

From: Alicea, Candido
Sent: Friday, April 26, 2019 4:58 PM
To: joan.robertson@grifols.com
Subject: Information Request #26: BLA 125683/0, Grifols Therapeutics LLC Immune Globulin Subcutaneous (Human), 20%

Our Reference: BLA 125683/0

Dear Ms. Robertson:

FDA will submit the labelling mark-up for XEMBIFY in the next few weeks and would like to communicate some of the areas that will need revision. There is no need to submit a revised label at this point, rather this is to help you prepare in advance of receiving the labelling mark-up.

Dosing and Administration:

- 1) We recognize that you performed a modeling and simulation study of subcutaneous and intravenous IgG dosing in PI patients (PopPK) submitted within the application; however, dosing based upon this modeling study has not been validated and therefore may not be used in labeling of the product.
- 2) We wanted to inform you in advance of receiving the label from FDA that the section on dosing and administration will need to be revised to reflect the dosing and administration per the clinical trial GTI1502.

Adverse Events

- 3) In reviewing the application and the label, you noted adverse events (AEs) that occur within 72 hours of infusion. The AEs noted in the label should reflect any AE that occurs in >5% of subjects in the trial regardless of time frame from the infusion. A sub-analysis of immediate adverse events in the 72 hour timeframe is acceptable; however, labeling will need to identify the most common adverse events.
- 4) In your analysis of local infusion site reactions (ISRs), you counted only ISRs that required an intervention with regard to the infusion. FDA considers all reactions AEs regardless of whether an intervention or cessation of infusion occurred. You provided a table that fully assesses such reactions, specifically, Table 10-18 Rates of Local Infusion Site Reactions Per Infusion During the SC Phase (> 0.02, non-TEAEs) (Safety Population). The AEs in the label will need to reflect the full scope of AEs that most commonly occur in >5% of subjects. For example, infusion site erythema (30%) and infusion site swelling (34%) of subjects who used the thigh as an infusion site. You may reference the smaller number of AEs that required intervention, if desired. Please revise this Table accordingly and submit Word files containing a Redlined Track Changes version and a Clean Copy version of this table or newly developed table that represents the full scope of AEs that most commonly occur in > 5% of subjects to the RPM as soon as feasible, preferably by 5/10/2019 .
- 5) Please submit a revised assessment of adverse events that occurred in > 5% of subjects in each Phase of the Study for the application review.

Please acknowledge receipt or provide questions by COB May 13, 2019.

If you have any questions, please contact me at (240) 402-8310.

Regards,

Candido

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