

EXECUTIVE SUMMARY

Since passage of the Drug Price Competition and Patent Term Restoration Act (or Hatch-Waxman Act) in 1984, generic drugs have become a mainstay for U.S. consumers and payers seeking safe, effective medication at a lower cost.

This legislation allowed manufacturers to produce generic versions of brand drugs when the patents for those brands expired. Because generic drug manufacturers do not incur the heavy upfront cost of research and development, generic pricing is lower. Subsequent competition between brand and generic drug manufacturers and among individual generic drug manufacturers also has contributed to lower prices.¹

This is changing dramatically, however, as factors converge to create unexpected price increases for formerly affordable drugs. These factors include industry consolidation, drug and raw material shortages and a myriad of business, economic and regulatory issues.²

As a result, payers, pharmacy benefit managers (PBMs) and retailers have scrambled to devise strategies to deal not only with the rising costs of generic drugs but also their frequent price fluctuations. This makes these stakeholders even more heavily reliant on drug pricing data, as a price just one day out of date can mean a difference between profit and loss – adding up to five and six figures in some cases.³

Adding fuel to the fire are specialty drugs, a significant number of which will lose their patents in 2020. Used to treat complex conditions such as cancer, rheumatoid arthritis and diabetes, these drugs already can cost tens of thousands of dollars per year, per patient.

Many of the highest-cost specialty drugs are biologics. Unlike traditional medications made from chemical compounds, biologics are complex molecules derived from living or biological sources. Given recent advances in medicine and biochemistry, biologics are experiencing dramatic growth.⁴

As biologics typically do not face generic competition after their original patent protection has expired, the threat of high prices continues due to lack of competition.⁵ This has led many to conclude that the answer can be found in biosimilar drugs.

The average annual retail cost of specialty drugs used to treat complex diseases such as cancer, rheumatoid arthritis and multiple sclerosis now exceeds the median U.S. household income, according to the AARP Public Policy Institute.⁶

WHAT ARE BIOSIMILAR DRUGS?

Simply put, biosimilar drugs are less costly versions of biologics that are built from chemical compounds. They are different from generics because the active ingredients in brand and generic drugs must match, whereas, in biosimilars, there may be other ingredients included, thus they are not exact copies. The two drug types are alike; however, in that much like a generic is similar to the brand drug, each biosimilar drug is similar to an already approved biologic drug. Thus, biosimilars have the advantage of being able to extrapolate and “piggyback” on the branded drug to get approval for all of the original drug’s indications.⁷

¹Elsevier Clinical Solutions, Generic Drug Price Increases: Causes and Impact, 2015, <https://www.elsevier.com/clinical-solutions/drug-information/insights/whitepapers/whitepaperrising-generic-drug-prices>

²Ibid.

³Ibid.

⁴AHIP, Issue Brief, Specialty Drugs Issues and Challenges, July 2015, <https://www.ahip.org/IssueBrief/Specialty-Drugs-Challenges-Issues/>

⁵Rand Corporation, The Cost Savings Potential of Biosimilar Drugs in the United States, 2014, https://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND_PE127.pdf

⁶AARP, Report: Rapid Rise in Cost of Specialty Drugs Exceeds Median Family Income, November 20, 2015 <http://www.aarp.org/about-aarp/press-center/info-11-2015/report-cost-rise-pharmaceuticals-exceeds-median-income.html>

⁷Erwin A. Blackstone, PhD and P. Fuhr Joseph, Jr, PhD, The Economics of Biosimilars, Am Health Drug Benefits. 2013 Sep-Oct; 6(8): 469–478, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732/>

Only now emerging in the United States, biosimilars are making significant gains in other areas of the world. The entry of biosimilars in the United States is projected to do for specialty drug pricing what generic drugs did for brands, that is, significantly lower costs.

