

**BLA for Coagulation Factor IX (Recombinant),
GlycoPEGylated [N9-GP]
STN 125611/0**

**Blood Products Advisory Committee Meeting
April 4, 2017**

Safety Concern

Preclinical findings related to the accumulation of polyethylene glycol (PEG) in the choroid plexus of animals exposed to N9-GP

DISCUSSION QUESTIONS FOR THE ADVISORY COMMITTEE



Discussion Question 1

Please discuss the clinical significance, if any, of the preclinical findings.



Discussion Question 2

Please discuss the nature and level of your concerns, if any, regarding the safety of the product in different age populations: e.g., from birth to < 6 years, 6 years to < 12 years, 12 years to 17 years, adults, and older adults.

Discussion Question 3

Considering the findings from the toxicology and clinical studies, please discuss whether the data provide sufficient evidence of the safety of the product for:

- (1) Intermittent use (i.e., for perioperative management and control of bleeding episodes)
- (2) Chronic, and possibly life-long, use (i.e., routine prophylaxis).



Discussion Question 4

Please discuss any clinical or laboratory assessments (including, but not limited to, assessments of neurologic function), either short-term or long-term, that you would recommend to help ensure the safety of patients (or study subjects) who receive the product.

Discussion Question 5

Please discuss your recommendations, if any, for additional preclinical or clinical studies, either premarketing or post-marketing, to support the safety of the product. For example, please discuss the clinical examinations and laboratory studies, the duration of follow-up, the inclusion or exclusion of specific age groups, and safety endpoints that you would recommend for any subsequent clinical trials or post-marketing studies.

Advisory Committee

- Preclinical findings related to PEG accumulation in the choroid plexus
- Risks for the intended population
 - Pediatric patients
 - Elderly patients
 - Chronic, including lifelong, administration
- Monitoring of neurologic function
- Additional preclinical or clinical studies



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