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Understand the intricacies of generic biologic drugs

New England's highly educated and entrepreneurial life sciences sector provides a deep talent pool for discovery, development and commercialization of therapeutic biologics. Biologics are extremely successful in treatment of certain diseases and constituted about a $78 billion market in 2009. Generic versions of these drugs — "biosimilars" — now have an abbreviated pathway for FDA approval, by virtue of enactment of the health care reform bill in March, which included the "Biosimilars Act."

In the upcoming months, the FDA will implement the Act by setting forth detailed requirements for approval of a biosimilar. There is a great deal of uncertainty around the final shape of the legislation, which is closely watched by biotech and pharma companies.

An abbreviated pathway for FDA approval of generic drugs was provided by Congress in 1984 under the Hatch-Waxman Act. Conventional generic drugs are chemically synthesized, whereas biologics are made by cells and therefore are more complex and subject to variability in their structure and function. Biologics include, for example, Herceptin (breast cancer), Erbitux (colorectal cancer), and Humira (arthritis). These drugs are FDA approved via a legal route called a BLA (biologic license application), which is a full clinical study of the drug.

The premise of the Biosimilars Act is that an FDA-approved innovator drug can enjoy 12 years of exclusivity in the U.S. market before a "biosimilar" can be approved to enter the market. This is a period of clear market protection for an innovated drug, even in the absence of patent protection. This period of time can be lengthened via other regulatory exclusivity periods, such as orphan and pediatric exclusivities.

Another premise of the Act is that a biosimilar must wait until four years after biologic approval before it can even submitted an application to the FDA. The filing of a biosimilar application is a critical time that kicks off a series of complex legal strategies on both sides involving both patent and regulatory exclusivity. The kickoff starts a demanding exchange of substantive scientific and patent information between the innovator and the biosimilar, commencing with the biosimilar providing a confidential copy of its FDA application to the innovator drug sponsor — this is the first time the innovator will have access to this detailed report. Within 60 days, the innovator must have in place its strategy, and provide a list of selected patents that protect the innovator's drug.

INSIDER VIEW

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A key issue in determining the actual date of biosimilars drug market entry, even given FDA approval, will be the innovator blocking patents. The patent exclusivity term is independent of the FDA exclusivity period. However, the biosimilar approval route intimately involves not only identification of relevant innovator biologics patents but also a detailed analysis of their strength and scope — by both the innovator drug sponsor and the generic challenger, as a patent list must be agreed on within several months after filing of the biosimilar application with the FDA.

To approve a "biosimilar," the FDA must decide how similar a biologic must be to the approved biologic in order to be considered "the same" drug. The Act sets forth a definition for "biosimilarity" which includes two requirements: the generic drug is "highly similar" to the approved drug, "notwithstanding minor differences in clinically active components," and must exhibit "no clinically meaningful differences" relative to the approved drug in terms of safety, purity, and potency. The FDA will determine what this definition really means by implementing detailed regulations. The FDA can request, on a case-by-case basis, any biosimilar data it wishes to see, and also has the power to waive any data requirements.

This immediately begs the question of what resources a biogenerics company should commit to testing of its biosimilar drug without specific guidance from the FDA. It also suggests there will be intense activity around the filing of citizen petitions, which are essentially letters to the FDA arguing why the FDA should or should not approve a given generic drug.

A significant provision of the Biosimilars Act is "interchangeability" status – but only if the biosimilar is shown to produce the "same" clinical result "in any given patient." To achieve "interchangeability" status, the biosimilar must demonstrate that the risk of alternating or switching between the biosimilar and innovated drug "is not greater than the risk of using the innovator drug without such alternation or switch."

Relatively few biosimilars have been launched to date due to high barriers to entry. However, those that have reached the market are discounted by 20 to 30 percent. Therefore, increasing pressure for drug price reduction and high market value for these drugs provide strong incentives for use of this new regulatory approval pathway. New challenges are presented by implementation of the Biosimilars Act, and also significant opportunities.

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