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NURTURING THE POTENTIAL OF THE BIOSIMILAR MARKET

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This report was commissioned by the Alliance for Patient Access (AfPA) and the Biologics Prescribers Collaborative.

Nurturing the Potential of the Biosimilars Market

Executive Summary

Almost a decade since the first approved biosimilar in the United States (U.S.), it is time to explore whether biosimilars are achieving three objectives -- decreasing costs to the overall health care system, increasing patient access/options and reducing patient cost sharing. And, beyond those objectives, what are the barriers to realizing the full potential of biosimilars?

The potential for a strong biosimilars market has been simmering for the past 15 years. While biosimilars have begun to fulfill their promise in terms of development, safety and efficacy, the progress of the biosimilar market in terms of utilization has been uneven. The U.S. did not have its first Food and Drug Administration (FDA)-approved biosimilar until the 2015 approval of filgrastim, an oncology supportive care product. Currently there are 52 approvals with 41 biosimilars launched in the U.S.[1]

Biosimilar Approvals and Launches to Date

Reference Product	Molecule	First Approved Biosimilar	# of Biosimilars on Market	Class
Neupogen	filgrastim	September 2015	3	Supportive Care
Remicade	infliximab	November 2016	3	Immunomodulators
Neulasta	pegfilgrastim	July 2018	6	Supportive Care
Epogen/Procrit	epoetin	November 2018	1	Supportive Care
Avastin	bevacizumab	July 2019	4	Oncology
Herceptin	trastuzumab	July 2019	5	Oncology
Rituxan	rituximab	November 2019	3	Oncology
Lantus	Insulin glargine	November 2021	2	Insulin
Lucentis	ranibizumab	July 2022	2	Ophthalmology
Humira	adalimumab	January 2023	10	Immunomodulators
Actemra IV/SC	tocilizumab	April 2024	2	Immunomodulators
Eylea	aflibercept	June 2024	1	Ophthalmology

From the patient's perspective, there can be a big difference in terms of access depending on whether the drug is covered under the pharmacy or medical benefit. Traditionally plans have been less restrictive on medical benefit drugs, that is those that are administered by providers, compared to their management of pharmacy benefit drugs, which are typically self-administered.

Drugs managed under the pharmacy benefit are often subjected to higher cost sharing and utilization management which asks for providers to provide additional justification for the use of the drug and/or may require a patient to try another drug before the one preferred by the provider.

Most biosimilars that have launched in the U.S. have been for provider-administered infused drugs covered under the insurance medical benefit. The first major pharmacy-benefit biosimilar was for adalimumab which launched in 2023.

Evaluating the Success of Biosimilars in the United States

Although biosimilar take-up has been gradual, with each biosimilar approved – particularly provider-administered drugs - the market has adapted, and the biosimilar market share has grown more quickly. Across all biologics, the downward pressure on reference biologic prices accounted for nearly two-thirds of estimated savings ($24.6 billion); the remainder resulted from lower biosimilar prices relative to their reference biologics.[2]

BIOSIMILAR SAVINGS

Projected $181 billion over next 5 years[3]

Biosimilars have provided some increased patient access and options to care, but access has been influenced by how the biosimilar is distributed and reimbursed. Compared to the medical benefit, biosimilars in the pharmacy benefit face a much harder path to success because many plans are financially motivated to pick a higher cost drug with a higher rebate. Rebates drop the price considerably for plans, but not always the patient.

With expected launches and uptake likely to increase overall spending on biosimilars to $20–$49B in 2027 and cumulative sales of $129B over the next five years, there is a need to understand the delta between the current landscape and the potential of biosimilars.[4] The biosimilar landscape could be more robust than it currently is; 86% of brand biologics that are eligible for biosimilar competition do not have a biosimilar under development.[4]

Regulatory uncertainties and intellectual property barriers can stifle biosimilar development. It takes six to nine years and cost between $100 million and $300 million to get a biosimilar approved and on the market.[5] More than half of the spend and half the time is due to clinical trials.[6]

After a biosimilar is approved and enters the market, it can face an uphill battle to gain utilization and market share. Uptake depends on physician prescribing which is influenced by their own judgement, understanding of the medicine and payer reimbursement. One found that only 16% of doctors and 13.4% of pharmacists said they felt “very prepared” to talk with patients about biosimilars.[7]

However, the biggest barrier to creating a long-term market for biosimilars will be reimbursement. Rebates motivate payers’ coverage decisions.[4] It is challenging for biosimilars to enter the market and quickly gain enough momentum to gain the scale necessary to be able to compete with established reference products that may be willing to dramatically increase rebates to be competitive with biosimilars.

