Biosimilars Market Access in the US
Hot Topic
Report extract

Ref Code: DMKC0170737
Author: Amanda Micklus
BIOSIMILARS ARE EXPECTED TO DELIVER CONSIDERABLE COST SAVINGS FOR THE US HEALTHCARE SYSTEM

High price of biologics is a key driver of increased drug spending

Biologics are generating significant annual sales and growth; US biologic sales are forecasted at $111bn in 2016, representing a compound annual growth rate of 9% since 2012 (Datamonitor Healthcare, PharmaVitae Analytics: Forecast Analysis, February 2017). This growth is being driven by two key factors: an increasing patient population due to indication expansion, new products launched, and greater awareness and diagnosis of target diseases; and price increases. Biologics are among the most expensive drugs in the world, with annual treatment costs of some of the most recently launched immunotherapies as high as $150,000 per patient (Weintraub, 2014). Moreover, as combination therapies come to market, those expenses are expected to increase – the approved combination of Opdivo (nivolumab; Bristol-Myers Squibb/Ono Pharmaceutical) and Yervoy (ipilimumab; Bristol-Myers Squibb) comes in at an annual cost of $256,000 (Bloomberg, 2015). Over the past few years, many biologics have seen their prices rise, and this trend has caught payers’ attention.

"I think the trend is what is the most alarming; I think for me the sort of astronomical jump in pricing has been a trend that does not show any sign of abatement, I think that is first and foremost the concern."

US payer

The cost of biologics varies depending on the disease

The cost of biologics varies considerably by therapy area and indication, with oncology drugs, for example, tending to have a higher price point than products used in more chronic conditions such as rheumatoid arthritis and psoriasis. Despite the low price of insulin, sales are high because the diabetic patient population is large. Many biologic agents are therefore considered big budget items by payers.

Payers look towards biosimilars as a means of decreasing specialty drug spend

The trend towards continued inflation-busting specialty drug spend is a worry for payers, and many are looking towards biosimilars as a means of reducing that segment growth and providing funding for new specialty drugs entering the market, especially in the field of oncology. Estimates for savings potential vary, but leading US pharmacy benefit manager Express Scripts has stated that filgrastim and infliximab could deliver an estimated $22.7bn in savings during their first decade on the market. Zarxio (filgrastim-sndz; Sandoz) is projected to account for $5.7bn, with biosimilar infliximab saving a further $17.0bn. These estimates are based on a 30% discount in price for the biosimilars and use in 30% of treatment-naïve patients only, without any switching from the reference products in existing patients (Maas, 2014). A further analysis by Express Scripts increases the cost savings benefit to $250bn during 2014–24 if biosimilars for other products are included, such as those for Avastin, EpoGen, Humira, Herceptin, Neulasta, and Rituxan (Zack’s Equity Research, 2016). Such estimates vary, however. A study by the IMS Institute pegs just the five-year savings during 2016–20 at $112bn (Pharmaceutical Commerce, 2016). Meanwhile, the Rand Corporation says biosimilars could provide a total of $44bn in cost savings during 2014–24 as a result of reduced direct spending on biologics, mainly anti-tumor necrosis factor drugs, long-acting insulins, and monoclonal antibody antineoplastics (Rand Corporation, 2014).
### Table 3: FDA guidance on biosimilars published to date

<table>
<thead>
<tr>
<th>Category</th>
<th>Title</th>
<th>Type</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biosimilarity, procedural</td>
<td>Reference Product Exclusivity for Biological Products</td>
<td>Draft guidance</td>
<td>August 2014</td>
</tr>
<tr>
<td>Biosimilarity</td>
<td>Scientific Considerations in Demonstrating Biosimilarity to a Reference Product</td>
<td>Final guidance</td>
<td>April 2015</td>
</tr>
<tr>
<td>Biosimilarity</td>
<td>Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product</td>
<td>Final guidance</td>
<td>April 2015</td>
</tr>
<tr>
<td>Biosimilarity, procedural</td>
<td>Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants</td>
<td>Final guidance</td>
<td>November 2015</td>
</tr>
<tr>
<td>Biosimilarity</td>
<td>Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product</td>
<td>Final guidance</td>
<td>December 2016</td>
</tr>
<tr>
<td>Naming</td>
<td>Nonproprietary Naming of Biological Products</td>
<td>Final guidance</td>
<td>January 2017</td>
</tr>
<tr>
<td>Interchangeability</td>
<td>Considerations in Demonstrating Interchangeability With a Reference Product</td>
<td>Draft guidance</td>
<td>January 2017</td>
</tr>
</tbody>
</table>

