Generic Biologics Still on Radar Screen in Congress

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A Congressional push for fast-track approval of generic biologics probably won't have any effect on insulin costs for most patients with diabetes, mainly because the types of insulins most patients use now are still on patent, according to an expert.

Patents for several insulin formulations—both regular and NPH—have expired in this decade: Humulin (Eli Lilly & Co.) in 2001 and Novo-Nordisk's Novolin in 2005. However, the Food and Drug Administration has not issued its in-progress guidelines for approval of several new follow-on biologics, each of which is claimed by its manufacturer to contain the identical active ingredient as the approved product and therefore, they argue, should not need additional testing.

Debate remains as to whether existing regulations would or should allow for approval of such products. Applications for new biologics are regulated by the 1944 Public Health Service Act. However, small-molecule drug products are regulated by the Food, Drug, and Cosmetic Act of 1938, which allows accelerated approval of new drugs based on prior evidence.

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In 2006, the FDA approved a follow-on of the recombinant human growth hormone Omnitrope, manufactured by Sandoz, but the agency said it considered that product to be not a generic but a "follow-on protein product," because it had made no determination of therapeutic equivalence.

According to the FDA, other proteins that have received fast-track approval in this manner include GlucaGen (glucagon recombinant for injection), Hylenex (hyaluronidase recombinant human), Hydase and Amphadase (hyaluronidase), and Fortical (calcitonin salmon recombinant) nasal spray. A member of his staff confirmed that Rep. Henry Waxman (D-Calif.) will reintroduce a bill submitted last session, H.R. 6257, that would effectively force the FDA to fast-track approvals of follow-on generic biologics—a bill that some believe will lead to the production of generic insulins and thus lower costs for state governments and insurers. The date of reintroduction has not been determined, the staff member said.

A Senate version of the same bill, S. 4016, was sponsored by Sen. Hillary Clinton (D-N.Y.), with Sen. Charles Schumer (D-N.Y.), Sen. Patrick Leahy (D-Vt.), and Sen. Debbie Stabenow (D-Mich.) as cosponsors. In each house of Congress, the bill was referred to committee but expired in December, when the 109th Congress ended, as do all pending bills not passed before the end of a session.

Dr. Bill Law Jr., an endocrinologist in private practice in Knoxville, Tenn., said in an interview that confusion in the lay media about the difference between nonanalogue human insulins and analogue human insulins is behind these legislative efforts and public support for them.

"It's only after the 20-year patent law has expired [on a human analogue insulin] that it would be eligible for a generic company to come in and make one," he noted. And as to the nonanalogue varieties, "unless the companies can sell one for less than $16 a vial, it's not going to change the cost" to the patient, he said. This confusion has given rise to false hopes for a drastic reduction in insulin costs for most patients, according to Dr. Law.

Regarding approval of follow-on biologics, "this is not like creating a pill," wherein only the active ingredient is important, he added. "Everything else that's in that pill was specifically added by the manufacturer of that pill, whereas the insulin we're talking about is a biologic system," and thus cellular byproducts can't be as easily modulated. "It's totally different from making a pill, where you have complete control over what goes in that pill."

Thus the safety of a generic biologic cannot be established as easily as that of a drug, Dr. Law said. "From my standpoint as a doctor treating patients, it's not enough just to show that in that bottle there's a certain amount of insulin. I want to know what else is in that bottle." ■