

From: Maruna, Thomas
Sent: Monday, May 02, 2016 4:11 PM
To: 'Angela.Azzara@cslbehring.com'
Cc: KevinDarryl.White@cslbehring.com; Khrenov, Alexey (CBER); Frost, Mitchell M
Subject: May 2. 2016 Information Request - BLA 125591.0 - Please Respond By May 6. 2016

Importance: High

CSL Behring Recombinant Facility AG
Attention: Mr. Kevin Darryl White
May 2, 2016
Sent by email

Dear Mr. White:

We are reviewing your May 29, 2015 biologics license application (BLA) for the following:

STN	Name of Biological Products
125591/0	Antihemophilic Factor (Recombinant), Single Chain

We have determined that the following is necessary to continue review:

Section 5.3, Monitoring Laboratory Tests, of the Prescribing Information (PI) warns prescribers that when monitoring Factor VIII activity in patients receiving AFSTYLA, the result using the one-stage clotting assay is approximately 45% lower than the chromogenic assay result, and that if the one-stage clotting assay is used the result should be multiplied by a conversion factor of 2 to align it with the chromogenic assay. Because the one-stage clotting assay is routinely used in US clinical laboratories, underestimation of FVIII activity in a substantial number of patients is probable if the result is not interpreted correctly, and could result in unnecessary additional dosing, higher chronic dosing, or unnecessary investigations for an inhibitor. Therefore, FDA believes that this warning should be accompanied by communications to health care providers in the form of a Dear Healthcare Provider (DHCP) letter. Please provide a letter of commitment to sending a DHCP and outline:

1. The issue to be addressed and the action required
2. The appropriate audience
3. A timeframe and means of communication of the letter

For recommendations on the content and format of DHCP letters please refer to FDA Guidance *Dear Health Care Provider Letters: Improving Communication of Important Safety Information – January 2014*

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM233769.pdf>).

This DHCP letter is an addition to the:

1. CSL-Behring communication plan submitted 17 February 2016, as part of a response to the FDA's Information Request of 09 February 2016 – FDA agrees with this communication plan with the caveats communicated to CSLB in an email sent 07 March 2016
2. Four additional actions to be incorporated into the communication plan as iterated in CSLB Response to FDA's 07 March 2016 FDA Comments, submitted 23 March 2016 – FDA agrees with these four additional actions

Please update the pharmacovigilance plan to include the communication strategies.

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

Please submit your responses as an amendment to this file by May 6, 2016, referencing the date of this request.

The action due date for this file is May 28, 2016.

If you have any questions, please contact me.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
Lieutenant, U.S. Public Health Service
Senior Regulatory Management Officer
Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Blood Research and Review
10903 New Hampshire Ave.
Silver Spring, MD 20993
thomas.maruna@fda.hhs.gov
O: (240) 402-8454
www.usphs.gov



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