Plasma Protein Therapeutics Association

Date: May 22, 2017
Reference No.: FDAA17006 **VIA EMAIL**

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

SUBJECT: Considerations in Demonstrating Interchangeability With a Reference Product; Draft Guidance for Industry; Availability
Docket No. FDA-2017-D-0154

Dear Sir or Madam:

The Plasma Protein Therapeutics Association (PPTA) thanks FDA for the opportunity to participate in the guidance development process and is pleased to provide these comments on the draft guidance for industry "Considerations in Demonstrating Interchangeability With a Reference Product" dated January 2017 (hereinafter "Draft Guidance").[1]

About PPTA

PPTA is the international trade association and standards-setting organization for the world's major producers of plasma-derived and recombinant analog therapies, collectively referred to as plasma protein therapies. Plasma protein therapies are used mostly in the treatment of several rare diseases. These diseases are often genetic, chronic, life-threatening conditions that require patients to receive regular infusions or injections of plasma protein therapies for the duration of their lives. These therapies include clotting therapies for individuals with bleeding disorders, immunoglobulins (IG) to treat a complex of diseases in persons with severe autoimmune deficiencies, therapies for individuals who have alpha-1 anti-trypsin deficiency, which typically manifests as adult-onset emphysema and substantially limits life expectancy, and albumin, which is used to treat individuals with severe liver diseases and, in emergency-room settings, shock, trauma, burns, and other conditions. PPTA members are committed to assuring the safety and availability of these medically needed, life-sustaining therapies.

Introduction

PPTA understands that the Draft Guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is interchangeable with a reference product for the purposes of submitting a marketing application or supplement under the Public Health Service Act (PHS Act) and is one in a series of guidances that the Agency has developed to implement the Biologics Price Competition and Innovation Act of 2009 (BPCI Act).[2] FDA, particularly the Center for Biologics Evaluation and Research (CBER), clearly recognizes the uniqueness of plasma protein therapies and their vital role for patients with several rare diseases; PPTA's comments are limited to the effects of the BPCI Act on plasma protein therapies.

[1] Considerations in Demonstrating Interchangeability With a Reference Product: Guidance for Industry, https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537135.pdf accessed Feb. 23, 2017
[2] *See* FR Notice, 82 Fed. Reg. 5579 (Jan. 18, 2017)

147 Old Solomons Island Road · Suite 100 · Annapolis, MD 21401 USA
tel: 202.789.3100 · 410.263.8296 · fax: 410.263.2298 · e-mail: ppta@pptaglobal.org · www.pptaglobal.org
PPTA Offices in Washington · Annapolis · Brussels · Tokyo

Comments

The Draft Guidance notes that FDA will determine a biological product to be interchangeable with a reference product if the Agency determines that the information submitted in the application is sufficient to show that:

- the biological product is "biosimilar to the reference product" and "can be expected to produce the same clinical result as the reference product in any given patient"[3] and
- "for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alteration or switch."[4]

PPTA reiterates its December 23, 2010, comments to FDA on the Approval Pathway for Biosimilar and Interchangeable Biological Products (Docket No. 2010-N-0477) as below.

*Can a **plasma protein therapy** be expected to produce the same clinical result as a reference product in any given patient?*

No: As small differences in manufacturing can result in significant changes in plasma protein therapies, **it is well-understood that plasma protein therapies are not interchangeable within their respective product classes.** The interactions of such changes with potentially relevant patient characteristics are numerous and highly variable. Further, within their respective product classes, plasma protein therapies are brand-specific and address unique patient needs.

*For a **plasma protein therapy** that is administered more than once to an individual, is the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product greater than the risk of using the reference product without such alteration or switch?*

Yes: While plasma protein therapies generally have favorable adverse-event profiles, rare but serious adverse events can occur (e.g. formation of inhibitors caused by immunogenicity in clotting-factor patients, thrombosis in intravenous IG (IVIG) patients). Such adverse events often result from interactions between product (e.g. pH, IgA) and patient characteristics; small differences in manufacturing also can result in different adverse-event profiles in patients due to excipients or contaminants in such therapies (e.g. IVIG).

Conclusion

PPTA appreciates the opportunity to comment on the Draft Guidance and looks forward to continuing to provide the perspective of the plasma protein therapeutics industry as FDA implements the BPCI Act. PPTA welcomes from FDA any questions regarding these comments. Thank you for your consideration.

Respectfully submitted,

Mary Gustafson
Vice President, Global Regulatory Policy
Plasma Protein Therapeutics Association

[3] Section 351(k)(4)(A) of the PHS Act
[4] Section 351(k)(4)(B) of the PHS Act