



The Cost Savings Potential of Biosimilar Drugs in the United States

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The U.S. Food and Drug Administration (FDA) is expected to release final regulations outlining lower-cost approval pathway requirements for so-called biosimilar drugs. The introduction of biosimilars is expected to reduce prices, albeit to a lesser degree than small-molecule generics. This Perspective combines prior research and recent data to estimate cost savings in the U.S. market. We predict that biosimilars will lead to a \$44.2 billion reduction in direct spending on biologic drugs from 2014 to 2024, or about 4 percent of total biologic spending over the same period, with a range of \$13 billion to \$66 billion. While our estimate uses recent data and transparent assumptions, we caution that actual savings will hinge on the specifics of the final FDA regulations and on the level of competition.

Context and Motivation

Biologics are complex, protein-based drugs including insulin, monoclonal antibodies to block inflammation in rheumatoid arthritis, and a range of drugs to treat cancer, multiple sclerosis, and other serious diseases. While biologics have revolutionized treatment for many conditions, they are often expensive in terms of cost per dose. Insurers are concerned about rising prices, acceleration in new approvals, and burgeoning pipelines for biologics compared with flat growth and few new nonbiologic “small molecule” drugs. In 2011, eight of the top 20 drugs in the United States in terms of sales were biologics, and year-on-year biologic spending grew at 6.5 percent, compared with 2.3 percent for small molecule drugs.¹ The American Society of Clinical Oncology is calling for value-focused moderation in the use of specialty drugs, many of which are biologics.² And patients—who are often asked to bear a share of the cost of expensive specialty drugs through cost sharing—

may face financial barriers that affect treatment initiation and adherence.

It is of particular concern that biologics typically do not face generic competition after their original patent protection has expired, thus extending high prices indefinitely. Under the Hatch-Waxman Act, FDA can approve generic copies of traditional small-molecule drugs like statins, oral chemotherapeutics, and antihistamines based on evidence from relatively small and inexpensive studies to demonstrate bioequivalence, or the rate at which the drug is available in the body over time. Competition between multiple generic manufacturers ultimately (after patent litigation and exclusivity periods) drives prices down by 50 to 80 percent in most small-molecule markets.³

FDA's approach to regulating small-molecule generic drugs cannot be applied to biologics, which are complex molecules manufactured in living systems. The 2010 Affordable Care Act (ACA) authorized FDA to develop a new regulatory framework for approving "biosimilars," which are biologics with highly similar molecular structures and equivalent safety and efficacy compared to already-approved reference biologics.

While FDA is still developing its final regulations, draft guidance documents released by FDA suggest that biosimilar manufacturers will face lower costs and less time to obtain approval

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compared with originator manufacturers, while still ensuring that there are no clinically relevant differences in safety and efficacy between the biosimilars and originator biologics.⁴ FDA has indicated that biosimilars and traditional generic drugs will be reviewed and regulated differently. For example, unlike generic drugs, not all biosimilars will be deemed "interchangeable" with their originator counterparts (at least initially), and nearly all biosimilars will require at least one head-to-head clinical trial to confirm similarity with the originator biologic as the basis for approval. These differences—in addition to complex biologic payment and delivery considerations—may limit the degree of competition and price savings in biosimilar markets compared with traditional generic drug markets.

European Union regulators developed a separate approval pathway for biosimilars in 2004 and have already approved several products. The pathway requires manufacturers to demonstrate similarity to a "reference" biologic (typically the originator) in terms of safety, efficacy, and quality, but not through a clinical research program of the scale that is demanded for initial approval of an originator biologic. While the EU biosimilars market is relatively new, studies suggest that biosimilars in some therapeutic areas are priced below reference biologics, often with discounts of 25 percent or more.⁵

FDA's new regulation, like the EU's biosimilar regulation, may potentially enable competition and lead to lower prices for payers and patients, limiting the de facto permanent monopoly that the high cost of regulatory approval under the usual biologics approval pathway creates. However, the magnitude of the price decrease depends in large part on the final FDA regulations. And it remains unclear how savings will be shared between payers, patients, providers, and taxpayers.

For over a decade, academics and policymakers have debated just how much savings biosimilars might create in the United States, drawing on the experiences with biosimilars in Europe and with generic small-molecule drugs and drugs that resemble biosimilars in the United States.⁶ There is little consistency in the factors that are considered key determinants of biosimilar cost savings, and there is considerable variation in assumptions, time frames, and perspectives across these estimates. This Perspective summarizes prior research, describes key policy issues and questions related to cost savings from biologics, and uses recent data to calculate a new cost savings estimate.

Cost Impact Framework

We developed a framework based on economic theory to describe the range of factors that will affect the potential cost savings from biosimilars. The framework identifies four categories of drivers—safety and efficacy, payment, acceptability, and competition—that together determine the magnitude of cost savings. These drivers are sequential in the sense that they build on one another and loosely follow the development and adoption process for new biologics. But they are also additive in the sense that a single strong driver can lead to significant cost savings even with lackluster results elsewhere in the framework. The framework can be applied overall or to specific biologic markets and therapeutic classes.

