

From: [Gildner, Jean](#)
To: [Janice Castillo \(jcastillo@Portola.com\)](mailto:jcastillo@Portola.com)
Subject: BL 125586 Information Request
Date: Thursday, November 16, 2017 7:57:18 AM
Attachments: [image001.png](#)
Importance: High

Dear Janice,

Please see the following information requests. Please respond by November 20, 2017. If you are not able to meet this deadline please let me know. Please acknowledge receipt of this email.

1. In the ADCM table, antiplatelet therapy and NSAIDs under CMSCAT column are listed. In the CMCAT column, these treatments are listed as subjects being on these treatments at least 7 days prior to screening, a dose is provided but the start or end dates (CMSTDTC and CMENDTC) as is the case with the Analysis reference date (CMSTDY) have missing information. It is unclear from this table as to whether the subjects continued to receive treatments with antiplatelet therapies or NSAIDs during the study period or whether it was stopped prior to the administration of andexanet. Could you please ask the applicant to update the ADCM datasets to provide information that includes information as to whether subjects continued to receive antiplatelet and NSAID treatments during the study by updating the appropriate columns.
2. Please conduct the following analysis (provide the analysis table(s) as well) to evaluate the overall rate of thromboembolic events and death from any cause (independent of attribution to the product) during the safety observation period (separately and combined please) in the ANNEXA 4 study (based on the cut-off date of April 20, 2017) in the safety evaluable subjects who
 - 1) received anticoagulation within the safety assessment period
 - 2) did not receive anticoagulation within the safety assessment period
 - 3) median time from andexanet to initiation of anticoagulation for item 1
 - 4) median duration of anticoagulation for item 1
 - 5) sub-group analyses based on high vs low dose andexanet for items 1 and 2.

Sincerely, Jean

Jean F. Gildner MSHS, MT (ASCP)

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