FDA = US Food and Drug Administration

Source: FDA, 2014; FDA, 2015c/f/g/h/k; FDA, 2016e; FDA, 2017a/b
Substitution and Naming Policy

BIOSIMILARS NAMING IS A CONTENTIOUS ISSUE

Naming policies for biosimilars and how they relate to substitution is one of the main ongoing issues around biosimilars and one that has courted a significant level of controversy. The originator companies insist that biosimilars should have a different International Nonproprietary Name (INN) to the originator product, largely due to the fact that biosimilars are not exact copies, and, at least in theory, could result in different efficacy or safety compared to the original biologics. This issue does not exist for small molecule generics as they are exact copies of the originator brand and can therefore be assigned the same INN. Further reasons given against using the same INNs for biosimilars include (Gaffney, 2012):

- concerns over inadvertent substitution if the same INNs were used, especially in healthcare systems where prescribing by INN is used
- confusion among prescribers and dispensers
- difficulty with reporting adverse events which would confound pharmacovigilance
- same INNs would infer interchangeability, even if the drugs are only designated as similar rather than highly similar.

On the other hand, biosimilars manufacturers and their supporters claim that there is no need to differentiate between the INN of the originator product and that of the biosimilar, and that the originator companies are creating this issue in order to hinder substitution. Supporters of the biosimilar industry have commented that the naming issue has not caused the same level of concern in Europe, and groups such as the Generic Pharmaceutical Association have noted the safety of biosimilar products used in the EU, where they have been approved for use for almost a decade, lessening the need for unique names (Gaffney, 2014).

WHO proposed a biologics qualifier system

The World Health Organization (WHO) has proposed that biosimilars have the same INN as originators but that a separate four-consonant code plus a two-digit checksum known as the biologic qualifier can be used as a differentiator. This system was proposed in July 2014 and it is yet to be seen if and when national regulators will adopt such a coding practice (Pink Sheet, 2015a). The WHO's INN Expert Group is planning a provisional implementation of the biological qualifier application, which would be voluntary, and would also conduct a prospective impact study. The primary advantage of the biological qualifier, according to the WHO, would be the improvement in drug traceability and pharmacovigilance. However, the generics and biosimilars industries believe that the qualifier is not needed and would make working with other naming and coding systems complicated (Pink Sheet, 2016).

Long-awaited final FDA naming guidance adds four-letter random suffix to the INN

In January 2017, the US Food and Drug Administration (FDA) released the long-awaited final biosimilar naming guidance, stating that a four-letter random code be added to the end of the INN, linked by a hyphen. Biosimilar sponsors are advised to submit up to 10 proposed suffixes at the time of Investigational New Drug (IND) or Biologic License Application (BLA) filing (FDA, 2017).
BILOGICS CURRENTLY HAVE FOUR YEARS OF DATA EXCLUSIVITY FOLLOWED BY EIGHT YEARS OF MARKET EXCLUSIVITY

The BPCI Act gives biologics approved via Biologic License Applications (BLAs) four years of data exclusivity followed by another eight years of market exclusivity, meaning that biosimilars cannot be marketed for at least 12 years after the originator biologic has been approved. The data exclusivity protection allows for a period of time following marketing approval during which competing firms may not use the originator company's safety and efficacy data that have been derived from proprietary preclinical and clinical trial results to obtain marketing authorization for a biosimilar version of the drug. This means the US Food and Drug Administration (FDA) cannot accept an application for a biosimilar within the first four years of approval of an originator product. Biosimilars developers can, however, rely on the originator's data in the latter eight years of the market exclusivity period, which ensures approval and entry of biosimilars is not delayed longer than necessary (FDA, nd).

The key benefit of data and market exclusivity is that, unlike patent protection, they provide the innovator company with a period of protection regardless of the length of time taken to bring the drug to market. In addition, data exclusivity is automatic upon new drug approval, whereas obtaining a patent requires proactive efforts and additional investment.

The 12-year market exclusivity period was seen as a victory for the originator lobby as it gives biologics a significantly longer period of market exclusivity compared to small molecule drugs. While there have been proposals and attempts to reduce the length of the exclusivity periods, this is unlikely to happen soon.

