Research

The New Frontier of Pharmaceuticals: Biosimilars

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Introduction

Biopharmaceutical medications, commonly referred to as biologics, are a rapidly growing sector of specialty drugs. While the concept of using living cells for specialized medical treatment is not new—live vaccine treatments have been around for some time—recent innovations in genetic engineering have precipitated more complex and specifically tailored drugs that are grown, rather than manufactured, and advanced the landscape of modern medicine. However, these innovations require large investments in both research and production.[1] Recent estimates indicate that research and development costs for biopharmaceuticals totaled $140 billion worldwide in 2014 alone.[2] A biologic treatment course can cost between $10,000 and $50,000 over the course of a year, with some treatments exceeding $100,000, and both public and private insurance programs are struggling to maintain access in the face of high price tags and increasing demand for specialty drugs.[3] In 2013, the IMS Institute for Healthcare Informatics estimated that 28 percent of prescription drug expenditures in the US were spent on biologic drugs,[4] and the market share of biologics globally is projected to continue growing at an annual rate of 10.6 percent through 2019.[5]

Traditional, small-molecule pharmaceuticals face aggressive competition from generic drug manufacturers after patent protections on the brand-name drugs expire, which has led to $734 billion in savings for payers and patients over the past decade.[6] However, the existing regulatory pathway for small-molecule generic drugs is not sufficient to accommodate the complexity of new biologics because identical biologics cannot be made like small molecule products. In 2010, Congress passed the Biologics Price and Innovation Act (BPCIA) as a part of the Affordable Care Act (ACA) to provide the FDA with new authority to approve follow-on biologic products—also known as “biosimilars”. These

products are “highly similar” to the biologic reference product, but not identical copies as is the case with generic pharmaceuticals. The FDA has issued draft guidance on many aspects of the approval process, including quality and scientific considerations related to biosimilarity, the clinical data necessary to demonstrate biosimilarity, and the relevant exclusivity period for brand-name biologics. In March 2015, the FDA approved the first U.S. biosimilar, filgrastim, through the new pathway. But due to a lack of final guidance from the agency, uncertainty remains on a number of key policy issues such as naming, extrapolation, and interchangeability, which will impact the entry of biosimilars to the market.

Studies indicate that savings associated with biosimilars will not reach the historically high level achieved in the small-molecule generic market. Unlike traditional generic drugs, it is expected that the relatively low discounts and high investment cost expected with biosimilars will create competition between biosimilars and brand-name biologic drugs that is more similar to competition between brands than between a brand and a generic. [7] Through an analysis of possible scenarios, the American Action Forum (AAF) estimates that biosimilar drugs approved through the BPCIA could save between $5.1 and $37.8 billion in total national biologic drug expenditures in the US over ten years. The federal government, which paid for roughly 36 percent of all prescription drug expenditures in 2013, has a significant stake in these savings.[8] In this paper, we further discuss the competitive implications and possible savings of the future biosimilar market.

Data and Methodology

Using publicly available Securities and Exchange Commission (SEC) filings, we collected information on $41.7 billion worth of biologic sales in the United States in 2013. Our data covers 37 brand-name drugs sold by 9 different pharmaceutical companies. Where applicable, we collected U.S. sales revenue for every year between 2009 and 2013. In 2009, 28 of the 37 drugs we examined were in production and accounted for $27 billion in U.S. revenue. Table 1 displays the 12 drugs that grossed over $1 billion in 2013. These 12 drugs accounted for 81 percent of all 2013 sales revenue in our data.

Table 1 – Biologic Drugs with over $1 Billion in US sales (2013)

Drug Name	**Exclusivity and Patent Expiration[9]**	**2013 US Sales (millions)**
Humira	2016	5,240
Remicade	2018	4,400

Enbrel	2028	4,260
Neulasta	2015	3,450
Rituxan	2013	3,410
Avastin	2019	2,640
Epogen/Procrit	2013	2,630
Avonex	2026	1,900
Herceptin	2019	1,830
Lucentis	2020	1,730
Prolia, Xgeva	2022	1,230
Neupogen	2013	1,170

