

From: Maruna, Thomas
Sent: Monday, March 07, 2016 10:54 AM
To: 'Angela.Azzara@cslbehrlng.com'; KevinDarryl.White@cslbehrlng.com
Cc: Khrenov, Alexey (CBER)
Subject: BLA 125591.0 - Communication Plan - FDA Comments

Importance: High

CSL Behring Recombinant Facility AG
Attention: Mr. Kevin Darryl White
March 7, 2015
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

On 17 February 2016, as part of a response to the FDA's Information Request of 09 February 2016, CSL-Behring submitted a communication plan to address possible lack of awareness of clinicians regarding the discrepancy in measured FVIII activity when using the one-stage assay instead of the chromogenic assay. FDA has reviewed the proposed communication strategies and has the following comments and additional suggestions:

Target Audience: HTC (Hemophilia Treatment Center) Hematologists Non-HTC Hematologists		FDA Comments
Communication points	<ul style="list-style-type: none">• rVIII-SingleChain is approved by FDA for treatment of Hemophilia A• For FVIII activity monitoring, both OS and ChS assays are acceptable• ChS assay is preferred for accuracy, request this assay if available at your lab	

Communication methods	<ul style="list-style-type: none"> Scientific communication <ul style="list-style-type: none"> Publications in scientific journals Education at professional society meetings, e.g., American Society of Hematology, Hemostasis & Thrombosis Research Society (handouts and discussions at CSLB promotional and Medical booths) Outreach by CSLB Medical experts Peer-to-peer education (rVIII-SingleChain speaker programs) Sales Force communication <ul style="list-style-type: none"> Training and education for CSLB sales representatives 	<ul style="list-style-type: none"> - Acceptable - Acceptable - Acceptable if consistent with the approved product label/medical experts may provide other information in response to unsolicited requests - Acceptable if consistent with promotional/ advertising regulations - Acceptable - Acceptable if consistent with promotional/advertising regulations - Acceptable - Acceptable - Acceptable
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Target Audience: Pathologists		FDA Comments
Communication points	<ul style="list-style-type: none"> Ensure that laboratory personnel indicate on FVIII activity level lab reports which assay was used (OS or ChS) When consulting with hematologists who ordered FVIII activity levels in patients treated with rVIII-SingleChain, advise him/her of the consistent and predictable difference in FVIII activity 	<ul style="list-style-type: none"> - It may not be possible to incorporate this into existing policies and procedures in the various healthcare environments.

Communication methods	<ul style="list-style-type: none"> • Scientific communication <ul style="list-style-type: none"> ○ Publications in scientific journals ○ Educational initiatives in partnership with professional societies, e.g., College of American Pathologists, American Society for Clinical Pathology ○ Audience-appropriate handouts/communications • Additional actions 	<ul style="list-style-type: none"> - Acceptable - Acceptable - Acceptable if consistent with promotional/advertising regulations - Acceptable - Acceptable - Acceptable
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In addition to the above components, FDA suggests the following additional communication strategies to maximize awareness of healthcare providers regarding the potency assay discrepancies and minimize dosing errors:

- a. Creation of webinar with case studies (ensure that this is consistent with the approved product label)
- b. Creation of a laboratory monitoring Instruction For Use (IFU) document accompanying the package insert (submit for approval)
- c. Outreach to pharmacy/medical informatics to include flagging of electronic physician orders or laboratory orders to display warning
- d. Dear Healthcare Provider letters
- e. Outreach to medical centers and their healthcare facility formularies
- f. Use of focus groups to evaluate the usefulness of the educational materials

FDA also plans to discuss other labeling strategies in future labeling meetings with you. This would include the addition of a boxed warning on monitoring laboratory tests and the need to use a conversion factor to align the results of the one-stage assay with those of the chromogenic substrate assay. Positioning this important monitoring information in a boxed warning would ensure its ubiquitous presentation in prescribing tools and in promotional materials.

Finally, FDA asks that you include communication plan activities regarding the potency assay discrepancy in future versions of the pharmacovigilance plan.

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 this file is May 28, 2016.

If you have any questions, please contact me.

Very Respectfully,

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

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