February 27, 2018

VIA FACSIMILE AND UPS (UNITED PARCEL SERVICE)

Kevin White
Senior Director, Global Regulatory Affairs
CSL Behring LLC
1020 First Avenue
P.O. Box 61501
King of Prussia, PA 19406-0901

Re: **IDELVION (Coagulation Factor IX (Recombinant), Albumin Fusion Protein**
BLA STN# 125582

Dear Mr. White:

The Advertising and Promotional Labeling Branch (APLB) at the U.S. Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) has reviewed your company website *www.idelvion.com*, patient brochure [IDL-15-10-0006], exhibit panel [IDL-16-02-0032(1)a], and sales aid [IDL-0072]. These promotional materials make misleading claims about the effectiveness of IDELVION. Such claims cause a drug to be misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act (Act) and make its distribution violative under sections 21 U.S.C. 352(a), 352(n), 321(n), and 331(a), and FDA implementing regulation, *Cf.* 21 CFR 202.1(e)(5).

Background

According to the FDA-approved prescribing information (PI) for IDELVION:

> IDELVION, Coagulation Factor IX (Recombinant), Albumin Fusion Protein (rIX-FP), a recombinant DNA-derived coagulation Factor IX concentrate, is indicated in children and adults with Hemophilia B (congenital Factor IX deficiency) for:
> - On-demand treatment and control of bleeding episodes
> - Perioperative management of bleeding
> - Routine prophylaxis to reduce the frequency of bleeding episodes
>
> Limitations of Use:
>
> IDELVION is not indicated for immune tolerance induction in patients with Hemophilia B.

The WARNINGS AND PRECAUTIONS section of the PI includes, but is not limited to, the following risks:

- Hypersensitivity reactions, including anaphylaxis, are possible. Should symptoms occur, discontinue IDELVION and administer appropriate treatment.
- Development of neutralizing antibodies (inhibitors) to IDELVION may occur. If expected Factor IX plasma recovery in patient plasma is not attained, or if bleeding is not controlled with an appropriate dose, perform an assay that measures Factor IX inhibitor concentration.
- Thromboembolism (e.g., pulmonary embolism, venous thrombosis, and arterial thrombosis) may occur when using Factor IX-containing products.
- Nephrotic syndrome has been reported following immune tolerance induction with Factor IX-containing products in hemophilia B patients with Factor IX inhibitors and a history of allergic reactions to Factor IX.
- Factor IX activity assay results may vary with the type of activated partial thromboplastin time reagent used.

The ADVERSE REACTIONS section includes, but is not limited to, the following:

The most common adverse reaction (incidence ≥1%) reported in clinical trials was headache.

Misleading Efficacy Presentation

Your website, patient brochure, exhibit panel, and sales aid contain the following claims and presentations:

"He's free to infuse only once every 14 days. Are you?" (Along with an image of a man about to engage in heading or kicking a soccer ball while jumping high in the air.)

"...[D]elivers high steady-state factor levels with up to 14 day dosing" (Along with the same image.)

The above claims and presentations misleadingly overpromise the effect that the drug will have on a hemophilic patient's activities and overall quality-of-life. Specifically, your promotional materials contain an image of a man playing soccer, which is considered a moderate to dangerous high-risk activity for hemophilic patients because of the bleeding risk associated with the cuts, scrapes, contusions, and similar injuries that occur when people engage in such activity. The soccer player depicted in your materials appears ready to engage in heading or kicking the ball while he is jumping high in the air. The initial impact of heading a ball could result in various injuries, including, but not limited to, intracranial bleeding from injury or trauma, a contusion, injury of the face, or concussion. Subsequently, the secondary impact from landing after jumping high in the air could cause injury to the joints or bones. A patient being treated through a routine prophylaxis regimen with IDELVION, and whose hemophilia is well-

controlled, will nevertheless still have a serious risk for bleeding while engaging in such activities.

In patients with hemophilia, once bleeding occurs, bleeding is prolonged, and such patients may experience bleeding even weeks after an injury. Persistent joint or muscle bleeding can lead to decreased mobility and function, or even permanent disability for these patients. Furthermore, one of the most serious types of bleeding that can occur within the body is intracranial bleeding from injury or trauma, possibly leading to strokes, which can threaten life, limb, and overall function. Without early recognition and treatment of a serious intracranial bleed, severe neurologic impairment or death can occur.

Overall, your claims and presentations misleadingly imply that hemophiliacs taking your product can engage in moderate to dangerous high-risk activity without consequences and that such activities are appropriate for typical patients with hemophilia using this product.

Conclusion and Requested Actions

For the reasons discussed above, your promotional materials misbrand IDELVION within the meaning of the Act and make its distribution violative under sections 21 U.S.C. 352(a), 352(n), 321(n), and 331(a), and FDA implementing regulation, *Cf.* 21 CFR 202.1(e)(5).

We request that CSL Behring immediately cease the dissemination of these promotional materials for IDELVION, as well as promotional materials with the same or similar claims and presentations. Please submit a written response within ten (10) business days of the date of this letter, stating whether you intend to comply with this request, listing all potentially violative promotional materials for IDELVION, and explaining your plan for discontinuing use of such materials.

Please direct your response to Lisa Stockbridge, Ph.D., Branch Chief at the Food and Drug Administration, Center for Biologics Evaluation and Research, Office of Compliance and Biologics Quality, Division of Case Management, Advertising and Promotional Labeling Branch, 10903 New Hampshire Ave., WO71-G112, Silver Spring, MD 20993-0002. In all future correspondence regarding this matter, please refer to the BLA/STN number. We remind you that only written communications are considered official responses.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for IDELVION comply with each applicable requirement of the Act and FDA implementing regulations.

If you choose to revise your promotional materials, APLB is willing to assist you in assuring that your revised materials comply with applicable provisions of the Act by reviewing your revisions before you use them in promotion.

Sincerely,

Robert A. Sausville
Director, Division of Case Management
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research