Securing the Biosimilar Marketplace

A sustainable biosimilar market will consider the needs of manufacturers who need to take the risk to invest in developing and marketing biosimilars, payers who need to see savings over the long term, providers who have incentives to switch to biosimilars and patients that have increased access and reduced costs when they take biosimilars.

TACKLE MISPERCEPTIONS ABOUT BIOSIMILARS

- Biosimilars are highly similar to their originator reference product, however, if the FDA were to remove the need for switching studies, it could help buoy the overall biosimilar market and increase access by allowing biosimilars to be used more broadly and ease the misperception that non-interchangeable products are not as safe as interchangeable products.
- While the FDA does have resources on biosimilars for providers, physicians and pharmacists need more biosimilar education.
- Specific payment codes could be used to pay to spend time educating patients on biosimilars.

INCENTIVIZE USE OF BIOSIMILARS

- While the add-on fee of 8% of the reference product's Average Sales Price (ASP) is helpful, it may not be enough to incentivize provider use of biosimilars because it uses average provider acquisition rates which may not reflect an individual provider's reality.
- The federal government, through Medicare and/or Medicaid, could incentivize providers through quality measures, to use biosimilars or, more boldly, institute reference pricing.
- Continue to review 340B utilization of reference products over biosimilars and consider Medicare changes to reimbursement that would incentivize use of biosimilars.
- Payers and providers could work toward a shared savings arrangement that compensates hospital outpatient departments for additional utilization of biosimilars.
- The Centers for Medicre & Medicaid Services (CMS) could directly call out and financially encourage the use of biosimilars through direct provider administration or through prescriptions in their Center for Medicare and Medicaid Innovation models like the Enhancing Oncology Model or the Accountable Care Model.

- CMS could institute reduced cost-sharing for biosimilars to incentivize patients to use them.

- Continue efforts to push transparency into pharmacy benefit manager dealings so that employers and patients can get the benefit of lower spending due to biosimilars.

Encouraging this market is good for payers and, more importantly, patients. Biosimilars are in development or approved but not launched for reference products that have almost $100 billion of invoice spending.[4] Nurturing biosimilars is about long-term savings and improved access, not just the next five years but the next 50.

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Nurturing the Potential of the Biosimilar Market

Utilization of generic medicine, that is small molecule drugs that are chemically derived, makes up 90% of the retail prescription drug market in the United States (U.S.) and has saved the U.S. healthcare system almost $3 trillion dollars over the past 10 years.[1] The hope is that more complex large molecule drugs – biologics - could follow a similar path, contributing to cost savings and greater access.

Biologics are typically proteins extracted from living organisms or manufactured in living cells. However, given the complexity of large macromolecules and the production process, biologics are usually more expensive to manufacture and thus command higher prices. Between 2014 and 2018, spending on biologic medicines increased by 50.1% in the U.S.[2] While utilization of biologics makes up only 2% of prescription drug utilization, it constitutes 46% of drug spending. The U.S. biologics market has grown on average, 12.5% annually over the last five years on an invoice-price basis.

Generics
- Typically small molecules
- Chemically synthesized
- Bioequivalent to brand name drug

Biosimilar
- Complex large molecules
- Made from living cells
- Highly similar to brand name biologic drug

With the continued development of effective, but expensive biologics, especially for cancer and immune-based therapies, it has never been more necessary to foster the biosimilars market.[4] Biosimilars are highly similar to an approved originator biologic drug (referred to as the reference product.) Because biosimilars and their reference products come from living organisms, they are not identical - but there are no meaningful differences in efficacy, safety, or purity between a biosimilar and its reference product.

