

A Prescription for Change?

FOCUS COLUMN

By Thomas Krzeminski and Marko Zoretic

The regulatory approval system for generic drugs, established in 1984 by the Hatch-Waxman Act, has been extremely successful in lowering the high cost of prescription drugs as a result of generic competition. But in the biotech drug industry, also known as biologics, generic competition is nonexistent. Presently there is no regulatory pathway for generic versions of biologics, even after all patents covering biologics expire. As a result, manufacturers of biologics have been able to price their drugs at a premium, without fear of generic competition. But President Obama's plans to drastically lower health care costs may end the boon being enjoyed by biologic manufacturers.

Congress is already considering multiple bills directed to streamlining the pathway for generic biologics. Bipartisan groups have introduced two bills in the House of Representatives - the Promoting Innovation and Access to Life-Saving Medicine Act (H.R. 1427) by Reps. Henry Waxman, D-Calif., Frank Pallone, D-N.J., Nathan Deal, R-Ga., and Jo Ann Emerson, R-Mo.; and the Pathway for Biosimilars Act (H.R. 1548) by Reps. Anna Eshoo, D-Calif., Jay Inslee, D-Wash. and Joe Barton, R-Texas. More recently, in the U.S. Senate, Sens. Charles Schumer, D-N.Y., Susan Collins, R-Maine, Sharrod Brown, D-Ohio, and Mel Martinez, R-Fla., introduced the Promoting Innovation and Access to Life-Saving Medicine Act, which is similar to the Waxman biologics bill. Although the bills all aim to create a faster regulatory pathway for generic versions of biotech drugs, there are serious disagreements on major components of the bills. Currently, there is no simple or universally accepted definition of what constitutes a biologic. In general, a biologic is produced only from a living system, such as humans, animals, plants and microorganisms (in contrast with most medicines, which are chemically synthesized). According to the Food and Drug Administration, "[b]iological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins."

In 1982, recombinant human insulin became the first biologic approved by the FDA. Since then, more than 250 biologics have been approved for sale in the United States. Examples of biologics on the market include Epogen, Aranesp, Procrit and Neulasta, all for treating anemia; Remicade, for treating rheumatoid arthritis and other inflammatory disorders; Avastin, for treating certain cancers; and Cerezyme, used to treat a genetic condition. There are over 600 potential biologics currently being developed, including treatments for cancer, infectious diseases, autoimmune diseases, HIV/AIDS, cardiovascular disease and diabetes.

Biologics are typically quite expensive. The cost of treatment associated with many biologics often exceeds \$10,000 per year. An annual supply of Cerezyme, for example, can cost \$200,000. The annual cost of Avastin can be up to \$100,000.

"Biologic drugs often cost on average 22 times more per daily dose than chemical medications," said Deal. "It is expected approximately 50 percent of all drugs approved in 2010 will be a biopharmaceutical [i.e., biologic], a projection which only underscores the need for this legislation as the strain on state and federal governments grows."

According to a 2007 study by Express Scripts, the estimated savings to the U.S. health care system that could be realized if Congress streamlined the approval process for generic biologics would be \$71 billion over a 10-year period.

A significant hurdle to any legislation for generic biologics will be the amount of market exclusivity provided to brand-name biologics. Market exclusivity prevents the marketing of a generic version of a name-brand drug for a set period of time after the name-brand product is approved. The market exclusivity period acts to protect the significant research and development investments by brand-name companies to develop biologics. Thus, the challenge is to establish an exclusivity period that adequately rewards innovation, while also encouraging competition.

In the case of chemical drugs, the Hatch-Waxman Act generally provides five years of market exclusivity. For biologics, the world's largest biotech trade organization, BIO (Biotechnology Industry Organization), would like a lengthy exclusivity period, i.e., 14 years. Generic drug makers, like Teva Pharmaceutical Industries, however, would like a significantly shorter period. Thus, brand-name companies appear likely to support the Eshoo bill, and generic drug makers appear likely to support the Waxman and the Schumer-Collins bills.

