

MAKERS OF PLASMA PROTEIN THERAPIES SUPPORT ESHOO'S BIOSIMILARS BILL

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The Plasma Protein Therapeutics Association, though opposed to including plasma protein therapies in biosimilars legislation, says a brand biologics-friendly bill by Rep. Anna Eshoo (D-CA) is the next best alternative. PPTA also supports Republican amendments to health reform legislation moving through the Senate that address biosimilars.

Eshoo's bill would require FDA to issue product class specific guidance for all biologics and ensure that biosimilars produce the same clinical results as reference products in any given patient for each condition prescribed in a product label. These provisions are absent in biosimilars legislation by Rep. Henry Waxman (D-CA), PPTA says.

Plasma protein therapies need special consideration if a biosimilar approval path is to apply to them, a white paper published by PPTA states. The nature of the therapies, the patients using them and the rare but serious adverse events that they can cause make it impossible to rule out all clinically meaningful differences in a follow-on product without testing the follow-on thoroughly in people, the paper states. Plasma protein therapies vary in manufacturing process and product characteristics from manufacturer to manufacturer.

Plasma protein is used to treat incurable, rare and chronic diseases, including hemophilia and genetic emphysema.

Eshoo's bill, the Pathway for Biosimilars Act, requires biosimilar applicants to provide clinical trial immunogenicity data showing that their products are safe, pure and potent for every indication for which the reference product is approved. FDA may waive that requirement, but it may do so only after receiving and considering public comment on a draft guidance and after publishing a final guidance. Thus, the bill would effectively require FDA to address the additional risks that plasma protein therapies pose for biosimilars regarding immunogenicity reactions, PPTA states.

Furthermore, the bill sets a standard that requires FDA to determine that the risk of switching between a biosimilar product and its reference product is not greater than risk that patients face with the reference product.

"Thus, under H.R. 1548, FDA would not be able to find two plasma protein therapies to be interchangeable before solving the conundrum that minor manufacturing process differences can produce product characteristic changes that can interact with patient-specific characteristics in ways that create different clinical results," the paper says.

The Waxman bill recognizes the risk of biosimilars causing immune reactions more frequently than reference products, but the bill addresses that risk insufficiently, the paper states. It only addresses immunogenicity in the context

of interchangeability, the paper states. The bill also does not require that the risk of immunogenicity in the context of biosimilarity or interchangeability is addressed in human clinical trial data, the paper states. But the interaction between the protein therapies' characteristics and the patients' own potentially relevant characteristics are too varied and complex to nail down without testing the products in people, the paper states.

“The rarity and unpredictability of relevant patient characteristics are such that manufacturers could not even set a baseline for each characteristic by performing clinical trials on a characteristic-by-characteristic basis,” the paper states. “Thus, manufacturers have no way to show that they have identified and analyzed all potentially relevant product characteristics.”

Absent legislative mechanisms like those in the Eshoo bill, Congress should create an exception for protein therapies, the paper says. It points out that in 2007 FDA urged Congress to statutorily exclude plasma-derived therapies. In addition, the European Medicines Agency has stipulated that an abbreviated application for complex biologics, including plasma-derived protein therapies, as well as recombinant blood clotting factor products, will not be accepted.

PPTA also said in an initial review of the numerous amendments posed to health reform legislation, it supports two: amendment 282 introduced by Sens. Michael Enzi (R-WY) and Orrin Hatch (R-UT), and amendment 297 by Sen. Kay Hagan (D-NC), Enzi and Hatch. “They best protect patient access to plasma protein therapies and allow for innovator non-patent exclusivity for a period of 12 years from the date of first licensure,” a PPTA spokesperson wrote in an e-mail. However, unlike the Eshoo bill, these amendments do not mandate FDA guidance.

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