The potential for a strong biosimilars market has been simmering for the past 15 years. The premise is that biosimilars, as close substitutes to biologics, will compete on price. While biosimilars have begun to fulfill their promise in terms of development, safety and efficacy, the progress of the biosimilar market in terms of utilization has been uneven. Each approved biosimilar was having more rapid adoption over earlier biosimilar launches. However, the recent launch of the first pharmacy benefit biosimilar, adalimumab, again calls into question the long-term prospect of biosimilars because even with ten biosimilars on the market biosimilars have very limited market share.[5]

Almost a decade since the first approved biosimilar in the U.S., **it is time to explore whether biosimilars are achieving three objectives: (1) decreasing costs to the overall healthcare system, (2) increasing patient access/options, and (3) reducing patient cost sharing.**

Beyond progress towards those objectives, what are the barriers to realizing the full potential of biosimilars? What policies have helped or hindered the market, and are some payers doing better than others? And, given the findings, what are the recommendations that would lead to a more stable and robust biosimilar market?

Encouraging this market is good for payers and, more importantly, patients. Biosimilars that are in development or approved but not launched for reference products constitute almost $100 billion of invoice spending.[4] Nurturing biosimilars is important for long-term savings and improved access; not just for the next five years, but the next 50.

Understanding the Here and Now of Biosimilars

The Drug Price Competition and Patent Term Restoration Act of 1984, otherwise known as Hatch- Waxman, established a generic drug pathway for small molecule medicines. However, it was not until 2010, with the Biologics Price Competition and Innovation Act (BPCIA) (passed as part of the Affordable Care Act), that an abbreviated regulatory pathway for biosimilars was established. In the European Union a similar pathway was approved five years earlier.[6]

The BPCIA provides four years of data exclusivity and 12 years of market exclusivity when an originator biologic receives approval from the Food and Drug Administration (FDA). Pediatric approvals can extend the exclusivity for another six months.[7] Reference products have market exclusivity until the 12-year period expires, but it is often much longer before a biosimilar is available.

The FDA approves biosimilars under Section 351(k) of the Public Health Service Act, which allows applicants to have less product-specific preclinical and clinical data compared to the reference product. Biosimilars are reviewed against the FDA-approved reference product, looking at whether the biosimilar is "highly similar" and possesses "no clinically meaningful differences" to the reference product.[8]

The U.S. had its first FDA-approved biosimilar with the 2015 approval of filgrastim, an oncology supportive care product. **Currently there are 61 approvals with 42 biosimilars launched in the U.S.**[9]

Table 1: Biosimilar Approvals and Launches to Date

Reference Product	Molecule	First Approved Biosimilar	# of Biosimilars on Market	Class
Neupogen	filgrastim	September 2015	3	Supportive Care
Remicade	infliximab	November 2016	3	Immunomodulators
Neulasta	pegfilgrastim	July 2018	6	Supportive Care
Epogen/Procrit	epoetin	November 2018	1	Supportive Care
Avastin	bevacizumab	July 2019	4	Oncology
Herceptin	trastuzumab	July 2019	5	Oncology
Rituxan	rituximab	November 2019	3	Oncology
Lantus	Insulin glargine	November 2021	2	Insulin
Lucentis	ranibizumab	July 2022	2	Ophthalmology
Humira	adalimumab	January 2023	10	Immunomodulators
Actemra IV/SC	tocilizumab	April 2024	2	Immunomodulators
Eylea	aflibercept	June 2024	1	Ophthalmology

Biologics and biosimilars are often considered "specialty medications" as they can be high-cost medications that treat rare or complex conditions and may require special handling. Specialty drugs are typically covered under either under the medical benefit when administered by a healthcare provider or under a plan's pharmacy benefit if self-injected/self-administered.

From the patient's perspective, there can be a big difference in terms of access depending on which part of the plan (pharmacy or medical) covers the drug. Traditionally plans have been less restrictive on medical benefit drugs compared to their management of pharmacy benefit drugs. Drugs managed under the pharmacy benefit are often subjected to higher cost sharing and utilization management, which asks providers to provide additional justification for the use of the drug and/or may require a patient to try another drug before the one preferred by the provider. This can vary plan to plan.