The Waxman biologics bill provides a five-year exclusivity term and provides a three-year exclusivity term to certain modifications of a previously approved product. The exclusivity scheme is consistent with the Hatch-Waxman Act. The exclusivity terms could be extended an additional year under certain circumstances. The bill also provides 180-day exclusivity to the applicant of the first interchangeable biosimilar product that receives FDA approval. An interchangeable product is one that could be switched one or more times with the reference product "without an expected increase in risk of adverse effects ... or diminished effectiveness." During the 180 days, the FDA could not approve another interchangeable biosimilar product. The Schumer-Collins bill closely mirrors the Waxman biologics bill.

In contrast, the Eshoo bill provides a 12-year exclusivity period. The exclusivity term could be extended an additional two under certain circumstances. The Eshoo bill also provides an additional six months of exclusivity for testing for use in pediatric groups. The bill also provides at least two years of exclusivity to the first approved interchangeable biosimilar product.

Various industry and health care groups have already chosen sides. The Generic Pharmaceutical Association supports the Waxman biologics bill, saying it, "achieves the right balance of fostering pharmaceutical innovation while also making affordable medicines available to consumers." The California Public Employees' Retirement System, which represents over 1.6 million California public employees, retirees and their families, "applauded" the Waxman biologics bill and stated that it "achieves a

balance between incentives for innovation and the competition that is required to reduce costs for patients and purchasers such as CalPERS." AARP, GM and the AFL-CIO have also expressed their support for the Waxman biologics bill.

Biotechnology Industry Organization CEO Jim Greenwood, however, described the bill as "filled with potholes" and said it "would take patients and industry down the wrong path - a path that jeopardizes the continued development of new breakthrough therapies and potential cures for debilitating diseases such as multiple sclerosis, HIV/AIDS and Alzheimer's." Referring to the Schumer-Collins bill, Greenwood said, "While well-intentioned, the bill ... follows its companion bill in the House [the Waxman biologics bill] through the looking glass to a world of biosimilars that would jeopardize patient safety and undermine future medical breakthroughs."

Expressing its support for the Eshoo bill, Greenwood said the bill "lays out an effective, reasonable and safe pathway to biosimilars" and that it "provides patients with the right balance between innovation and competition." Eli Lilly commended Eshoo, Inslee and Barton.

"Making biotech discoveries entails many years of research, massive investments and high risk," said Robert Armitage, Eli Lilly's senior vice president and general counsel. "This bill makes certain that innovator companies can continue to make these types of investments in new therapies for patients, and that, once a reasonable period of time has passed for recouping its investment, generic companies can copy those innovations in a safe, scientifically sound manner."

According to Debra Barrett, senior vice president of government affairs of Teva Pharmaceutical Industries, the Eshoo bill "is clearly written to protect brand-name drugs and their innovator's government-granted monopoly at the expense of access and innovation. This bill will dampen innovation and deny Americans access to more affordable health care."

Kathleen Jaeger, president and CEO of the Generic Pharmaceutical Association, said that the Eshoo bill "is the wrong road for patients looking for safe and affordable biogeneric medicines, particularly during these difficult economic times. It is a long route filled with needless roadblocks that will keep patients from getting needed medicines in a timely manner."

President Obama's plans to drastically lower health care costs may ultimately decide the fate of the exclusivity period.

During the election, Obama pledged his support for short exclusivity periods in order to get affordable biogenerics to market. He reiterated that promise in his first budget proposal, which was announced in late February: "The administration will accelerate access to make affordable generic biologic drugs available through the establishment of a workable regulatory, scientific, and legal pathway for generic versions of biologic drugs," according to the budget documents. "In order to retain incentives for research and development for the innovation of breakthrough products, a period of exclusivity

would be guaranteed for the original innovator product, which is generally consistent with the principles in the Hatch-Waxman law for traditional products."

Based on the president's remarks, it appears that he favors an exclusivity period closer to five years. Regardless of the length of exclusivity ultimately adopted, there can be no doubt that there is strong support in the White House and in Congress for new legislation that would create a pathway toward cheaper, generic versions of biologic drugs.

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