

From: Do, Yu  
Sent: Thursday, October 01, 2015 12:00 PM  
To: Erik.Bjornson@baxalta.com  
Cc: tung.koh@baxalta.com; Thompson, Edward  
Subject: Information Request: Response Due by TUESDAY, October 06, 2015 - Original BLA, BL 125566/0, Antihemophilic Factor (Recombinant), PEGylated [ADYNOVATE]

Importance: High

Dear Mr. Bjornson:

We are reviewing your original November 25, 2014 submission to BLA 125566/0 for Antihemophilic Factor (Recombinant), PEGylated. We are providing the following comments and request additional information to continue our review:

1. Regarding ongoing pediatric safety, efficacy, PK, and immunogenicity trial #261202 in PTPs under age 12 years, please add efficacy hypothesis testing for both indications:
  - a. On-demand treatment and control of bleeding episodes
    - i. For example, using a confidence interval approach, please specify a minimum acceptable percentage of bleeding episodes for which no more than two product infusions were administered for treatment and control of the bleed.
    - ii. Alternatively, using a confidence interval approach, please specify a minimum acceptable percentage of bleeding episodes for which the hemostatic efficacy rating was good or excellent.
  - b. Routine prophylaxis to reduce the frequency of bleeding episodes
    - i. Please compare, using a confidence interval approach, the observed annualized bleeding rate (ABR) during routine prophylaxis with ADYNOVATE to one or more appropriate pre-specified historical controls for the ABR during (a) routine prophylaxis with (an) approved Antihemophilic Factor (Human) product(s), such as Advate, and (b) on-demand therapy with (an) approved Antihemophilic Factor (Human) product(s), such as Advate.
2. We continue to recommend eliminating PK sampling following administration of ADVATE during the PK substudy of trial 261202. Dosing with ADVATE and PK sampling following ADVATE are unnecessarily burdensome in this pediatric population, are expected to provide little useful information given the availability of comparative PK data for ADYNOVATE and ADVATE in adults, and are expected to be an impediment to enrollment in the trial.
3. Please submit the revised milestone dates for PREA PMR study 261202, most particularly a revised milestone date for when the final (further amended) protocol is expected to be submitted. Please submit the protocol amendment, SAP for the study, and its revised milestone dates to the IND within 15 calendar days from the date of this request.
4. Please submit the revised milestone dates for the PMC PUP study 261203, most particularly a revised milestone date for when the final (further amended) protocol is expected to be submitted. Such revisions are based on our information request for changes to the protocol dated October 01, 2015.

The review of this submission is ongoing and issues may be added, expanded upon, or modified as we continue to review this submission. Please submit your response as an amendment to this file by October 06, 2015, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is November 25, 2015.

Please acknowledge receipt of this request and contact me at (240) 402-8343 or Yu.Do@fda.hhs.gov if you have any questions.

Sincerely,

Yu Do, M.S.  
Regulatory Project Manager  
FDA/OMPT/CBER/OBRR/IOD/RPMS  
(240) 402-8343  
yu.do@fda.hhs.gov

"THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender by e-mail or phone."