

From: Maruna, Thomas
Sent: Tuesday, April 05, 2016 8:48 AM
To: 'Denloye, Aderonke O'
Cc: Landow, Laurence
Subject: April 5. 2016 (Clinical) Information Request - BLA 125596.0 - Please Respond by April 15. 2016

Importance: High

Baxalta US Inc.
Attention: Ms. Aderonke Denloye
April 5, 2016
Sent by email

Dear Ms. Denloye:

We are reviewing your September 14, 2015 biologics license application (BLA) to treat primary immune deficiency disorders associated with defects in humoral immunity for the following:

| STN | Name of Biological Products |
|------------|--|
| 125596/0 | Immune Globulin Subcutaneous (Human), 20% Solution |

We have determined the following information is required to continue our review:

1. Concerning study 170903, please submit narratives justifying an assessment of "unrelated to study product" for 4 severe intensity TEAEs in Subject (b) (6) (bronchitis, influenza and epilepsy) and Subject (b) (6) (headache).
2. Please submit justification for an assessment of "unrelated to study treatment" for an SAE pneumonia in Subject (b) (6) in Study 170904.
3. Please submit justification for an assessment of "unrelated to study treatment" for an SAE pneumonia in Subject (b) (6) in Study 170903.
4. Subject (b) (6) withdrew prematurely from Study 160601. The narrative on page 131 of 152 states that he developed sickle cell crisis during routine care with GAMMAGARD LIQUID. Later, the narrative goes on to state that the subject had been on chronic IVIG infusions, but usually received another product rather than GAMMAGARD LIQUID. In addition, the narrative states that he did not receive treatment in the context of the study and is therefore not included in the FSDS.

Please clarify the following:

- a. What was the "other product(s)" the subject was receiving at the time of enrollment, and for how long had he been receiving it?
- b. When was the first and last time GAMMAGARD LIQUID was administered as part of "routine care" to this subject?
- c. How does excluding an enrolled subject from the FSDS, for whatever reason, comport with an intent-to-treat analysis?

Please submit your responses as an amendment to this file by April 15, 2016 referencing the date of this request.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

The action due date for these files is September 13, 2016.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH

Lieutenant, U.S. Public Health Service

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