SPECIALTY PHARMACY NEWS

Reading of Biosimilar Law Could Mean One Day or Years Until Competitors on Market

Although the health reform law included a provision for an approval pathway for follow-on biologics, the legislation left the details of how that process would work to the FDA. With many questions still remaining on how the agency will interpret various aspects of the biosimilars provision — known as the Biologics Price Competition and Innovation Act of 2009 (BPCIA) — stakeholders have begun offering their opinions on how that portion of the law should be interpreted. And, in the same way that exclusivity was an issue of debate under earlier bills, it is once again at the center of a public debate, with various congressional and industry representatives penning letters to the FDA in December and January in which they weigh in on what kind of exclusivity the bill actually provides for.

At stake is the amount of time before follow-on products could come onto the U.S. marketplace — a difference that could be one day or years before innovator products face biosimilar competition. With various studies showing billions of dollars in estimated savings from follow-on products, the clarification is huge for stakeholders.

Payers, both commercial and government — and particularly Medicare — have been hoping to soon reduce their tremendous spend on specialty drugs. And even if biosimilars offer only a 20% discount off the price of the innovator product, as most experts expect, that can add up quickly with drugs that cost tens and even hundreds of thousands of dollars per member per year.

But payer interests are weighed against the interests of innovator manufacturers — "preserving innovation and receiving a return on their investment," says Mark Armstrong, a member of the Health Care and Life Sciences practice of Epstein Becker Green Wickliff & Hall in the firm's Houston office.

In addition, "a number of manufacturers that are weighing this as an area they want to jump into" are waiting to find out "as much information as possible on what the ground rules will be," says Genia Long, managing principal of Analysis Group, an economic consulting firm. For these companies, it "comes down to the level of investment required, both of time and money."

And, points out Ralph Loren, a partner with Edwards Angell Palmer & Dodge LLP, the amount of data the FDA requires follow-on companies to produce versus using the reference product's data is important because "the more clinical testing required, the more costs" to manufacturers. "And with more costs, these products are less likely to be cheaper."

"There is so much money at stake that everyone is trying to find some way to craft an argument to back their position," says Armstrong. "Pursuing research and being able to receive less expensive alternatives…are both good objectives.…The FDA has to find a way to balance this so there is a not a winner and a loser."

Exclusivity Section Is Very Brief

In the "Exclusivity for Reference Product" section, the law states that "approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed." In addition, it says, an application that used the biosimilar pathway "may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed."

"The law itself is both very clear — and maybe not so much," says Long. "The section that refers to exclusivity for reference products is really very brief. And it doesn't use any words about exclusivity" except in the title of the section.

"The exclusivity language is not perfect," says Eric Hargan, a shareholder in Greenberg Traurig, LLP's health and FDA business practice. And although it "looks like it is [12 years of] market exclusivity,…given the concerns on both sides,…the FDA must consider the intent of Congress."

At issue is whether the reference products will get 12 years of data exclusivity — during which follow-on manufacturers will not have access to the innovator's data that is needed for the FDA application — or 12 years of marketing exclusivity — which would mean the FDA could consider applications during those 12 years but not actually approve them until after the period has expired.

"I think the exclusivity period is arguably intended to allow generic competitors to be on the market in 12 years" after the reference product's licensing, Armstrong tells *SPN*. Follow-on manufacturers could file an application that uses data from the innovator product after four years, the FDA could consider it during the period between four

and 12 years from the innovator product's initial licensing, and then the agency could approve it after 12 years.

However, if the 12 years refers to data exclusivity, the provision on four years "doesn't make sense," says Hargan. "But Congress could say, 'Oh, we didn't mean to put that in; that's an error.'" Likewise, the FDA could say that it could accept an application without the innovator data, but it could not approve it until it had those data, he says.

The act's language, contends Long, "left open room for debate on what the data exclusivity period is."