As many leading biologics, worth more than \$81 billion in global annual sales, will lose their patient protections by 2020, the opportunities for biosimilars are huge for both manufacturers and consumers.⁸

According to the Federal Trade Commission (FTC), biosimilars have the potential to save the U.S. healthcare system \$250 billion through 2022. Furthermore, the global biosimilars market, according to an analysis by Frost & Sullivan, “will see exponential growth” over the next decade. This growth will not only save the healthcare system money; it also can improve patient outcomes and be a significant economic driver.⁹

POLICY ISSUES

Obviously, the potential of biosimilars to treat those with chronic diseases at less cost has drawn a great deal of attention and comment from market stakeholders, consumers and regulators, among others. Topics include:

Licensure

The Biologics Price Competition and Innovation Act (BPCIA) created an expedited licensure pathway, section 351(k) of the Public Health Services Act, for biosimilar approval. Most biologics were originally licensed through the traditional 351(a) pathway, which requires comprehensive data and does not rely on findings from any other pharmaceutical approved by the FDA.¹⁰

On March 6, 2015, the U.S. Food and Drug Administration approved Zarxio (filgrastim-sndz), the first biosimilar product approved in the United States. On April 5, 2015, it approved a second, Pfizer Inflectra (infliximab-dyyb).

Still, licensed biosimilars are required to meet the Agency’s rigorous standards of safety and efficacy. It has been noted, however, that the licensure pathway is provided “to demonstrate biosimilarity between the proposed [biosimilar] product and the reference product, not to independently establish safety and effectiveness of the proposed [biosimilar] product.”

Details on issues such as interchangeability, naming conventions, market exclusivity for originators and clinical research requirements will have a direct impact on biosimilar competition and uptake. The FDA’s gradual release of draft guidance is shedding increasing light on the form of the final regulation.¹¹

Naming Conventions: On April 1, 2016, the FDA issued for comment draft guidance on naming conventions, which has been a point of great contention among stakeholders.

Biosimilar makers say the drugs should carry the same non-proprietary name as their brand-name counterparts to avoid confusion about the safety and efficacy of their products. Critics want biosimilars to carry vastly different names from biologics to avoid confusion among physicians and pharmacists and prevent adverse reactions.¹²

How issues such as interchangeability, naming conventions and market exclusivity are resolved will have a direct impact on biosimilar competition.

In response to the FDA proposal of adding a four-letter suffix to the nonproprietary names shared with brand-name biologics, the FTC went on record in opposition. Such a convention, it said, “could result in physicians incorrectly believing that biosimilars’ drug substances differ in clinically meaningful ways from their reference biologics’ drug substances.” The Commission also suggested it would hinder competition that was intended to lower prices on expensive biologic medications.

⁸Fortune, Biosimilars may one day save your life. But what are they? February 6, 2015, <http://fortune.com/2015/02/06/BioSimilars-what-are-they/>

⁹The American Spectator, Unleashing the Potential of Biosimilars, <http://spectator.org/articles/62714/unleashing-potential-biosimilars>

¹⁰Alliance for Health Reform, Biosimilars: Unpacking Complex Issues, August 2015, http://www.allhealth.org/publications/Prescription_drugs/Biosimilars-Toolkit_167.pdf

¹¹Rand, Op. cit.

¹²Modern Healthcare, One year after Zarxio approval, future of biosimilars remains unclear, March 23, 2016, <http://www.modernhealthcare.com/article/20160323/NEWS/160319919?template=print>

Interchangeability: The BPCIA established two designations for biosimilars: “highly similar” and “interchangeable.” An “interchangeable” biological product is biosimilar to the reference product and can be expected to produce the same clinical result as the reference product in any given patient. If administered more than once to an individual (as many biological products are), the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product will not be greater than the risk of using the reference product without such alternation or switch. A biosimilar should only be considered interchangeable with the reference product if the FDA has approved it as a biosimilar and designated it as interchangeable, once additional criteria have been met.¹³

Switching is a practice wherein a prescriber (or the prescriber’s delegate, under direct supervision of the prescriber) may change the prescription from one biologic medicine to another biologic medicine.¹⁴

Substitution, on the other hand, is a practice allowed by law wherein a pharmacist may dispense an alternative biologic medicine for a prescribed biologic medicine without the prior approval of the prescriber. In some U.S. states, there is ongoing dialogue regarding post-dispensing notification and documentation. Private organization management of substitution may vary based on formulary decisions and other factors.¹⁵

The issue here is that while a biosimilar product can be prescribed by a healthcare provider in place of the FDA-approved reference product, an interchangeable biological product may be substituted for the reference product by a pharmacist without the intervention of the healthcare provider who prescribed the reference product.

As generic drugs made their mark based on substitutions of identical medicines at the pharmacy level, it is conjectured that biosimilars, too, will need “interchangeability” status to gain widespread acceptance. The FDA has promised guidance on this issue in 2016.

