A PBM Perspective on the Evolving Biosimilars Landscape

The first biotechnology drug, insulin sold under the name Humulin, was patented in 1982. Since then, biologic medicines have revolutionized the treatment of conditions such as diabetes and cancer, multiple sclerosis and rheumatoid arthritis. Biologic drugs are developed from living organisms, which makes them expensive to develop and produce. Today the cost of biologics is increasing at a faster pace than any other component in health care.¹ These high-tech drugs are often the only effective treatments for the most severe diseases, but their high price tags can put them out of reach for many patients.

The development of biosimilars represents an important opportunity to make biologic drugs more accessible. Increased product competition may lead to lower prices and help hold down health care costs, according to the Generic Pharmaceutical Association (GPhA).² But no one knows how quickly or how widely biosimilars will become available – or how much they will cost. This paper summarizes key issues related to biosimilars and presents a pharmacy benefit manager’s perspective on the opportunities and challenges these drugs represent for pharmacy benefit managers and plan sponsors.

What are biosimilars?

Biosimilars are copycat versions of biologic drugs. Like traditional generic drugs, they can only be sold after the original drug’s copyright, or patent, has expired. Unlike traditional generic drugs, biosimilars are not exact chemical copies of the original medication. Because they are created from organic material, they can never be exactly the same as the original biologic. This makes it difficult to determine whether a biosimilar is as effective as the original, and is the main reason biosimilars have been slow to come to market.

The Biologics Price Competition and Innovation Act of 2009 (BPCIAct) established a pathway for biosimilar drugs to be reviewed and approved by the U.S. Food and Drug Administration (FDA). This act was signed into law as part of the Affordable Care Act of 2010, and cleared by the U.S. Supreme Court in June 2012. Additional guidance from the FDA has helped to clarify how biosimilar drugs may be evaluated and approved. As the path to market becomes clearer, investment in biosimilar research and development is increasing.³

Making the most of opportunity

Rising demand for biologic drugs and the potential to charge relatively high prices for these products make biosimilar development attractive to pharmaceutical companies.

Manufacturer revenues from biologics – most of which are classified as specialty drugs – have been growing at an average annual rate of about 20 percent since 2000.⁴ In 2010, sales of biologics reached $100 billion worldwide.² Demand for biologics will accelerate in coming years as the number of people above age 65 increases in the U.S.⁵ Biologic drugs are used to treat chronic and complex conditions (such as kidney disease or cancer) that are more prevalent in an older population.
Expiring patents will give biosimilar manufacturers an opportunity to compete for a share of biologic drug profits. Major biologic drugs, including Roche’s Herceptin® and Rituxan®, Sanofi’s Lantus®, and Amgen’s Neulasta®, are expected to lose patent protection starting in 2012.6 By 2015, biologics responsible for $20 billion in annual sales will go off patent, leaving the field open for competitors.7

Back Door Biosimilars?
A few biologic drugs (Hylenex, GlucaGen, and Omnitrope) have been approved through the pathway for traditional generics. In approving these drugs, the FDA relied on a combination of new scientific data and information from the original drug review.

Biosimilar approvals could follow a similar model, or could require costly independent clinical trials.

Unresolved questions will affect biosimilar availability, management and costs
While the BPCIA established a pathway for biosimilar drugs to be reviewed and approved by the FDA, significant questions remain.8 Among the unanswered questions are several that will affect the availability of biosimilars, their cost, and the ease with which they can be managed by health plans and pharmacy benefit managers.

The first is how the FDA will determine similarity, since a biosimilar is not an exact replica of an innovator product. Currently, the ruling states that a biosimilar must be both highly similar and clinically comparable in safety, purity and potency to the original product. But it is not yet clear how the FDA intends to evaluate these factors.

No two proteins or enzymes are precisely identical and slight changes in the production process can produce subtle variations. These characteristics will make it tricky for regulators to confirm whether a biosimilar drug is as safe and effective as the original product. The burden of proof will fall to manufacturers. To gain approval, biosimilars are likely to require independent and extensive clinical trials which would increase the time and money required to develop them. If the outlay required is too great, manufacturers may be reluctant to invest in biosimilar development.

Substitution is another unresolved question that will affect biosimilar management. Traditional generic drugs are substituted for the brand name drug every day. But because biosimilars are not exact copies, they must meet certain criteria before they can be substituted without the patient’s consent (see Figure 1).

