Can The Life Sciences Industry Bank On Biosimilars?

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The latest U.S. Food and Drug Administration biosimilar approval has many industry observers wondering about the likely ensuing economic impact. Inflectra, biosimilar to Janssen's anti-TNF immunosuppressant Remicade, is the second biosimilar approved by the FDA[1]. This development comes approximately one year after the FDA's first such approval of Zarxio (biosimilar to Amgen's bone marrow stimulant Neupogen) and a little more than six months after Zarxio's launch[2].Given the very limited experience in this context to date, there has been much speculation concerning the likely impact of these and future approvals. Interest in better understanding the potential impact of biosimilar entry is heightened by the fact that the FDA is currently reviewing biosimilar applications referencing other top-selling innovative biologic drugs[3].

As a point of comparison, it is instructive to consider the experiences involving large molecule biologics in the context of empirical findings concerning generic competition for small molecule chemical drugs. Previous research by Professor Henry Grabowski and Analysis Group Inc. found that small molecule drugs facing initial generic entry in 2011-2012 rapidly lost sales, leading to average brand unit shares of just 25 percent within four months[4]. In contrast, Neupogen's share has seen a much more modest decline, falling to 76 percent four months after the entry of Zarxio[5]. It remains to be seen whether Inflectra

and the many other biosimilars currently in development will follow a pattern similar to Zarxio or to their small-molecule generic counterparts. But there are a few distinguishing characteristics of biosimilars that suggest the Zarxio pattern may not be an anomaly. These relate to regulatory features as well as financial incentives and evaluation of risks on the part of patients, payers and physicians.

From a regulatory perspective, one notable difference between generics and biosimilars concerns the nature of FDA approval. When the FDA approves a small-molecule generic, it is often deemed bioequivalent to and interchangeable with the reference product and, by extension, comparable in terms of its safety and efficacy profile for all uses. For biosimilars, FDA approval means something different. The FDA assures that the product in question is similar to its originator counterpart in terms of its safety and efficacy. Furthermore, in some cases it may do that only with respect to particular uses. Inflectra, for example, was approved for a limited set of indications relative to Remicade's label. Moreover, the studies on which approval was based pertained to only a subset of those indications, because the FDA engaged in what is referred to as "indication extrapolation[6]. "This was the case for Zarxio as well, where FDA approval encompassed all of the indications on Neupogen's label, despite the fact that clinical trials for Zarxio were only undertaken for some of those indications[7].

The difference in approval for generics versus biosimilars is likely to affect uptake in at least two ways. First, because the biosimilar is not deemed interchangeable with the reference product, there is no mechanism for automatic substitution to occur at the pharmacy as is the case with most generics. This is likely to limit the biosimilar's market penetration relative to the generic experience. In addition, the absence of data with respect to some indications may make some physicians and patients wary of switching to the biosimilar, even in cases where the FDA allows for indication extrapolation. This too could make it harder for biosimilars to achieve steep growth rates.

With respect to financial incentives, Zarxio launched at a list price just 15 percent lower than its reference product[8]. Small-molecule generics, in contrast, typically offer a much steeper discount immediately upon patent expiration (or, in other instances, following a six-month exclusivity period for the first-to-file generic). This may be because the technological hurdles to develop biosimilars and the costs to commercialize them are usually higher than for generics (i.e., in terms of research and development, manufacturing and marketing), resulting in lower profit margins, fewer entrants and less competition. Regardless of the reason, patients, payers and physicians may be reluctant to incur the risks associated with switching in return for only a relatively small savings. That is, since biologics are typically indicated for severe chronic conditions such as cancer and rheumatoid arthritis and can have serious adverse effects, the initial choice of a particular therapy and dosing can be very involved and critical to the patient's well-being. Therefore, once physicians and patients become accustomed to treatment with a particular biologic, they may be hesitant to try a new alternative, particularly if it is not deemed interchangeable by the FDA and is not associated with substantial savings.

While incentives to switch existing patients to a biosimilar may be low, initiating new patients on the biosimilar still provides a substantive pathway for biosimilar uptake. This may be particularly true as physician experience with the biosimilar evolves over time. As a result, we might expect biosimilar adoption to be far more gradual compared with the rapid and almost complete shift to generics observed for many small molecule chemical drugs.

Another factor that benefits innovator biologics is the formula for Medicare reimbursement. The current payment rule for physician-administered biologics provides incentives to favor higher priced products. That is, many biologics are purchased by physicians, administered to patients in an outpatient setting and subsequently reimbursed by Medicare. Since the current formula for reimbursement is average sales price plus 6 percent, physicians will obtain higher levels of reimbursement when they prescribe a higher priced treatment[9]. Thus, all else equal, physicians have a financial incentive to prescribe higher-priced products in this context. Such incentives could work to preserve shares of reference products facing competition from lower-priced biosimilars.

Biologics are projected to account for more than 50 percent of global sales of the top 100 drugs by 2020[10]. The advent of biosimilars has generated substantial attention as stakeholders attempt to assess their potential economic impact. The expectation is that they will reduce systemwide costs substantially, but there are several features of the U.S. marketplace that may temper those savings. These include the FDA's current approach to approvals and existing regulations concerning substitution at the pharmacy along with the financial incentives and risk tolerance of payers, physicians and patients. As a result, biosimilars are likely to face greater challenges compared with small molecule generics in penetrating the U.S. market.

Endnotes

1 http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm494227.htm (viewed 4/7/16).
2 http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm436648.htm (viewed 4/7/16).
3 http://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/Documents/IMS_Institute_Biosimilar_Brief_March_2016.pdf (viewed 4/7/16).
4 Grabowski H, Long G, Mortimer R, Recent trends in brand-name and generic drug competition, J Med Econ 2013; 1–8.
5 http://www.biopharma-reporter.com/Markets-Regulations/Sandoz-s-biosimilar-Zarxio-gradually-eroding-Amgen-s-Neupogen-sales (viewed 4/7/16).
6 http://www.law360.com/articles/779591/fda-backs-celltrion-biosimilar-of-janssen-s-remicade (viewed 4/7/16).

7 http://www.sandoz.com/media_center/press_releases_news/global_news/2015_03_06_fda_approves_first_biosimilar_zarxio_from_sandoz.shtml (viewed 4/7/16).

8 http://www.fdanews.com/articles/173036-sandoz-launches-zarxio-at-15-percent-lower-price-than-neupogen (viewed 4/7/16).

9 https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/Part-B-Biosimilar-Biological-Product-Payment.html (viewed 4/7/16).

10 http://info.evaluategroup.com/rs/evaluatepharmaltd/images/EP240614.pdf (viewed 4//7/16).