Most biosimilars that have launched in the U.S. have been for provider-administered infused drugs covered under the insurance medical benefit; these biosimilars follow the buy-and-bill model for reimbursement. In the buy-and-bill model, providers purchase products, treat patients, then seek reimbursement from the payer post-treatment. This means that providers carry the financial risk between the time they purchase the product and their reimbursement.

Biosimilar reimbursement in Medicare Part B, for example, is at the Average Sales Price (ASP) plus 8% of the reference product's ASP. Commercial payers often provide higher reimbursement. Payer decisions on formulary coverage can have a substantial effect on provider economics.

Two key, closely linked factors, have been instrumental in the trajectory of the biosimilar landscape:

1. **Provider choice:** While it is changing, traditionally payers have left treatment decisions for provider-administered drugs to the provider. Providers, depending on the care setting and their facility/health system, could make these decisions on their own or work with their system's preferred treatment.

2. **Not all biosimilars are interchangeable, unlike small molecule generics:** Where pharmacists can dispense generics in place of brand name drugs at the pharmacy counter, most biosimilars are not interchangeable in the same way. Unlike small molecule generics, the FDA does not (yet) view all biosimilars as interchangeable with their reference products. This has not been an issue for the biosimilars that are directly clinician-administered drugs but will be with the newly emerging self-administered biosimilars covered under the pharmacy benefit.

In addition to the evidence required for approval, currently manufacturers can conduct a switching study as part of an application for a new interchangeable biosimilar product.[10] A switching study is where a manufacturer studies patients who alternate between the reference product and the biosimilar and compares them to patients who did not alternate. As of November 2024, seven launched biosimilars and six yet-to-be-launched biosimilars have FDA interchangeability designations in the U.S.[9]

Evaluating the Success of Biosimilars in the United States

Currently, **biosimilars make up only 2 to 3% of the biologics marketplace**.[11] While some might be tempted to rush to judgement and declare the biosimilar landscape a failure; these are still the early days of biosimilars. Over the past nine years, we have just started to comprehend their market potential and evaluate their success based on how biosimilars are decreasing costs to the system overall, increasing patient access/options and reducing patient cost sharing.

Decreased Costs to the System Overall

Thus far, biosimilars have decreased costs to the system overall by ~$25 billion without impacting quality or delivery of care.[1] It took time, but eventually there was significant uptake in the first biosimilar. Three years after market entry, the use of filgrastim biosimilars increased to almost half of all filgrastim claims paid by Medicare Parts B and D, and to over one third of filgrastim products in Medicaid. Both Medicare and Medicaid saw significant discounts in 2018 from filgrastim biosimilars and the increased biosimilar utilization. This uptake translated to an annual total savings of $59 million for Medicare and Medicaid.[12]

Although biosimilar adoption has been gradual and far less than what is now seen in small molecule generic drug markets, it has followed a similar trend to that observed among generic drugs in the years that immediately followed the passage of the Hatch-Waxman.[13] With each biosimilar approved, the market has adapted, and the biosimilar market share has grown more quickly.

One of the main ways that biosimilars save the healthcare system money is by simply being on the market and presenting competition for the reference product. For example, infliximab's reference product price continued to increase in price until 13 months after approval of a biosimilar. It then **decreased** 45% over four years instead of the anticipated 20% increase without a biosimilar. Thus, the infliximab biosimilars contributed to a decrease, at least in theory, of 55% in the cost of the reference product.[14]

On average, Medicare reimbursement for reference products increased 9.2% in the two years prior to the launch of biosimilars. **Following the launch of a biosimilar, Medicare reimbursement rates for reference products fell 32.7%, while biosimilar reimbursement rates fell much faster at 50.3%.** However, most biosimilars started with a reimbursement price below that of the reference product; only 20% did not.[15] Biosimilars that are provider-administered and covered under the medical benefit typically launch at a wholesale acquisition cost (WAC) that is between 10% to 57% lower than that of the reference product.[16]

