glass vial.
6. You have proposed that for the stability of the rFVIII Fc drug substance the acceptance criterion of –b(4)---- be set at –b(4)----. However, the available data from long-term storage showed that the test results of –b(4)--- were only –b(4)--- over time, with no significant upward trend in –b(4)----- . To better control the quality of drug substance and to better represent manufacturing capability, please tighten the acceptance criterion of –b(4)----- in the stability study based on long-term stability data.
7. For the reconstitution (in-use) stability study,
 1. Please include the parameters b(4) and –b(4)----- in the in-use stability study
 2. Please make the acceptance criteria for the in-use stability be consistent with the commercial stability protocols
 3. Please provide a complete in-use stability protocol
 4. Please resubmit in-use stability data under *Module 3.2.P.8*
8. You did not specify the temperature range for the “Room temperature” in the temperature cycling study. Please clarify the temperature range of “Room temperature” in this study.

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 this information request by August 29, 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