The first category is the safety and efficacy of biosimilars and their originator equivalents relative to other products that are available in the market in the same therapeutic class. Price competition will be greater to the extent that biosimilars are substitutes (in terms of safety and efficacy) for other approved drugs with similar uses. This is an important factor in some markets (e.g., erythropoi-

etins and anti-tumor necrosis factor [TNF] products) with multiple originator drugs. It may also be an important driver when patients and providers can choose between biologics and other treatment alternatives, including traditional drugs. To the extent that differences do exist, payers will need to compare the cost-effectiveness of biosimilars versus other treatments, including possibly second- and third-generation biologics (i.e., improved versions of successful first-generation biologics like recombinant erythropoietin).⁷

The second category is payment and relates to the approach that insurers use to pay providers (including physicians, pharmacies, and facilities) for biosimilar drugs relative to other biologics and to small-molecule drugs. Equivalent or higher payment rates for biosimilars relative to other drugs will encourage prescribers to substitute biosimilars for more expensive originator biologics. We discuss different approaches to payment below.

Another factor is the acceptability of biosimilars to patients, payers, and the medical community. Prescribers must support the use of biosimilars, and patients must agree to take biosimilars in place of originator products in order to realize cost savings. These changes could potentially disrupt longstanding prescribing practices.

Competition is the final and most important driver of cost savings. The number of competitors and the extent of competition in the biosimilars market will depend on factors such as the costs of entry; the costs of manufacturing; firm-specific scientific, regulatory, and commercial expertise; and the overall return that biosimilar manufacturers believe they can realize from their investment in advancing a product. Additionally, the presence or absence of legal barriers or facilitators of entry, such as time limits on patents, data or market exclusivity, or regulatory uncertainty, will modify the

incentives facing potential biosimilar manufacturers. We view the link between competition and price through the lens of economic theory—in other words, that more competitors will drive biologics prices downward. Several studies point to a clear relationship between the number of competitors and price in small-molecule generic drugs.⁸ However, this relationship is driven by incentives for competition and substitution that may not apply to biosimilars, especially for physician-dispensed biosimilars.

Our framework predicts that increased competition, comparable or better safety and efficacy relative to alternative drugs in the same therapeutic class, greater acceptance, and payment policies favoring biosimilars will lead to greater savings, while fewer competitors, worse safety and efficacy relative to alternative drugs, low acceptance, and payment policies disincentivizing biosimilars will lead to less overall savings.

Health Care Cost Impact of Biosimilars

The advent of a U.S. biosimilar approval pathway and market can affect health care spending through two mechanisms:

1. **Decreased unit cost.** The unit cost of biologics with biosimilar competitors will decline.
2. **Increased volume.** The entry of lower-cost competitors will cause patients and payers to choose biologic treatment options to a greater degree.

The net effect on pharmaceutical spending will depend on the relative magnitude of unit cost reductions and increased volume. In this Perspective, we focus on the impact on unit cost, for two reasons. First, there is limited evidence for the effects of increased volume, as most studies focus on the impact of lower unit cost. We

summarize some of these estimates below, describe their strengths and weaknesses, and suggest how these estimates can be updated to fit a more contemporary context. Second, the impact on unit cost is likely to apply across the fragmented U.S. health care system, while the volume effect will depend on context—for example, clinical factors, insurance coverage, and delivery system structure.

Existing Estimates of Potential Cost Savings

We searched the peer-reviewed literature for studies on potential direct cost savings from biosimilars. We also scanned the non-peer-reviewed literature to identify relevant industry perspectives, government publications, and reports from various consulting firms. The box on page 5 describes our search methods and the number of publications that we identified in our search.

Description of Existing Estimates of Cost Savings

Overall, studies estimating the short to mid-term (i.e., within ten years) savings from biosimilars arrive at a range of 10 to 50 percent reduction in unit price. In other words, if all else is held constant, and if every patient is transitioned to a biosimilar, spending on biologics will fall by between 10 and 50 percent. Some of these studies separately estimate the impact on total spending on biologics of between 1 and 10 percent (when a baseline spending estimate is available). The impact on spending is smaller than the difference in price because it is unlikely that every patient will transition from originator to biosimilar products. One study estimates how lower biosimilar unit prices and cost sharing could encourage patients and payers to increase utilization.⁹

Table 1 summarizes key published estimates of U.S. biosimilar cost savings. For each study, we describe which product markets are

Literature Review Methodology

Search terms: Search terms included “biosimilar,” “follow-on biologic,” and “biogeneric” combined with terms focusing on economic and financial impacts, such as “cost,” “price,” and “savings.” Searches for the term “biosimilar” produced the most results, while searches for “follow-on biologic” and “biogeneric” returned relatively few results. In addition to the search terms used above, we also mined citations and performed forward searches to identify other articles that cited key publications. Each study abstract or summary was reviewed by one of the authors. Studies reporting the actual or predicted impacts of multi-source biologics (i.e., similar biologics produced by different manufacturers) on (a) prices, (b) utilization, or (c) health outcomes were reviewed in full, and we catalogued key outcomes using an abstraction sheet. We did not review editorial, opinion, or perspective articles without empirical analyses.