Our methodology for estimating baseline biologic drug spending is an extrapolation of growth trends over the past 5 years. We compare the average growth in sales revenue for the first 12 years a drug is on the market to the average growth in sales revenue for drugs that have been on the market for longer than 12 years. This division attempts to capture the effects of competition from other drug brands—the FDA grants exclusivity for the first 12 years of most biologic drug approvals—as well as the general slowdown in sales over time as modern medicine develops new treatments that make older ones less valuable. We find that the average year-over-year growth in U.S. revenue for biologic drugs in our sample is 12.1 percent for the first 12 years and 8.9 percent thereafter. We use these rates to estimate the growth of total sales revenue for a given biologic drug over the next ten years.

In order to estimate potential savings from biosimilars, we estimate two scenarios of biosimilar penetration, a low-savings and high-savings scenario, which are determined by assumptions on the average price of biosimilar drugs relative to the brand-name counterparts and the penetration of biosimilars into the total number of biologic prescriptions.

The Federal Trade Commission (FTC) estimates that producers of biosimilars will likely be limited to manufacturers that already produce biologic drugs of some kind and that discounts will likely be between 10 and 30 percent rather than the 70 percent typical of small-molecule generics.[10][11] Producers of traditional, small-molecule generics are able to exploit relatively cheap and easy-to-replicate chemical processes to realize steep discounts

from the price of a reference product. However, the same economic efficiencies do not apply to biosimilars. Therefore the complexity of the manufacturing process remains a significant barrier to entry for biosimilar manufacturers. High start-up costs are likely to reduce the size of the discount a biosimilar manufacturer will be able to offer relative to the brand-name biologic. In AAF's high-savings scenario, we assume that biosimilars offer an average discount of 30 percent relative to the reference brand-name product, and we assume that biosimilars offer an average discount of 10 percent in the low-savings scenario.

Biosimilars also differ from traditional generics through the very nature of "similarity." A biosimilar cannot be manufactured—or grown—to be identical to the reference drug and relies on a determination by the FDA that the product is "highly similar," and that switching between the reference product and the biosimilar does not lead to any "clinically meaningful differences in any given patient." The issues of similarity and interchangeability will have a substantial effect on the ability of biosimilars to gain market share. Currently, generic drugs account for 86 percent of all prescriptions, which has led to large savings and increased access to small-molecule prescription drugs.[12] But the success of generic drugs has depended on the confidence of physicians, pharmacists, patients, and payers that those drugs were substitutable. In contrast, there is research to suggest that substitution between biosimilars and reference biologics may have unintended impacts on patients and clinical outcomes.[13] Physicians understand the uncertainty surrounding biosimilar treatments and may hesitate to substitute away from a successful biologic treatment in exchange for modest savings. In a recent study by the Biotrends Research Group, 86 percent of rheumatology and gastroenterology physicians surveyed indicate they would prevent biosimilar substitution for some, if not all, prescribed biologic medicines.[14] In our high-savings scenario, we assume that biosimilars enter the market with an average market share of 10 percent of the relevant prescriptions and grow to a maximum 30 percent market share over the first 5 years on the market.[15] In our low-savings scenario, we assume that biosimilars will capture an average of 10 percent of the relevant prescriptions throughout the analysis period.

Biosimilars in Europe

In 2003, the European Union (EU) became the first jurisdiction to establish a robust biosimilar approval pathway. Unlike the FDA, the European Medical Agency (EMA) does not have a mandate to determine whether a biosimilar is "interchangeable" with a reference product.[16] The EMA only determines whether the product is biosimilar. The key to generating savings is left to national payers at the country level and national policymakers through substitution policies. Authorities in each EU member country may allow automatic substitution between biologics and biosimilars, but generally patients currently on biologics

are not automatically substituted. The market for biosimilars and biologics in the EU also differs from the US in that European member nations generally have greater negotiating power to lower drug prices, in part due to heavier price regulations and payer structures.[17]