Medicare Reimbursement: On October 30, 2015, The Centers for Medicare & Medicaid Services (CMS) finalized a rule explaining how Medicare will pay for physician-administered biosimilar drugs. Essentially, it said it would treat biosimilars as it does generics, assigning all biosimilars of a single reference product one Healthcare Common Procedure Coding System (HCPCS) code and would reimburse biosimilars with the same HCPCS code based on the weighted average of their average sales price under Medicare Part B.

Criticism, up to and including calls for Congressional action and presidential invalidation, followed from a number of venues whose constituents felt their previous comments had gone unheard. Among them were chain drug stores and health insurers who felt the payment structure would stifle competition, increase costs and fail to realize the savings anticipated, as the development costs of follow-on biologics are high, even with an abbreviated approval pathway.

FACTORS AFFECTING SUCCESS

Safety: Some safety concerns regarding biosimilars are those that accompany all biologics. Because biologics are more structurally complex than chemical drugs, even slight changes in their manufacture can cause undetected changes in the biological composition of the product. These changes can in turn affect the safety and effectiveness of the product in patients.¹⁶ Immunogenicity is a related and significant concern, as all biologics have the potential to stimulate antibody production when administered, causing a variety of potentially serious outcomes.¹⁷

Pricing and Incentives: The Affordable Care Act requires that Medicare Part B reimbursement for biosimilars be based on the sum of the drug’s average selling price plus a fixed percentage (6 percent as of December 2015) of the average selling price of the reference product. Critics say this will eliminate the economic incentive to preferentially prescribe biosimilars.¹⁸

¹³Amgen, Biosimilar Frenzy: Facts, Fiction, and Future, an AHIP Webinar, December 11, 2015, http://www.amgenbiosimilars.com/~media/amgen/full/www-amgenbiosimilars-com/downloads/usa-bio-114753_biosimilar_frenzy_class_i.ashx?la=en

¹⁴Ibid.

¹⁵Ibid.

¹⁶Biotechnology Innovation Organization, Why is Patient Safety A Concern in the Biosimilars Debate? <https://www.bio.org/articles/why-patient-safety-concern-biosimilars-debate>

¹⁷Ibid.

¹⁸Surya C. Singh, MD, and Karen M. Bagnato, The Economic Implications of Biosimilars, AJMC.Com, December 28, 2015, RPhhttp://www.ajmc.com/journals/supplement/2015/ace0039_dec15_biosimilars/ace0039_dec15_biosimilars_singhbagnato

Further, a CMS ruling that exempted biosimilars from the mandatory 50 percent discount in the Medicare Part D coverage gap could reduce the cost gap between these drugs and biologics while patients are in the “doughnut hole,” that places temporary limits on what the drug plan will cover.¹⁹

Also, while private insurers, qualified health plans and employers may legally offer physicians financial incentives to prescribe generic drugs and follow-on biologics, the National Institutes of Health has noted that “marginally greater risks” could affect newer market entries.²⁰

Brand loyalty: Though use of generics has grown, there is still significant loyalty to brand names on the part of patients.

Pushback: Brand manufacturers are expected to compete with biosimilars by coordinating rebate contracts with payers.²¹

Provider Acceptance: Physicians are expected to display caution when deciding on prescribing biosimilars to existing patients.²² New data, however, shows that nearly half of U.S. doctors in five specialty areas surveyed anticipated expanding their prescribing of biosimilars in the next three years, as availability increases.²³

For now, the mindset is the same for physicians with biosimilars and biologics. When a patient is doing well on a treatment, don't change them. And once a response is lost due to immunogenicity, it is lost forever. New patients will be a different story.²⁴

IMPACT ON PAYERS

Payers have a significant financial incentive to consider biosimilars as an alternative to biologics. The Congressional Budget Office estimates the BPCIA will result in a total cost reduction of \$25 billion from 2009 to 2018. For the U.S. government, cost savings are estimated at \$5.9 billion.

Based on market research, most payers are taking action to plan for biosimilars, including evaluations of alternative payment models and restructuring of historical drug tiers. For instance, some biosimilars may be placed on preferred tiers, further reducing patients' cost-sharing burden. Insurers also could choose to eliminate cost sharing for biosimilars altogether to incentivize patients to switch from more expensive innovator products. They also can invoke mechanisms such as formulary exclusion.

It also is anticipated that PBMs will apply some of the same tried-and-true strategies used to increase generic market share.