Databases: To create the library of peer-reviewed literature, we searched databases including PubMed, Web of Science, and Google Scholar. We searched for non-peer-reviewed “gray” literature using Google and reference mining.

Summary: We subdivided the peer-reviewed literature into three categories: retrospective studies, which examined existing markets for biosimilars in European countries; prospective studies, which projected prices and impact for biosimilars on American and European markets; and case studies, which examined European experiences with individual biosimilars. In the final library, there were 18 retrospective studies, 37 prospective studies, and six case studies, for a total of 61 peer-reviewed articles. In total, 23 non-peer-reviewed articles and reports were added to the library, six of which were industry perspectives. The final library contains 84 articles and reports. It contains a mixture of prospective studies, retrospective analyses, case studies, government reports, and reports from industry and various consulting firms.

included, the methodologic approach, the time frame considered in the estimate, biosimilar price relative to originator price, and estimated savings in absolute and relative terms.

Discussion

Our review identified a range of studies, some presenting retrospective empirical analyses and others reporting prospective modeling or prescriptive policy analysis. The studies drew on a variety of sources for the basis of their estimates, including evidence from U.S. generic markets and from the EU’s experience with biosimilars. Many studies included analysts’ assumptions and other expert opinion.

Many studies grounded their cost savings estimates in comparisons to small-molecule generics. The 1984 Hatch-Waxman Act introduced a generic approval pathway alongside patent extensions for originator drugs. Hatch-Waxman is often viewed as a policy that “worked.” The resulting robust U.S. generic drug market promotes competition and lower prices. U.S. market share of small-molecule generics is high because both pharmacists and patients have incentives to prefer generic drugs. Despite this success, there are important differences between small-molecule generics and biosimilars, including differences in the competitive landscape, in financial incentives for dispensers and prescribers (which are sometimes the same entity for biosimilars), and in substitutability. As a result, we caution against expecting savings similar to those from small-molecule generics for biosimilars but rather view those as an upper bound of the potential savings. Still, given the paucity of other evidence, it is an obvious starting point.

Some studies leveraged data from the EU’s experience with biosimilars. There are many important differences between Euro-

Table 1. Select U.S. Biosimilar Cost Savings Estimates

Study	Approach	Scope	Time Frame	Price Reduction	Savings
Grabowski et al., 2007 as applied in Goodman et al., 2009 (base case) ¹⁰	Economic model	6 major categories of biologics, top 20 biologics by sales only, all payers	2009–2019	12% to 20%, varies by product	\$10 billion (2.4% of baseline spending)
Grabowski et al., 2007 as applied in Goodman et al., 2009 (sensitivity analyses)	Economic model	6 major categories of biologics, top 20 biologics by sales only, all payers	2009–2019	12% to 40%, varies by product	\$1 billion to \$44 billion (0.2% to 10.5% of baseline spending)
Ahlstrom et al., 2007 (Avalere Health) ¹¹	Actuarial model	Federal payers only	2008–2017	10% to 51%, varies by product and increasing over time.	\$3.6 billion (0.6% of baseline spending)
Engel and Novitt, 2007 ¹²	Actuarial model	Excludes Enhanced Primary Care, Medicare Part B only (office-based, physician-administered biologics)	2007–2016	Unknown	\$14.4 billion
Miller and Houts, 2007 (Express Scripts) ¹³	Actuarial model	Select markets, all commercial payers	2007–2016	25%	\$71 billion (baseline not reported)
CBO, 2008 ¹⁴	Actuarial model	All biologics	2009–2018	20% to 40%, varies by product and increasing over time.	\$25 billion (baseline not reported), \$7 billion of which accrues to the federal government
Shapiro et al., 2008	Actuarial model	Top 12 biologic classes	2010–2019	25% to 35%, varies by assumption	\$67 billion to \$108 billion

pean and the U.S. health care systems, including well-developed branded generic markets in the European Union but not in the United States and pharmaceutical price controls in many EU countries. Price controls, for example, could limit the savings from biosimilars in the European Union compared with the United States if originator prices are already at a lower baseline. While the U.S. small-molecule generic and EU biosimilar markets provide some

insight into what the U.S. biosimilar market could look like, none of these comparators is a perfect match, and caution is indicated when drawing any comparisons.

Grabowski et al. (2007) developed an economic model to estimate potential biosimilar cost savings. They used data from small molecule generic markets to estimate two interconnected models. First, how many competitors were there in each drug market, and

how does the number of competitors vary with the characteristics of the market that we can observe, like originator drug sales? And second, how does the price of generics vary with the number of competitors? Grabowski et al. used information from these models to estimate how many competitors and how much of a price reduction we should expect to see in the biosimilars market. Others have updated and built on this approach.¹⁵

The key assumption underlying these studies is that competition and pricing for biosimilars will resemble competition and pricing in small-molecule markets. These studies also rely on estimates of the costs associated with manufacturing, studying, and obtaining regulatory approval for biosimilars. Because of the limited U.S. experience with biosimilars and the lack of final FDA regulation, these estimates are often “best guesses” based on anecdotes, even though they incorporate microeconomic modeling.