In total, biosimilars of six different molecules have been approved through the European pathway.[18] Biosimilar penetration over the past decade has been modest, accounting for only 6.6 percent of relevant sales according to one 2009 study.[19] The slow start in Europe is a result of exclusivity restrictions, uncertainty among physicians, and limited discounts—leading to limited data by which to estimate the impact of biosimilars on health care budgets. Analysts are still optimistic about total savings, projecting between €11.8 and €33.4 billion in potential savings across the continent by 2020, but documentation of those savings so far has been sparse.[20] In Germany, one biosimilar manufacturer claims the generic versions of epoetin—for which there are 5 approved biosimilars—have saved €551 million, a small portion of projected national savings of between €4.3 and €11.7 billion by 2010.[21],[22] However, the success of biosimilars in the EU is highly variable across therapeutic categories and member nations, and pharmaceutical markets and regulations are still adapting.[23]

Potential Savings in the United States

Savings in the United States may accrue more rapidly than in Europe simply because biosimilar technology has advanced substantially in the last decade, and patent protection for many biologic drugs are set to expire over the next few years. However, approximations of the magnitude of potential savings are highly uncertain—demonstrated by widely varying estimates. Some industry projections are as high as $250 billion over the next ten years, while the Congressional Budget Office estimated a ten year savings of about $25 billion.[24],[25] AAF estimates two savings scenarios over the next decade: a low-savings scenario characterized by relatively smaller discounts and prescriptions rates, and a high-savings scenario characterized by relatively larger discounts and prescription rates. These two scenarios encompass the range of savings that could be achieved, depending on the acceptance of biosimilars in the U.S. by regulators, health care providers, patients, and payers.

Table 2 – Change in Total Spending on Biologic Drugs in the United States (billions)

	2015	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2015 – 2024**

Low-Savings Scenario	0	-0.2	-0.3	-0.4	-0.5	-0.6	-0.7	-0.7	-0.8	-0.9	-5.1
High-Savings Scenario	0	-0.7	-1.2	-2.0	-3.1	-4.4	-5.2	-6.1	-7.1	-8.0	-37.8

The low-savings scenario might occur if the FDA places significant requirements on biosimilar manufacturers to perform independent clinical trials to support claims of "similarity." Such regulations would increase the fixed costs of developing biosimilars and likely reduce the discount that a manufacturer would be able to offer relative to the reference product. This scenario could also be the case if the market lacks significant competition, and biosimilar manufacturers find it more profitable to set prices close to those of the reference product. The response of insurers, physicians and patients will also have a significant impact on possible savings. The low-savings scenario reflects low enthusiasm among both physicians in prescribing and filling biosimilar scripts and payers in providing insurance coverage for biosimilars.

Alternatively, the high-savings scenario would be characterized by less burdensome requirements for data supporting treatment indications and little restriction on a pharmacists ability to automatically substitute biosimilars for the reference product. These regulations might encourage widespread adoption of biosimilars but come at the cost of oversight and quality control that preserve physician and patient confidence.

Conclusion

Biologics, as well as traditional specialty drugs, are stimulating an important policy debate over maintaining access to high cost medications for populations in need, while preserving the incentives to innovate new treatments. Unfortunately, biosimilars cannot bring the same degree of savings and access to biologics that generic small-molecule drugs have for traditional pharmaceuticals. Regardless of the favorability of the regulatory environment, the prices of biosimilar treatments will likely be measured in the thousands and far exceed the maximum out-of-pocket expenses of any commercial or public health insurance product, which are capped at $6,850 per person in 2016. The high prices limit the incentives for patients to seek out biosimilars as pocket-book relief.

However, biosimilars do present an opportunity to establish meaningful competition and downward pricing pressure for many of the most expensive drugs, which could be instrumental in mitigating rising prescription drug costs in the future. Health insurance providers are eager to find ways to combat the rising cost of prescription drugs, and

biosimilars may find success through favorable treatment by payers. Savings estimates exceeding $100 billion are improbable, but if the pathway is established clearly and provides an environment through which physicians can safely and confidently prescribe biosimilars, AAF expects savings of at least $5.1 billion and up to $37.8 billion over the next decade. Advancing policy that will seek to maximize biosimilar savings will depend on policymakers balancing the need to establish confidence in biosimilar products and the goal of reducing overall healthcare costs.

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[1] http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18,_2014..pdf