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Health-care reform creates large-dollar biosimilar drug market

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Health-care reform brought about sweeping changes to our nation's health-care system. Much of the commentary has been focused on Medicaid expansion and the individual coverage mandate, punctuated by the U.S. Supreme Court finding the law constitutional in a 5-4 decision last June. The general public has not concerned itself with most of the act, particularly its establishment of a regulatory pathway for biosimilar versions of biologic medicines. The act created the Biologics Price Competition and Innovation Act (BPCIA), thereby starting the multibillion-dollar, biosimilar drug market of tomorrow and enhancing our future health-care savings. Its creation is analogous to a 1984 law, which established our current generic drug market and is colloquially referred to as the Hatch-Waxman Act in reference to its eponymous, congressional sponsors. Unlike today's generic drugs, there are no generic or biosimilar versions of biologic drugs.

The biosimilars market is expected to be $19.4 billion by 2014 with an astonishing compound annual growth rate of about 85 percent. That value provides a glimpse into the $100 billion in branded, biologic sales expected to lose patent protection by 2020. The increasing demand to reduce health-care costs created numerous opportunities in the global market and the BPCIA will increase the shares and profit margins of the few market players. While we witness the rare birth of a multibillion-dollar market, how will that differ from generic drugs?

What are drugs as compared to biologics?

A typical drug is often-referred to as a "small molecule" due to its simple structure relative to a biologic. Think of a bicycle as compared to a car. A small molecule drug is generally made using standard chemical synthesis by combining specific ingredients in a defined reaction scheme. In contrast, a biologic is manufactured in a living system such as a microorganism, plant or animal cells. Most biologics are very large, complex molecules or a mixture thereof.

Small molecule drugs have well-defined chemical structures, which can be positively confirmed through well-known analytical techniques found in any college chemistry laboratory. By contrast, it is difficult — with some opining impossible — to fully characterize a biologic using current methods, meaning that the structure of any corresponding biosimilar product will also be unknown. Comparative analytical data will thus be a cornerstone in this evolving market and related intellectual property landscape.

Branded biologic companies argue that the process defines the product and that small changes may significantly alter its effects in and on the body. Consequently, manufacturing controls are not likely to be publicly disclosed (e.g., through patent applications or other publications) and will remain confidential. Without such patent protection, one would expect a corresponding uptick in nonpatent efforts, such as citizen petitions and the like, to block the approvals of competing biosimilar products.

Generics drugs v. biosimilars

Under current U.S. Food and Drug Administration (FDA) regulations, generics of small molecules are submitted in what is known as an Abbreviated New Drug Application (ANDA) and must have the same active ingredient, strength, dosage form and route of administration as the branded drug.

A generic product will also need to show bioequivalence, meaning there is no significant difference in the rate and extent that the generic product is available as compared to the brand. Bioequivalence is generally determined through relatively simple in-vivo and-or in vitro studies and without the need for full-scale, expensive clinical trials. Once these criteria are satisfied, the FDA may classify the generic as therapeutically equivalent to the brand, meaning that the generic can be fully substituted at the pharmacy. This is the generic drug market in the United States.

In contrast, the BPCIA establishes requirements for a biosimilar product application, which are more comprehensive than an ANDA. A biosimilar application must contain, among other things, information demonstrating that the biologic product is biosimilar to a brand product based upon data derived from analytical and animal studies. Also required is one or more clinical studies, if FDA determines them necessary, making this the largest financial risk in developing a biosimilar product; this is the key differentiator from an ANDA.

Any required clinical studies must include an assessment of immunogenicity and pharmacokinetics or pharmacodynamics, sufficiently demonstrating the safety, purity and potency of the biosimilar product.

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Regarding the degree of sameness to the brand product, the BPCIA uses the concepts of "biosimilarity" and "interchangeability." Under the statute, "biosimilarity" means the product is highly similar to the brand despite any minor differences in clinically inactive components and there are no clinically meaningful differences between the products as to safety, purity and potency. 42 U.S.C. § 262(i)(2).

Going a step further, "interchangeability" means the product can satisfy the biosimilarity standard and also that the product is expected to have the same effect as the brand in any patient and there is no increased risk of safety or diminished efficacy when switching from the brand product. 42 U.S.C. § 262(k)(4). Importantly, like therapeutically equivalent generic drugs, interchangeable biologic products "may be substituted for the reference product without the intervention of the prescribing health-care provider" (42 U.S.C. § 262(i)(3)) just as is done with generic drugs.

But how soon will we see a biosimilar product? Like Hatch-Waxman, the BPCIA contains various market and data exclusivities to balance the incentives for brand and generic-biosimilar companies alike. Most notably, the BPCIA establishes a four-year exclusivity period from the date of first approval of the brand product, during which a biosimilar application may not be filed, and another eight years after that before the biosimilar application can be approved and marketed. These inherent delays mean we are several years from the first approval of a biosimilar product.

While those years may pass quickly, the market effects will be long-term and are long-awaited. We are at the very beginning of a bona fide market evolution whose time has come. Only time will tell if our health-care savings on biosimilars will approach the nearly $1 trillion saved on generic drugs over the last decade.