Other cost savings estimates were actuarial analyses using growth trends and informed guesses on price differences and other key parameters to model savings from biosimilars over a fixed time horizon. The price differences in these models are sometimes from studies like Grabowski et al., and other times they are based on analysts’ estimates. These studies all adopted the payer point of view (some with a narrow federal payer perspective) and focused on a ten-year time horizon.

Distilling an Updated Estimate

We used 2013 U.S. sales data on more than 100 biologics, including all blockbuster biologics with sales over \$1 billion and many products with smaller markets, to estimate the potential direct cost savings from biosimilars.¹⁶ These products had combined 2013 sales of \$66.3 billion across all distribution channels. We expect the

biosimilar market for insulins and human growth hormones—where there are already multiple competing products—to look different than the market for other biologics. We divided the \$66.3 billion total into two parts, leaving \$13.7 billion in 2013 sales for the “established” insulin and human growth hormone markets and \$52.6 billion for all other biologic markets.

We assumed year-on-year originator growth of 10 percent, an increase in the share of originator sales exposed to biosimilar competition from 10 percent in year 1 to 20 percent in year 10, biosimilar market penetration of 60 percent, and a biosimilar price discount due to competition of 35 percent.¹⁷ We assumed that 100 percent of the established insulin and growth hormone markets will be exposed to biosimilar competition in year 1 but with half the biosimilar penetration and price discounts of other markets. These assumptions—while informed by previously published studies and our expert opinion—are informed guesses, and as a result we vary many of the assumptions with sensitivity analyses.

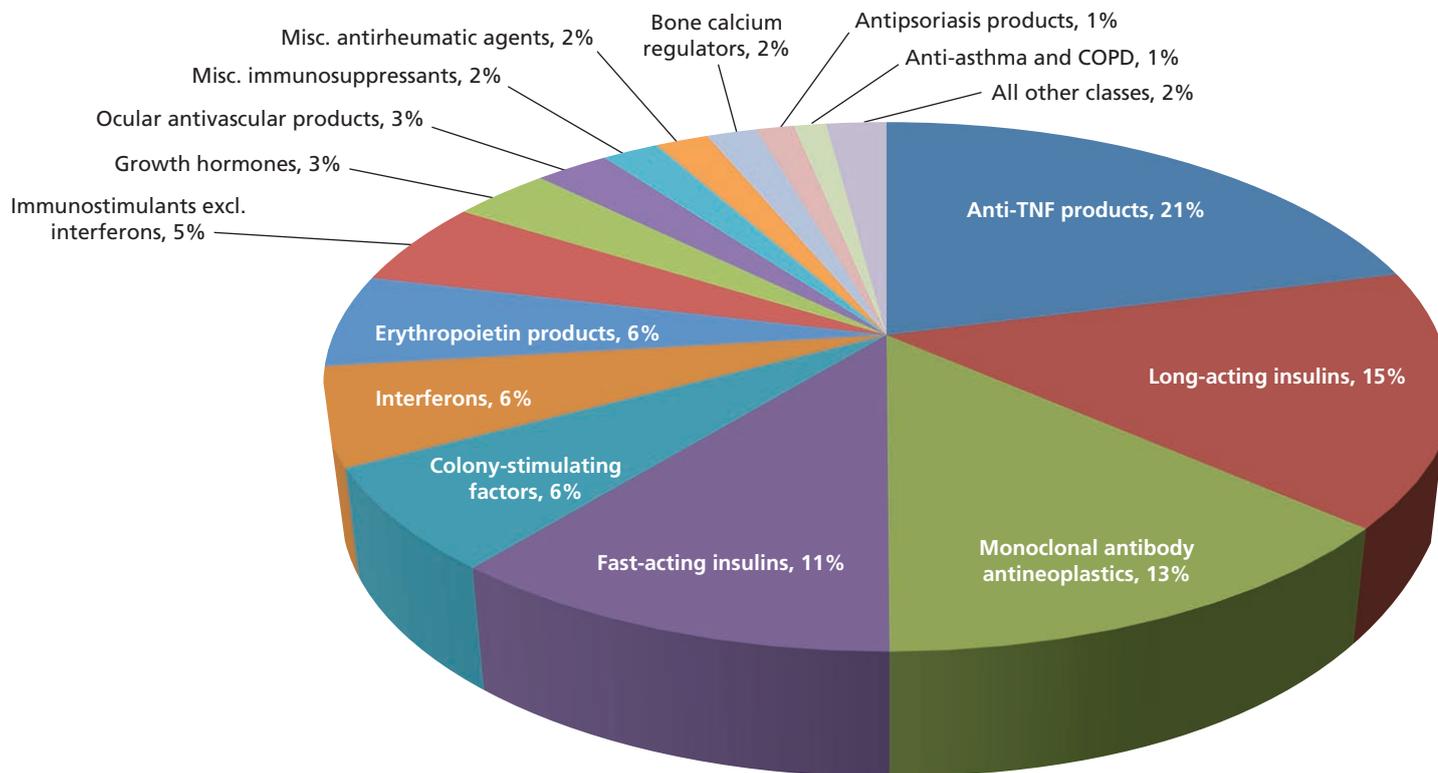
Given these assumptions, we calculate potential direct cost savings of \$44.2 billion over ten years, or about 4 percent of total biologic sales over the same period.¹⁸ The 35 percent price reduction estimate is on the high end of those included in the models described above, although the Congressional Budget Office anticipates an even larger 40 percent reduction in the long term. Reducing the price discount to 10 percent (the low end of assumptions in the models described above) cuts potential savings to \$12.6 billion over ten years. Biosimilar penetration is also a key driver of potential cost savings. Increasing penetration to 90 percent (with a 35 percent reduction in price) raises cost savings to \$66.2 billion over ten years, while decreasing penetration to 30 percent results in cost savings of \$33.9 billion over ten years.

