

Dehdashti, Seameen (Jean)

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)
- 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_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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