Trend toward Generics Puts Spotlight on Biopharmaceuticals: FDA Slow to Develop Guidelines as Congress and Public Wait Impatiently

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One of the few “positive” notes—and I use this term advisedly—in the surveys on federal health spending, published in January, was that prescription drug prices increased by only 8.2% in 2004, the smallest increase in the past decade. A major reason, according to the Centers for Medicare & Medicaid Services (CMS) and published in the current edition of Health Affairs, was an increasing use of mail-order pharmacies and a corresponding decrease in the number of customers who used retail pharmacies. Mail-order pharmacies, of course, are more likely to switch customers to lower-priced generic drugs—hence the lower rate (8.2%) of drug inflation in 2004.

This small decrease in drug price inflation is good news, of course, but it is not as good as it could be. Substitutions of generic brands are available only for large-molecule drugs manufactured by conventional means; they are not available for “biotech” drugs, which are proteins made from living cells, often using recombinant DNA technology.

The U.S. Food and Drug Administration (FDA) does not allow generics to be substituted for biotech drugs, mainly because no drugs of this type had been developed back in 1984, when Congress passed the Hatch–Waxman law. This law lays out the requirements for the FDA approval of generics for conventional drugs.

The lack of generic substitutes for biotechnological therapeutic products is problematic because of their high costs. “Some of these new wonder therapies can cost over $10,000 per course of treatment,” said Senator Orrin Hatch (R-Utah) (one of the sponsors of the Hatch–Waxman Act) in a speech to the Generic Pharmaceutical Association (GPhA) last September. “For example, human growth hormone can cost $25,000 per year.”

More than 1,000 FDA-approved biological products are now on the market, another 350 are in various stages of human clinical testing, and more than 1,000 others are in the development pipeline. Many of these products are irreplaceable lifesavers, albeit expensive ones.

Those high prices weren’t much of a concern to Congress before January 1, 2006. But because that date signaled the start of the Medicare outpatient drug benefit, the high prices of these biotech drugs have become a concern for a Congress struggling to wrestle a Sumo-like federal deficit to the ground. This drug benefit, which was initially forecast to cost about $400 billion over a period of 10 years, now may cost the U.S. Treasury closer to $700 billion. That prospect has focused Congress’s attention on strategies for drug price reductions.

As a result, Senator Hatch told the GPhA: “As I have said for more than five years now, cost factors alone compel a full examination and public discussion of the merits of developing and implementing a fast-track review and approval system that can reduce the price of biopharmaceuticals once patents expire.”

He didn’t go as far as to say that he and his Democratic partner, Representative Henry Waxman (D-Calif.), would introduce legislation to force the FDA to establish a process for allowing generic companies to file abbreviated New Drug Applications (NDAs) for biotech copies. The agency has resisted this, arguing that it would be impossible for a generic company to duplicate the manufacturing process used by a biotech company. Instead, the FDA requires generic companies to develop their own manufacturing process for a generic drug that has gone off-patent and to submit an NDA, based on clinical trials, for a generic biotech drug. Whether justified or not, and whether they are based on safety concerns, those requirements have kept generic versions of Amgen’s Epogen (epoetin alfa), Eli Lilly’s Humulin (insulin of recombinant DNA origin), and other important, expensive biopharmaceuticals off the market.

Instead of introducing legislation, Senator Hatch seems willing to wait for the FDA to issue long-awaited guidelines, which will ostensibly make it easier for generic companies to gain approval for biotech copies. Those guidelines have been in the works for more than a year.

In early 2005, former FDA Commissioner Lester Crawford told the GPhA at its annual meeting, “I think we now have the science to fashion a generic biologics program.”

Scott Gottlieb, deputy commissioner for medical and scientific affairs at the FDA, told The Wall Street Journal on December 27 that the guidelines had been delayed because of their complexity.

Senator Hatch thinks those guidelines should cover process validation, allowing them to be used to help establish the critical manufacturing steps and assay parameters for certain medically or commercially significant off-patent biological products. He also believes that the FDA should consider collaborating with an organization such as the U.S. Pharmacopoeia, the Institute of Medicine, or another interested party, to help address the technical issues that need to be resolved in order to expedite “fast-track” approvals for off-patent biopharmaceuticals.

The senator says that he is willing to wait for the FDA for the time being. However, the agency has been without a commissioner since Lester Crawford left last fall, and the absence of a top leader makes it much more difficult for the agency to move forward on this kind of controversial issue.