First biosimilar approved as interchangeable will have a commercial advantage

There is a significant commercial incentive for biosimilars manufacturers to be the first to gain approval for an interchangeable biosimilar for a given originator product. Under the BPCI Act, the first biosimilar approved as interchangeable will receive its own period of market exclusivity, which would expire on the earliest of the following (Bonilla and Beaver, 2011):

- one year after first commercial marketing of the interchangeable product
- 18 months after the resolution of patent litigation with the sponsor of the reference product
- 42 months after initial approval of the interchangeable product if patent infringement litigation is ongoing
- 18 months after approval of the first interchangeable biosimilar if the biosimilar applicant has not been sued for patent infringement by the sponsor of the reference product.

This means that no other interchangeable biosimilar product of the same reference product can be approved during that period. This protection is similar to the 180 days of exclusivity awarded to generics that are seeking accelerated approval if accompanied by a Paragraph IV certification and where the applicant is successful in challenging the innovator's patent in court. The magnitude of this commercial advantage will depend largely on the benefit of having the interchangeability designation, as according to the BPCI Act, other biosimilar products may be approved. The extent to which the FDA’s interchangeability designation governs the states’ substitution rules, and the payers’ strategies to promote cheaper products whether they are interchangeable or not, will therefore be key.
Originators are likely to reduce their prices to counter biosimilar competition

The high cost of biologics means that even with a discount, there is still significant value in the market which both originator and biosimilar companies will want to capture. As such, some pharmaceutical companies may be considering reducing the price of the originator product to one that is comparable to the biosimilar, preferring to take a price reduction in order to secure ongoing market share.

This approach is likely to be favored by payers as it ensures continuity for patients, physicians, and payers, and avoids the costs and disruption involved in switching. This means that biosimilars manufacturers must be prepared to offer a higher discount by contracting with individual health plans.

“*There are two ways that the originator company can approach it; they can just ignore it and hope that they will get as much revenue as they can on whatever they can get, or they can actively compete and try to match discounts, which will make it easier for plans as it means that we do not have to deal with the disruption to our members and our patients. They could offer further discounts if we do not do a substitution with the biosimilar.*”

US payer

“We would be likely to stay with the branded company if they were competitive. We would not have to move anything.”

US payer

The example of generic Copaxone (glatiramer acetate; Teva/Takeda) supports this latter idea. It has been reported that Sandoz’s generic Copaxone, marketed as Glatopa, has only managed to capture 20% market share as many payers have retained coverage of Copaxone or even have Copaxone listed as a preferred product due to Teva’s willingness to contract and match or better Sandoz’s price (Helfand, 2015).

**THERE ARE SOME PERCEIVED BENEFITS OF USING THE ORIGINATOR PRODUCT**

US payers recognize that originator products deliver several benefits compared to their biosimilar equivalents. These benefits include:

- **Guarantee of manufacturing quality and stability** – This is an issue that causes concern among payers and physicians alike. There are concerns about some biosimilars being manufactured in countries where standards are not perceived to be as high as in the US and that they do not necessarily follow good manufacturing practice, which may lead to variations in the efficacy and, more importantly, the safety of biosimilars.

- **Supply stability** – The complex nature of the biologic manufacturing process means that it is relatively inflexible and it can take a long time to modify and react to unexpected increases in demand. In addition, several biologics have experienced product shortages in the past, giving rise to the concern that this could happen with biosimilars, which could lead to a lack of supply for patients when it is needed.

Therefore, payers are more favorably disposed to biosimilars that are manufactured in the US or the five major EU markets (France, Germany, Italy, Spain, and the UK), as well as those developed by larger, more well-known companies such as Sandoz and Amgen.
The best coverage.  
The best forecasts.  
The best analysts.  
The best support.  
The Best of Health.

We’ve just made strategic investments in Datamonitor Healthcare to give you the best of health.

Introducing The New Datamonitor Healthcare.

We’ve quadrupled our business intelligence which covers more than 90% of prescription medicines in the major markets. Our forecasts are tailored to your needs as events occur and are powered by a new forecasting tool built in collaboration with a leading analytics technology provider. We’ve increased our global analyst resources by 300%, and Live Support replies to your queries in real time, not hours, for the fastest support in the market.

Discover the best of health.  
Request a live demo and see how The Best of Health supports smarter, faster decision-making.