Examined on an annual basis, ASP prices of biosimilars have decreased at 9% to 24% per year while most reference products have decreased at a rate of 4% to 21% following the introduction of a biosimilar.[16] Across all biologics, the downward pressure on reference biologic prices accounted for nearly two-thirds of estimated savings ($24.6 billion); the remainder resulted from lower biosimilar prices relative to their reference biologics.[17] Biosimilar savings over the next five years are projected to reach $181 billion.[3]

And payers are seeing the savings; according to survey work done by Cencora, 78% of payers felt that biosimilars have provided meaningful cost savings to their organization. This is up from 53% in 2022.[18]

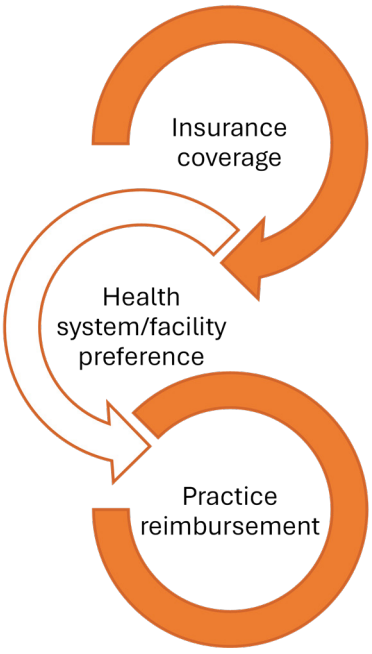
Increasing Patient Access and Options

Biosimilars have provided some increased patient access and options to care, but access has been influenced by how the biosimilar is obtained and reimbursed.

Physician-administered drugs and/or those covered under the medical benefit

To date, the biosimilar market has been focused primarily on products that are provider-administered. All things being equal in terms of clinical efficacy, providers decide what to administer based on the patient's insurance coverage/what payers will reimburse, what the provider's health system/facility prefers, and what is financially viable to their practice.

Factors in Provider Decisions



Influence of Insurance Coverage/Payer Choices

Patients with employer coverage or Medicare Advantage have been driven toward biosimilars by their insurance coverage.[19] The reason? Financial liability.

Biosimilar uptake was greater in Medicare Advantage than traditional fee-for-service Medicare for 6 of 7 product types, ranging from 1.1 times greater for trastuzumab to 2.3 times greater for epoetin.[20] For Medicare Advantage and employer plans, the financial liability often stays with the payer. As a result, payers tightly manage costs and often prefer biosimilars.

Overall, biosimilar uptake in traditional fee-for-service Medicare, which maintains a largely hands-off approach to coverage decisions, has been uneven but growing. With the payer not being a deciding factor, the provider may consider the care setting in their treatment.

Influence of Care Setting

Through buy-and-bill, under a payer's medical benefit, providers are typically key decision makers in drug selection. However, beyond their obligation to their patient, providers are also accountable to their practice or facility.

When a provider is part of a larger system or facility, the utilization preferences of that system may override individual provider choice for provider-administered drugs. Medical practices and hospital outpatient departments may steer utilization toward preferred products with a higher profit margin, and reference products may qualify for different discounts and rebates (including 340B pricing) that make them a more financially lucrative choice.

Finally, entities that qualify for the 340B program receive discounts from brand manufacturers on the purchase price, but payers reimburse them at the same rate as non-340B entities. Hence reference products are often more profitable for 340B entities than biosimilars.

Table 2. Biosimilar Purchases by 340B eligible entities

	ASP	340B Price (-22.5%)	Reimbursement	Net
Reference	$1,200	$930	$1,272	$342
Biosimilar	$900	$697	$996	$299

Note: This example is illustrative and not based on any specific product.
Source: Apteka Analysis

As seen in Table 2, a reference product with an ASP of $1,200 would result in a net profit of $342 for a provider versus $299 for the biosimilar. And while this example is purely illustrative, it demonstrates directionally the challenges of biosimilar uptake with 340B entities.

