



Our Reference: BL 125582/0

CSL Behring Recombinant Facility AG  
Attention: Mr. Kevin D White  
January 29, 2016  
Sent by email

Dear Mr. White:

We are reviewing your December 5, 2014 biologics license application (BLA) for Coagulation Factor IX (Recombinant), Albumin Fusion Protein. We are providing the following comments and request for additional information with a post marketing commitment to continue our review:

1. We have reconsidered your request to allow a labeling claim for both 7-day and 14-day dosing regimens, and are willing to allow a claim for a 14-day regimen for patients  $\geq 12$  years who will be treated on the 7-day regimen and meet the same switching criteria as was used in clinical trial 3001 providing that you:
  - a. Submit a summary of all relevant pharmacokinetic (PK) data that demonstrate that FIX trough levels are maintained above 1% and above 3% at the proposed dose of 50-75 IU/kg body weight every 14 days.
  - b. Commit to conducting a postmarketing study to evaluate the PK and safety of the 14-day regimen. We reiterate our previous comment that because FIX activity trough levels may be lower after repeat dosing, we are concerned that patients maintained on a 14-day regimen may not be able to maintain appropriate FIX activity levels over time and therefore may pose a safety risk to patients. Depending on the PK information that you provide as per the request above, we may need additional data from new subjects to address this issue. We may request additional post-marketing studies to evaluate trough levels at day 7, 10 and 14 in subjects  $\geq 12$  years who switch from the 7 day regimen to the 14 day regimen.
2. Regarding your proposed pediatric dosing, please:
  - a. Provide a justification, based on PK information, for the proposed pediatric dosing of 35-50 IU/kg body weight every 7 days and show your calculations.
  - b. Provide a list of subjects  $< 12$  years that received doses for routine prophylaxis or on-demand treatment of bleeding episodes that were greater than 50 IU/kg. For each subject, please include descriptive statistics to summarize the dose, number of

infusions received, and any adverse events associated with the higher dose range of 50-75 IU/kg. FDA needs this information to evaluate the safety of the higher dose.

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 as an amendment to this file by February 3, 2016 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 March 5, 2016.

Please send an acknowledgement for receipt of this request.

If you have any questions, please contact me at (240) 402-8443.

Sincerely,  
Edward Thompson  
Regulatory Project Manager  
FDA/CBER/OBRR/RPMS

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Thank you.