The potential for cost savings will vary across biologic classes based on sales, the degree of competition, and the timing of bio-similar entry. We used the same assumptions as outlined above to generate estimates of potential savings for specific classes of biologics (Figure 1). Monoclonal antibody antineoplastics, anti-TNF alpha products, and insulins together account for more than 60 percent of estimated savings.

Gaps in Current Cost Saving Estimates

The estimates of cost savings that we identified in our review focused on a relatively narrow set of inputs, including growth in the biologic market overall, growth in the proportion of the biologic market eligible for competition, prices, and penetration rates. Data describing several key dimensions of our cost savings framework were rarely, if ever, noted in cost savings estimates. These important dimensions include:

Figure 1. Potential Cost Savings Across Biologic Classes



Payment models. Today, insurers pay for biologics using a range of approaches depending on insurance plan features, coverage decisions, place of service, and type of product. In the future, Medicare and commercial payers may adopt these same payment approaches for biosimilars, or they may develop new approaches entirely. Reference pricing, value-based-purchasing, and bundled payment have been discussed in the context of Medicare payment for self-administered and physician-administered biologics.¹⁹ Changes in payment models may have profound impacts on physician and facility incentives to shift to biosimilars, leading to changes in utilization and spending. Reviewed studies generally assumed that current payment practice would continue into the future. Few studies distinguished at all between self-administered and physician-administered biologics or different sites of service or provider incentives.

Nonprice competition from originators. Originator companies in some markets are developing second- and third-generation biologics that offer improvements over their older products. These products will compete with biosimilars for market share. Whether or not payers, patients, and prescribers will switch to these next-generation biologics rather than to biosimilars depends on the safety, efficacy, convenience, and cost of biosimilars, not just relative to originator products, but also to these next-generation biologics, and on how payers structure the relative reimbursement incentives. In addition to the development of new products, manufacturers of originators and biosimilar drugs may differentiate their products by offering value-added services, for example, patient support and medication therapy management.

Regulatory uncertainty. Several critical features of the biosimilar regulatory pathway have yet to be finalized, such as guidance on clinical trial requirements, criteria for a finding of similar-

ity and interchangeability, and whether or not a biosimilar approval will apply across all originator indications. These policy decisions will have a significant impact on the evolution of the U.S. biosimilars market. Every study that projected biosimilar cost savings assumed (out of necessity) some final form of the FDA regulations that may or may not resemble the actual regulation. In addition to regulatory uncertainty, there is also significant legal uncertainty surrounding the new patent litigation processes introduced by the Biologics Price Competition and Innovation Act that will affect the timing of and barriers to biosimilar entry.

Indirect health and cost impacts from broader biologic use. Widespread biosimilar use has the potential to cause gains in health for patients taking biosimilar medications; if lower prices of biosimilars relative to reference products result in lower copayments for patients, patients' adherence to medication regimens may increase, improving their health. Several studies outside the scope of our search suggest this is the case for pharmaceuticals in general.²⁰ None of the studies that we reviewed modeled biosimilar cost savings from this point of view. Only a handful of studies considered a change in biologic prescription volume at all.²¹

Who Will Benefit from Biosimilar Cost Savings?

Biologics include self-administered drugs obtained from retail and specialty pharmacies, drugs administered in hospital settings, and drugs administered in physician office settings. The balance of cost savings to health care payers, providers, and patients is different for those three different settings due to differences in payment and cost-sharing arrangements (see the box on page 10). Table 2 summarizes these actors and the degree to which they are likely to benefit from lower-priced biosimilars.

Common Payment Arrangements for Biologics

Self-administered, pharmacy-dispensed biologics: Most self-administered outpatient drugs are paid for on a fee-for-service basis, and the final amount paid by insurers reflects several transactions, including a confidential rebate payment. First, wholesalers and pharmacy chains purchase biologics from manufacturers at market rates. Patients then obtain biologics from pharmacies, often with cost sharing in the form of a copay or coinsurance. Next, pharmacies bill insurance companies for the market rate net of cost sharing, plus a dispensing fee. As a final step, manufacturers often deliver a rebate payment to insurers in exchange for favorable placement on the insurers' formulary.

Biologics used in the inpatient facility setting: Most inpatient procedures are paid for on a prospective, bundled basis (through, e.g., diagnosis-related group payments). The costs associated with biologics administered in the inpatient setting are incorporated into these prospective payments. Facilities purchase and stock biologics directly from manufacturers and wholesalers or through Group Purchasing Organizations (GPOs). Health care professionals may bill separately for administration of the drug and related services.

