Experts Divided on Biologics Becoming Generic

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ARLINGTON, Va. — With the annual price tag of biologic agents reaching well into the tens of thousands, pressure to find lower-cost alternatives caused scientists and drug companies to air their concerns at a workshop on biologics becoming generic.

At the heart of the discussions were fundamental questions such as the degree to which follow-on proteins could be judged to be similar enough to already approved agents and how the federal government might compare agents to certify whether a generic was ready for the marketplace.

Brand-name manufacturers argue that generic companies need to do clinical tri- als to prove interchangeability, and generic firms make the case that product characteristic alone should suffice.

The issue of generic versus brand-name biologics is reminiscent of the fight to get more generic small-molecule drugs on the market in the late 1970s and early 1980s. At that time, generic drug manufacturers could only get approval for their medications if states independently proved their safety and efficacy, without using any data from the brand-name manufacturer.

Then, in 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act, otherwise known as the Hatch-Waxman Act. This law allowed generic manufacturers to get their drugs approved if they could simply demonstrate that their drug was bioequivalent to the brand-name counterpart. The law also allowed generic drug manufacturers to begin testing a new generic before the patent expired on the brand-name drug.

These changes helped shorten the average time it took for a new generic drug name’s expiration and the introduction of the generic from 3 years to 18 months. But the law excluded biologics because there were only a few biologics on the market and because bioequivalence was difficult to prove.

Demonstration of bioequivalence may work really well for determining the comparable safety and efficacy of two chemi- cal generic drugs, “but there’s little evidence that this chemical drug paradigm would work for biopharmaceuticals,” said Anthony Lubinecki, S.C.D., vice-president for technology transfer at Centocor, a brand-name pharmaceutical manufacturer in Radnor, Pa.

The Generic Pharmaceutical Association (GPhA) supports an abbreviated approval process for generic biologi- cals, but at the same time it’s recognized that “biophar- maceuticals comprise a continuum of complexity, from relatively simple bio- pharmaceuticals, such as penicillin, to those that are highly complex….”

As such, a one-size-fits-all paradigm for technical and regulatory approaches would be inad- equate,” said Gordon Johnston, vice-president for regulatory affairs at GPhA.

Another issue is the potential for pa- tients taking generic biologics to develop immunogenicity, said Dawn Viveash, vice-president for regulatory affairs at Agen, a biologies manufacturer in Thousand Oaks, Calif. Depending on the individual, such effects can range from “none at all to an allergic or anaphylactic type of reaction, or they may have an impact on clear- ance, which could reduce efficacy,” she said at the workshop sponsored by the Food and Drug Administration and the Drug Information Association. Many of these issues aren’t likely to be settled any- time soon.

The FDA started working on two bio- logic ‘guidance documents’ on insulin and human growth hormone 4 years ago.

At the time, “those documents were ex- pected to be issued within 60 days,” said GPhA’s Mr. Johnston. “More than 1,000 days later, we’re still waiting.”

The FDA also is developing a general guidance document on the development and approval of generic biologics, however, there is no timeline for issuing the final product, according to Dr. Darrell Royal, Ph.D., deputy director of the Center for Drug Evaluation and Research’s Office of Pharmaceutical Science.


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