

## Dehdashti, Seameen (Jean)

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**From:** Dehdashti, Seameen (Jean)  
**Sent:** Thursday, December 13, 2018 6:51 AM  
**To:** 'BDV (Barbara Davies)'  
**Cc:** Dehdashti, Seameen (Jean)  
**Subject:** FDA Information Request - Clinical: BLA 125671/0

Good morning Barbara,

We are reviewing your BLA submission for Antihemophilic Factor (Recombinant), GlycoPEGylated, turoctocog alfa pegol (STN 125671), and have the following information request (IR), outlined below in **bold text**. Please send us your response by close of business, Friday, December 14, 2018, if possible.

### **FDA Information Request (IR) – Clinical:**

**In your response to FDA’s information request dated December 11, 2018, you state that:**

- 1. Only treatment requiring bleeds were included in the analyses of ABR. Thus, non-treatment requiring bleeds were excluded from the ABR analyses in both pivotal trials 3859 and 3885.**
- 2. The main objective of the trials was to evaluate the prophylactic effect of N8-GP for prevention of clinically relevant bleeds. Non-treatment requiring bleeds (e.g., bruises, minor nose/gum bleeds) were not considered relevant for the assessment of ABRs in the clinical trials. These non-treatment requiring bleeds are bleeds that resolved by themselves or by the RICE principle (rest, ice, compression, elevation), which is in line with common clinical practice.”**

However, we note that the following subjects had joints bleeding, some of whom had severe, spontaneous, or multiple joint bleeds:

- NN7088\_3859/(b) (6) (severe)
- NN7088\_3859/(b) (6)
- NN7088\_3859/(b) (6) (2 bleeds)
- NN7088\_3859/(b) (6)
- NN7088\_3859/(b) (6)
- NN7088\_3859/(b) (6)
- NN7088\_3859/(b) (6)
- NN7088\_3859/(b) (6) (2 bleeds)
- NN7088\_3859/(b) (6)
- NN7088\_3859/(b) (6)
- NN7088\_3885/(b) (6) (3 bleeds)
- NN7088\_3885/(b) (6)
- NN7088\_3885/(b) (6) (2 bleeds)
- NN7088\_3885/(b) (6)
- NN7088\_3885/(b) (6)
- NN7088\_3885/(b) (6)

And

- NN7088\_3776/(b) (6)

**Please clarify the reason why each subject's bleeds were not included in the ABR analysis, given that joint bleeds are significant in hemophilia patients.**

Please confirm receipt of this communication, and do not hesitate to contact me, should you have any questions and/or concerns.

Warm regards,

**Jean Dehdashti, MSc, RAC**  
***Regulatory Project Manager***

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