Biologics used in the outpatient facility setting: As in the inpatient hospital setting, in most cases facilities purchase drugs for

use in an outpatient setting from manufacturers and wholesalers or through GPOs. Some facilities are eligible to use the 340B Drug Discount Program²² to obtain biologics for outpatient use at reduced prices. Unlike the inpatient setting, many insurers pay for biologic drugs separately under fee-for-service arrangements. Some low-cost biologics are "packaged" into Medicare outpatient hospital payments for other services and are not separately reimbursed. Health care professionals may bill separately for administration of the drug and related services.

Biologics administered in the physician office setting:

Physician offices purchase drugs directly from wholesalers and manufacturers or through GPOs. Medicare pays physicians a reference price (ASP, which is reported to the Centers for Medicare and Medicaid Services by manufacturers) plus a margin to cover acquisition and stocking costs (now 4.3 percent in the case of Medicare). It is expected that Medicare will reimburse biosimilars at the lower biosimilar ASP plus 4.3 percent of the reference product's ASP. Commercial insurers also use a cost plus margin payment approach, although the base and margin can differ from the Medicare rates. In most cases, physicians bill separately for administration of the drug and related services.

Insurers benefit from lower biologic prices across all four delivery settings in the short term, and over time commercial insurers may transfer savings to payers and patients in the form of lower insurance premiums. Lower Medicare spending on biologics will ultimately benefit taxpayers.

Providers—such as physicians—purchase the biologics that they administer to patients in their offices and are reimbursed retrospectively. As a result, they may benefit from lower prices for

the biologics that they administer in their offices. In Medicare, physician-administered drugs are reimbursed at a price called "average sales price" (ASP) plus a fixed percentage (which was recently reduced from 6 percent to 4.3 percent as part of the 2013 sequester cuts). The ACA requires that Medicare reimburse physicians for biosimilars at the lower biosimilar ASP plus the fixed percentage of the higher reference biologic ASP to avoid financial disincentives for switching patients to biosimilars. Hospitals and other facilities

Table 2. Where Will Biosimilar Cost Savings Accrue?

Setting	Self-Administered from Retail or Mail-Order Pharmacy	Physician-Administered		
		Inpatient Facility Setting	Outpatient Facility Setting	Office Setting
Insurers	++	+	++	++
Facilities	NA	+/-	+/-	NA
Physicians	NA	NA	+/-	+/-
Patients	++	+	+	+

NOTE: ++ Significant share of savings. + Share of savings. +/- Ambiguous. NA: Not applicable.

purchase the biologics that are administered in the inpatient and outpatient facility settings and in a similar way will benefit from lower prices, and in the long run public and private insurers may adjust prospective payment and fee schedule rates to realize savings from biosimilars.

Whether or not and for how long physicians and facilities benefit from cost savings hinges on insurers. If insurers aggressively lower fee-for-service payment levels to biosimilar levels, the savings will accrue to insurers rather than providers. Insurers may, however, be slow to reduce payment levels, or they may choose to incentivize the use of lower-cost biosimilars by sharing savings. As noted above, Medicare is already committed to pay for Part B biosimilars at a lower biosimilar-specific ASP plus 6 percent of the reference biologic ASP. In some cases (e.g., prospective payment for inpatient health care), insurers make a single payment for a bundle of services, and it may be challenging to adjust payment rates to reflect lower biologic prices.

Patients are subject to cost sharing for biologics. Many biologics are “specialty drugs” that are on separate specialty formulary tiers with coinsurance rates of 20 percent to 35 percent. Cost

sharing often applies to self-administered biologics and can apply to physician-administered biologics depending on the patient’s insurance coverage. Deductibles and copays also factor into total patient out-of-pocket spending. In most cases, and especially when coinsurance plays a major role in patient out-of-pocket spending, lower biologic prices will benefit patients.

The range of biologic products, treatment locations, and providers complicates any analysis of biosimilar cost savings. To further complicate matters, the same biologic can be administered in all three settings. We designed our framework to be compatible with this variation.

Key Policy Issues

The immediate key policy issue centers on the final FDA regulation. Details on interchangeability, naming conventions, market exclusivity for originators, and clinical research requirements will have a direct impact on biosimilar competition and uptake, and therefore on cost savings. FDA’s gradual release of draft guidance is shedding increasing light on the form of the final regulation. For example,

FDA recently released draft guidance outlining its current thinking on similarity between a biosimilar and a reference biologic.²³ This draft guidance lists four categories of similarity that will help manufacturers and FDA determine the evidence required for approval: (1) not similar, (2) similar, (3) highly similar, and (4) highly similar with fingerprint-like similarity. FDA’s release of a first version of the “Purple Book” list of potential reference biologics in September 2014 offered insight into FDA’s use of nonproprietary and proprietary names and the terms “interchangeable” and “biosimilar.”²⁴

The following sections introduce other issues that are related to cost savings and other impacts from biosimilars but are not directly linked to FDA regulation. These issues focus on secondary and potentially unintended impacts of biosimilars.

