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CBER-04-005

May 11, 2004

Food and Drug Administration
Center for Biologics Evaluation
and Research
1401 Rockville Pike
Rockville MD 20852-1448

VIA FACSIMILE AND CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

Jan Robertson Vercelli, Manager
Global Regulatory Affairs
Baxter Healthcare Corporation
One Baxter Way
Westlake Village, CA 91362

Re: **BLA STN # 103133**
Polygam® S/D [Immune Globulin Intravenous (Human)]

Dear Ms. Robertson Vercelli:

The Advertising and Promotional Labeling Branch (APLB) in the Food and Drug Administration's Center for Biologics Evaluation and Research (CBER) has reviewed a professional print advertisement (2003-72) for Polygam® S/D [Immune Globulin Intravenous (Human)] submitted by Baxter Healthcare Corporation (Baxter) under cover of Form FDA 2253. This advertisement fails to include risk information in the main part, 21 CFR 202.1(e)(3)(i), and is misleading with respect to risk information, 21 CFR 202.1(e)(5)(i), and thus does not include a true statement in brief summary as required by section 502(n) of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 352(n). The advertisement presents a serious public health issue, because it could encourage the unsafe use of Polygam S/D.

Background

Polygam S/D is a solvent/detergent treated, sterile, freeze-dried preparation of highly purified immunoglobulin G (IgG) derived from human plasma. Polygam S/D is distributed by the American Red Cross and manufactured by Baxter Healthcare Corporation. According to the FDA-approved labeling (PI), Polygam S/D is indicated for the treatment of primary immunodeficiency diseases, B-cell chronic lymphocytic leukemia (CLL), idiopathic thrombocytopenic purpura (ITP), and Kawasaki Syndrome. The PI contains a black box warning that states, in relevant part, "Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death." According to the contraindications section of the PI, patients may experience severe hypersensitivity reactions or anaphylaxis in the setting of detectable IgA levels following infusion. A bolded warning in the PI states that Polygam S/D may carry a risk of transmitting infectious agents, such as viruses and Creutzfeld-Jacob disease. The warnings section states, further:

Polygam S/D is not indicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern. It should be given with caution to patients with antibodies to IgA or IgA deficiencies that are a component of an underlying primary immunodeficiency disease for which IGIV therapy is indicated. In such instances, a risk of anaphylaxis may exist despite the fact that Polygam S/D contains only trace amounts of IgA.

Brief Summary Violations

The main part of the advertisement makes numerous claims of safety and effectiveness, but fails to provide any risk information. As noted, Polygam S/D is associated with numerous risks, including serious and sometimes fatal risks of renal dysfunction, acute renal failure, osmotic nephrosis, severe hypersensitivity reactions or anaphylaxis, and infectious disease. Information about these risks is pertinent to the safety and effectiveness of Polygam and, therefore, must appear in the main part of the advertisement along with the claims of safety and effectiveness information. 21 CFR 202.1(e)(3)(i).

Moreover, the advertisement states that Polygam S/D "has one of the lowest IgA content levels of any IgIV product to accommodate patients with antibodies to IgA or selective IgA deficiencies." This statement is misleading because it appears in the main body and is not accompanied by the pertinent qualifying information from the PI regarding patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern. The statement is also not accompanied by the pertinent qualifying information from the PI regarding the risk of anaphylaxis in patients with antibodies to IgA or IgA deficiencies that are a component of an underlying primary immunodeficiency disease for which IGIV therapy is indicated. The advertisement is thus false or misleading with respect to product risks, in violation of 21 CFR 202.1(e)(5)(i).

Conclusion and Requested Action

The advertisement makes claims of safety and effectiveness but omits risk information in the main part, and also fails to include qualifying information with the safety claim regarding use in patients with antibodies to IgA or selective IgA deficiencies. The advertisement thus fails to include a true statement in brief summary as required by section 502(n) of the Act, and Polygam is misbranded under that provision. 21 U.S.C. 352(n).

We request that you immediately cease the dissemination of promotional materials for Polygam S/D that are the same as or similar to the advertisement. Because of the significance of the violations described above, we request, further, that you disseminate truthful, nonmisleading, and complete information to the audience(s) that received the advertisement. Please submit a written response to this letter within ten [10] business days of the date of this letter stating whether you intend to comply with this request, providing a plan of action to disseminate corrective information, listing all promotional materials for Polygam S/D that are the same as or similar to the advertisement, and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, Center for Biologics Evaluation and Research, Office of Compliance and Biologics Quality, HFM-600, 1401 Rockville Pike, Rockville, Maryland 20852-1448. In all future correspondence regarding this matter, please

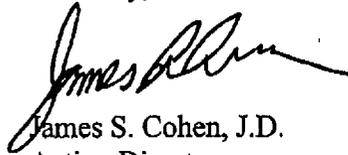
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refer to the BLA/STN number and to CBER-04-005. We remind you that only written communications are considered official responses.

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

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

A handwritten signature in black ink, appearing to read "James S. Cohen". The signature is fluid and cursive, written over the printed name.

James S. Cohen, J.D.
Acting Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: American Red Cross

Enclosure – Print Ad