The difference has tremendous ramifications for when these products could come onto the U.S. market. "If it's marketing exclusivity, we're really talking about 12 years plus one day" until a follow-on product could be approved. But if it's data exclusivity, "it could take years at the end of the 12 years for the FDA to go through the process of evaluation," Hargan says.

FDA Notice May Have Spurred Response

Experts contend that a few factors have pushed the exclusivity issue to the forefront. "Exclusivity is what really resonates now because of the costs [of biologics], and everyone is focused on the cost of health care," Armstrong says.

"At one point or another, the exclusivity issue would have come up," Long says. But, she tells *SPN*, wording in a *Federal Register* FDA announcement may have spurred some of the current attention.

The Oct. 5, 2010, *Federal Register* announcing the early November public hearing on the law says the act "provides for a 12-year period of marketing exclusivity from the date of first licensure of the reference biological product" in the section in which it seeks comments on factors it should consider for granting "a second 12-year period of marketing exclusivity."

"The use of 'marketing exclusivity' got a strong reaction," notes Long.

The co-sponsors of the follow-on biologics bill that became the BPCIA — Reps. Anna Eshoo (D-Calif.), Jay Inslee (D-Wash.) and Joe Barton (R-Texas) — sent a letter Dec. 21 to "clarify the Congressional intent behind our legislation" and "address what appears to be an error" in the *Federal Register* question. They claim that the act "does not provide 'market exclusivity' for innovator products. Rather, it provides data exclusivity for 12 years from the date of FDA approval."

However, a letter from Sens. Sherrod Brown (D-Ohio), John McCain (R-Ariz.), Charles Schumer (D-N.Y.) and Tom Harkin (D-Iowa) contends that "the statute is clear that the FDA can begin reviewing biogeneric applications during the 12 year exclusivity period."

Other members of Congress and industry groups also have sent letters on the issue to the FDA.

Biosimilars are not a new issue for the FDA, particularly with the numerous bills calling for an approval pathway that have been introduced over the past several years (SPN 4/09, p. 1).

Hargan, a former deputy secretary and regulatory policy officer with HHS, says that during his tenure at the agency — 2003 to 2007 — there were "a lot of conversations" about biosimilars, including the issue of exclusivity. "Often with issues, there is a clear view among the staff," he explains. But, he tells *SPN*, noting that many of the career staffers now are the same players as when he was there, "the staff seems to be very much in the center of the debate," and there "is not a clear view" or bias for one side or the other. Staffers are in an "umpire or referee role."

According to Armstrong, "it's more likely than not that the FDA will be able to issue guidance that provides the detail people are looking for."

Nevertheless, Hargan says, "I don't know what the result will be when it [i.e., FDA guidance] comes out." And although there have been two stakeholder meetings and the FDA has gotten a lot of feedback, "I wouldn't be surprised if they reach back to Congress" for further input.

FDA Guidance Is Expected This Year

Hargan, does, however, believe that the FDA will issue some kind of guidance this year. Loren ventures a guess that the agency could release guidelines as early as "late spring." But he also says there will "probably be more hearings" as the FDA works through various issues.

Contending — as many industry experts have — that the biosimilars provision, as well as the overall reform bill, is "clearly not a final product," Loren tells *SPN* that he "would not be surprised to see a substantial portion of this thing rewritten over time" until a biosimilar product is approved. "This is one of those sections that will get revised, in part based on recommendations from the FDA and others."

The only potential problem that could affect the approval pathway is if the entire reform bill is deemed invalid — the chances of which "are real," Hargan asserts. Nevertheless, "the FDA is working to implement the law as soon as possible.…They are not waiting to see if the constitutional case comes down to yea or nay. They have a lot of stuff to do here, there and everywhere.…It's a high priority for the agency."

The FDA, Hargan contends, "has the capacity to get guidance out this year.…It's not like they haven't been here before. People are well aware of the back and forth within the industry. This is not their first rodeo."

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