Provider skepticism and limited competition from biosimilars will challenge payers and pharmacy benefit managers to reduce prices and maximize uptake of follow-on biologics. Successful payers and pharmacy benefit managers will employ various strategies, including tiered formularies and innovative fee schedules that can control spending by promoting uptake of biosimilars across both the pharmacy and medical benefits.

IMPACT ON RETAIL PHARMACY

As a primary source of validated information for prescribers and consumers, pharmacists will have a central role in ensuring the safe and effective adoption of biosimilars. As trusted patient advisors, they will be expected to be knowledgeable about biosimilars, even if they don't dispense them. They also will play key roles in mitigating any resulting confusion between brand drugs and biosimilars. Much depends on the final rule on interchangeability, which could reduce prices and encourage patients to use non-branded products.

¹⁹Ibid.

²⁰PLoS Medicine, Paying Physicians to Prescribe Generic Drugs and Follow-On Biologics in the United States, Ameet Sarpatwari, Niteesh K. Choudhry, Jerry Avorn, and Aaron S. Kesselheim, published online 2015 Mar 17. doi: 10.1371/journal.pmed.1001802

²¹Donald J. Dietz, RPh, MS, Ann Johnson, PharmD, Dave Schuetz, Rph, Patient Care, What's Old Is New Again...Biosimilars Are a Repeat of Yesterday's Generics, June 2015, Vol 3, No 6 - The First Word, <http://www.insidepatientcare.com/issues/2015/june-2015-vol-3-no-6/2015-whats-old-is-new-again-biosimilars-are-a-repeat-of-yesterdays-generics>

²²Abigail E Felix, BA, Anumeha Gupta, MD, Joshua P Cohen, PhD, Kim Riggs, MPH, Generics and Biosimilars Initiative Journal, Volume 3 / Year 2014 / Issue 3, <http://gabi-journal.net/barriers-to-market-uptake-of-BioSimilars-in-the-us.html>

²³InCrowd, Nearly Half of US Physicians Say They Will Prescribe More Biosimilars, According to New Data from InCrowd, March 03, 2016 <https://www.incrowdnow.com/2016/03/nearly-half-of-us-physicians-say-they-will-prescribe-more-biosimilars-according-to-new-data-from-incrowd/>

²⁴PharmExec.Com, Biosimilars in the US: Five Potential Sticking Points Apr 21, 2015, <http://www.pharmexec.com/BioSimilars-us-five-potential-sticking-points>

From a business standpoint, as noted, pharmacists will have to be sure they are working with the most accurate information and biosimilars potentially add increased fluidity to an already mercurial pricing environment.

And still unresolved is whether pharmacists will have to notify physicians when they substitute an interchangeable biosimilar for the innovator biologic – an issue left to individual states to decide.

By opening markets to biosimilar competition, healthcare systems could realize a 30 percent reduction in price per treatment day compared to originator biologics, according to IMS Institute for Healthcare Informatics. The extent of actual savings, it says, will depend on policy decisions made and actions taken around incentives, education and pricing.

IMPACT ON PROVIDERS

In addition to their concerns regarding notification of substitutions of biosimilars by pharmacists, physicians fear that third-party payers could substitute one medication for another without the patient's knowledge or permission. There also are concerns that biosimilars could become first-line therapies, as they are in parts of Italy,²⁵ even though other pharmaceuticals are physician-preferred.

Overall, however, there is hope that physicians' ability to prescribe less expensive therapies for high-cost specialty drugs will promote adherence to medication regimens, improving health.

CONCLUSION

The impact of biosimilars on drug costs and healthcare will continue to play out as more of these therapies enter the U.S. market. It is important that stakeholders take steps now to understand the potential of, and issues related to, biosimilars, arming themselves with the right tools and data to effectively manage their dispensing and coverage.

While there is no immediate or simple solution for rising drug prices, truly current and accurate drug price data ensures that pricing decisions are made with correct information, that reimbursements are fair and balanced and that pricing analysis and reporting is both strong and vigilant.

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²⁵Ajpb.Live, How Will the Emergence of Biosimilars Impact the Marketplace? - See more at: <http://www.ajpb.com/articles/how-will-the-emergence-of-BioSimilar-impact-the-marketplace#sthash.7JbDWayF.dpuf>, Feb 18, 2016. <http://www.ajpb.com/articles/how-will-the-emergence-of-BioSimilar-impact-the-marketplace>