To be eligible for substitution, a biosimilar must deliver the same clinical result as the original drug, and must not create an additional safety risk as a result of switching. Together, these criteria add up to “interchangeability.” It is not yet clear how much evidence the FDA will require from drug makers in order to establish interchangeability.

Figure 1 Requirements for Interchangeability

1. Biosimilar
   - The FDA has declared the product “biosimilar” to the reference product.

2. Same clinical result
   - Any patient would receive the same clinical result with the biosimilar as with the reference product.

3. No switching risk
   - Risks of switching are not greater than with repeated use of the reference product.

= Interchangeable
   - May be substituted without a doctor’s authorization.
A biosimilar’s interchangeability will affect the ease with which patients can switch from the original drug to the biosimilar drug. Biosimilar drugs that do not meet the standards for interchangeability will require outreach to educate physicians and patients about alternate or preferred treatments. Without the ready ability to move patients to biosimilars, manufacturers of these drugs would need to actively market their products. The need for advertising would increase the cost of biosimilar drugs.

Other unresolved questions, such as how biosimilar drugs will be named, add to the uncertainty in this emerging market. Guidance from the FDA will continue to shape the issues, but it is likely that some questions will not be resolved until the laws and limits are tested through real-world experience.

**Will biosimilars rein in drug spending?**

Competition from biosimilars is expected to bring down the cost of biologic medicines. The Congressional Budget Office (CBO) has estimated that the resulting increase in competition from biosimilars will yield lower prices for these medicines. Estimates from various economic impact studies pin the projected savings from $42 billion on the low end to as high as $108 billion over the first 10 years of biosimilar market formation.

However, it is important to be realistic about biosimilars’ savings potential. Current market examples indicate biosimilars may sell for 10 to 30 percent less than the original products. Biopartners has announced that it will offer its Valtropin® growth hormone biosimilar at a 20 percent to 25 percent discount, and Sandoz says it will sell its generic EPO for 30 percent less than the original. This is nowhere near the 80 to 90 percent price reduction payers are accustomed to with traditional generic drugs.

In fact, discounts for biosimilars will probably never be as deep as payers would like them to be. Ultimately, the long development cycle, clinical trial expenses, ongoing manufacturing costs and the need for sales and marketing may limit the number of manufacturers in the market. Less competition translates directly to less competitive prices for biosimilars.

**What should plan sponsors do to prepare for biosimilars?**

Today there are over 400 biosimilars in development. Yet the lack of clarity and the untested regulatory pathway suggest that it may be 2014 or beyond before these drugs become more widely available. Still, now is the time to prepare for the eventual reality of biosimilar competition. Prime Therapeutics (Prime) is actively preparing for this reality, and has the following recommendations for plans and plan sponsors:

- **Reconfigure benefit designs now to capitalize on biosimilar savings opportunities.**
  The level of co-pay will be a crucial factor in biosimilar adoption; unless the member’s out-of-pocket costs for biosimilars are significantly lower, there will be little incentive to drive use of lower-cost or preferred biosimilar drugs. Prime recommends a benefit design that allows for clear distinction between preferred and non-preferred specialty drugs.
• Prepare for heightened communication with physicians and patients.
A lack of experience and the newness of the regulatory pathway may make physicians reluctant to prescribe biosimilars. Health plans and pharmacy benefit managers will need to actively educate prescribers about preferred treatments and coverage guidelines. Patients are likely to trust their physician’s advice on biosimilars, but will also need extra education about benefit coverage, questions to ask and the benefits of using preferred treatments.

• Publicly promote biosimilars.
Biosimilar products can exist only if drug manufacturers are willing to assume the risk to bring their products to market. If manufacturers do not see potential for a return on investment, the approval pathway for biosimilars may go unused and savings potential will wither. Showing public support for biosimilars may be one way to keep the pathway open and the pipeline robust. It will signal to manufacturers that health plans and plan sponsors are in favor of biosimilar development. Promotion may also help members accept these new drugs as safe and effective treatment options.

• Help shape thoughtful legislation.
Right now, several states are considering laws that would make it difficult for biosimilar drugs to be deemed interchangeable. To compete, biosimilar manufacturers would need to adopt advertising and marketing strategies that would add to their costs, and could reduce the savings from these drugs. Prime believes legislation that places limits on the potential clinical uses of biosimilars is premature. Health plans and plan sponsors should consider getting involved in shaping legislation that will support, rather than hinder, biosimilar development.

1 http://www.gphaonline.org/issues/biosimilars
6 http://www.prweb.com/releases/biosimilars/follow-on_biosimilars/prweb9386524.htm