Links Between Benefit Design, Out-of-Pocket Costs, and Utilization

While the introduction of biosimilars will have direct and significant effect on patients, none of the cost savings estimates we analyzed considered the patient perspective. Lower-priced biosimilars will reduce patient out-of-pocket spending. Biologic drugs—and specialty drugs in general—are often placed on specialty tiers, especially when there are nonbiologic therapeutic alternatives (e.g., in rheumatoid arthritis). Patient out-of-pocket costs are much higher when biologics are placed on specialty tiers—up to 35 percent of the cost of the drug. Patients’ out-of-pocket burden can vary across clinical settings. For example, physician-administered drugs covered under medical benefits may or may not require coinsurance-based cost sharing. Cost sharing may be higher for some patients with few other health expenditures and a high deductible, and it may be lower for other patients who have reached a catastrophic spending cap.

To the extent biosimilars reduce the direct cost of drugs, they will also reduce cost sharing, and in particular cost sharing based on coinsurance. A 25 percent direct price reduction on a \$40,000-per-year drug would reduce out-of-pocket spending for an individual facing a 30 percent coinsurance rate by \$3,000 a year (Table 3). Coinsurance savings will be smaller for less expensive biologics, although some of these biosimilars may be placed on preferred tiers, further reducing patients’ cost-sharing burden. Insurers could choose to eliminate cost sharing for biosimilars altogether to incentivize patients to switch from more expensive innovator products.

Indirect Outcomes in Terms of Uptake, Adherence, and Health Outcomes

Regardless of the mechanism, lower cost sharing for biosimilars will increase utilization of biologic drugs. Studies suggest that patients’ demand for biologics (and other types of health care) is relatively inelastic—i.e., a proportional decrease in out-of-pocket costs will lead to a relatively small proportional increase in utilization. Still,

Table 3. Potential Cost Savings for Patients

Biosimilar Price Reduction Relative to Originator (%)	Co-insurance Rate		
	10	20	30
10	\$400	\$800	\$1,200
15	\$600	\$1,200	\$1,800
20	\$800	\$1,600	\$2,400
25	\$1,000	\$2,000	\$3,000
30	\$1,200	\$2,400	\$3,600
35	\$1,400	\$2,800	\$4,200

NOTE: Savings in relation to a \$40,000-per-year reference biologic.

estimates in the literature on small-molecule drugs suggest that a 10 percent reduction in cost sharing would result in a 2 to 6 percent increase in spending.²⁵ We expect a smaller—but still potentially significant in terms of spending—response for biologics.

Some of this increase in spending comes from patients who previously were not on medication who decide to seek a biosimilar prescription. Less-expensive biologics may also incentivize some patients to switch from relatively inexpensive small-molecule therapies to more expensive biologics, even if they switch to biosimilars that are less expensive than originator biologics. As a result, the net impact of lower biosimilar cost sharing on total drug spending is unclear.

The potential impacts of biosimilars on total health spending and health outcomes—while potentially significant—are even less clear at this point. Higher biologic prescription rates could improve adherence and could match patients with appropriate drug treatments.

Understanding the Impact of Payment and Clinical Context on Cost Savings

While national estimates of cost savings are relevant to some policymakers and industry strategists, we believe there is a need for cost-savings estimates targeted more narrowly at specific payers, specific delivery systems, and specific patient populations. As we outlined at a gross level previously, payment policies and incentives for biosimilar substitution vary significantly depending on who purchases biologics and where they are administered. Actual payment policies can vary at a finer-grained level across insurers and delivery systems. On the other hand, the distinctions between providers and places of service may blur in integrated health care systems, like Kaiser Permanente, and in new health care delivery

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and payment arrangements such as accountable care organizations (ACOs). In either case, additional contextual detail could help inform more targeted and accurate cost estimates for specific entities that have a financial stake in biologic prescribing.

Delivery system and patient population-oriented studies are also a useful context to investigate the impacts of biosimilars on uptake, adherence, and health outcomes. Analyses using claims data will be useful to identify these indirect impacts once the U.S. biosimilar market develops in earnest.

Conclusion

We estimated the cost savings potential of biosimilars to be \$44.2 billion over ten years using available information and a survey of the literature. Actual savings will hinge on the details of FDA's final biosimilar regulation. Payment arrangements, competition, and acceptability will also influence the magnitude of potential savings. Savings will accrue to a range of stakeholders in the short term, though in the long term patients and taxpayers will benefit. Aside from the FDA regulation, other key policy issues include the impact of cost sharing on the use of biologics and on links between costs, adherence, and health outcomes. Future research in these areas will provide helpful

context for policymakers, patients, and providers and will strengthen the foundation for future cost savings estimates and analyses.

Notes

¹ IMS Health, “Shaping the Biosimilars Opportunity: A Global Perspective on the Evolving Biosimilars Landscape,” 2011.

² American Society of Clinical Oncology, “ASCO in Action Brief: Value in Cancer Care,” web page, January 21, 2014. As of September 16, 2014: <http://www.asco.org/advocacy/asco-action-brief-value-cancer-care>

³ Berndt, E. R. and M. L. Aitken, “Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century After the 1984 Waxman-Hatch Legislation,” NBER Working Papers, 2010.

⁴ U.S. Food and Drug Administration, “Drugs: Biosimilars Guidances,” web page, September 9, 2014. As of September 16, 2014 <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm290967.htm>

⁵ Grabowski, H., et al., “Biosimilar Competition: Lessons from Europe,” *Nature Reviews Drug Discovery*, Vol. 13, No. 2, 2014, pp. 99–100.

⁶ Including situations where multiple, similar drugs were approved in the United States through the full New Drug Application (NDA) or Biologics License Application (BLA), or via the 505(b)(2) “paper” NDA pathway.

⁷ Simoens, S., “Biosimilar Medicines and Cost-Effectiveness,” *ClinicoEconomics and Outcomes Research*, Vol. 3, No. 29, 2011.

⁸ For example, Reiffen, D., and M. R. Ward, “Generic Drug Industry Dynamics,” *Review of Economics and Statistics*, Vol. 87, No. 1, pp. 37–49, 2005.

⁹ Shapiro, R., et al., *The Potential American Market for Generic Biological Treatments and the Associated Cost Savings*, 2008.

¹⁰ Grabowski, H. G., et al., “Entry and Competition in Generic Biologics,” *Managerial and Decision Economics*, Vol. 28, Nos. 4–5, pp. 439–451, 2007; and Goodman, C., et al., *Economic Analysis of Availability of Follow-On Protein Products*, Report to the U.S. Department of Health and Human Services, Assistant Secretary for Planning and Evaluation 2009.

¹¹ Ahlstrom, A., et al., *Modeling Federal Cost Savings from Follow-On Biologics*, Avalere Health, 2007.

¹² Engel and Novitt, *Potential Savings that Might be Realized by the Medicare Program from Enactment of Legislation Such as the Access to Life-Saving Medicine Act (H.R. 6257/S. 4016) That Establishes a New CBLA Pathway for Follow-On Biologics*, Pharmaceutical Care Management Associates, January 2007.

¹³ Miller, S., and J. Houts, *Potential Savings of Biogenerics in the United States*, Express Scripts, 2007.

¹⁴ Congressional Budget Office, *Cost Estimate: S. 1695 Biologics Price Competition and Innovation Act of 2007*, 2008.

¹⁵ Goodman, C., et al., “Economic Analysis of Availability of Follow-On Protein Products.” Report to the U.S. Department of Health and Human Services, Assistant Secretary for Planning and Evaluation, 2009 and Chauhan, D., et al., “The Markets for Biosimilars: Evolution and Policy Options,” Office of Health Economics briefing, November 2008.

¹⁶ We used 2013 IMS MIDAS data for 110 individual biologic drugs. These drugs included all products in major biologic Anatomical Therapeutic Classification classes (e.g., insulins, growth hormones, interferons, anti-TNF alpha products, and monoclonal antibody neoplastics) as well as select biologics in other classes (e.g., “other antineoplastics”). We excluded vaccines and blood products due to unique manufacturing and market considerations for these products.

¹⁷ Year-on-year growth of 10 percent is consistent with recent sales growth and forecasts from IMS Health. The assumed increase in biologic sales exposed to biosimilar competition over time is due to patent expiration. The initial 10 percent rate assumes that the initial biosimilar entrants will rely on first-generation biologics as reference products. Biosimilar market penetration of 60 percent is a conservative estimate that is considerably lower than typical small-molecule penetration rates. Finally, the price discount assumption is informed by the discount factors reported from other studies in Table 2.

¹⁸ From 2014 to 2024. We chose 2013 as a base period because it was the last year for which complete status quo sales data were available. We estimated cost savings discounted at 3 percent from 2014 to 2024.

¹⁹ MedPAC, *Report to the Congress: Improving Incentives in the Medicare Program*, “Chapter 5: Medicare Payment Systems and Follow-on Biologics,” 2009.

²⁰ See, for example, Goldman, D., et al., “Prescription Drug Cost Sharing: Associations with Medication and Medical Utilization and Spending and Health,” *Journal of the American Medical Association*, Vol. 298, No. 1, 2007, p. 61.

²¹ See, for example, Shapiro (2008).

²² The 340B Drug Discount Program creates a ceiling price for outpatient drugs that is based on Medicaid's payment rate for drugs. A variety of safety net provider organizations can access 340B pricing, including federally qualified health centers and disproportionate share hospitals.

²³ U.S. Department of Health and Human Services, Food and Drug Administration, "Guidance for Industry: Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product," draft guidance, May 2014. As of September 16, 2014:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM397017.pdf>

²⁴ U.S. Department of Health and Human Services, Food and Drug Administration, "Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations," web page, September 9, 2014. As of September 16, 2014:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411418.htm>

²⁵ Goldman et al., 2007.

About This Perspective

This Perspective combines prior research and recent data to estimate cost savings in the U.S. market for so-called biosimilar drugs, in anticipation of the U.S. Food and Drug Administration's release of final regulations outlining lower-cost approval pathway requirements. This research was sponsored by Sandoz, a Novartis Company, and conducted within RAND Health, a division of the RAND Corporation. A profile of RAND Health, abstracts of its publications, and ordering information can be found at www.rand.org/health.

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