This could explain why uptake for biosimilars between provider practices and hospital outpatient departments has been inconsistent and varied by drug. In one analysis, a patient in the hospital outpatient setting was 42% less likely to receive a filgrastim biosimilar than a patient in an office setting, but 73% more likely to receive an infliximab biosimilar.[21] Utilization patterns indicated that product selection occurred at the facility level, rather than being at the discretion of the prescribing physician or driven by patient characteristics and could have been driven by facilities/systems steering physicians toward certain products when they can earn higher profits.[22]

Influence of Provider Choice

After providers factor in any payer or system/facility dynamics, they consider their reimbursement for the biosimilar or the reference product. If a biosimilar is seen as clinically effective and equally or more financially advantageous to the provider in terms of reimbursement, providers will administer the biosimilar.

For instance, practices participating in Medicare's Oncology Care Model (OCM) adopted biosimilars at significantly higher levels than non-participants, with average biosimilar uptake at 76% after two years in the model compared to 64% in non-model practices.[4] These practices had an incentive to seek the lowest price per treatment.

Overall, payer and provider decisions have given some patients improved access to provider-administered biosimilars.

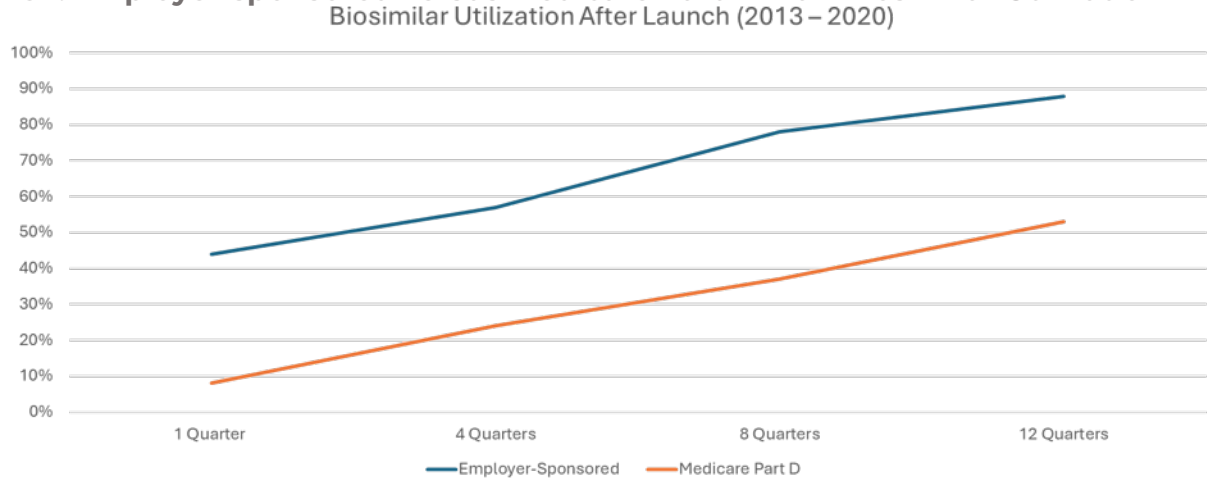
Self-administered drugs and/or those covered under the pharmacy benefit

While there has been relatively strong biosimilar uptake in the provider-administered buy-and-bill environment that operates under a patient's medical benefit, the limited experience in biosimilars market covered under the pharmacy benefit has shown weaker adoption.

Adalimumab, launched in 2023, was the first big pharmacy benefit biosimilar. Unlike most medical benefit products, pharmacy benefit products must be on a formulary: a list of drugs that the insurance plan will allow patients to access. As more pharmacy benefit biosimilars enter the market, payer preference will be a larger factor in biosimilar market share than provider preference, particularly if interchangeable biosimilars gain momentum. This could increase patient access to treatments; if patients are presented with less costly alternatives at the point of sale, they are more inclined to switch to the biosimilar.

Although based on relatively limited data, as seen Figure 1, employer-sponsored coverage had far greater coverage of biosimilars compared to Medicare Part D. **Employer-sponsored plans covered biosimilars at a rate of 44% compared to Part D plans which only covered 8% one quarter after biosimilar market entry.**[19]

Figure 1. Employer-sponsored versus Medicare Part D Plan Biosimilar Utilization



Source: Bertuzzi, L. & Maini, L. Benefit Design And Biosimilar Coverage In Medicare Part D: Evidence And Implications From Recent Reforms. Heal. Aff. 43, 717–724 (2024).

Compared to the medical benefit, biosimilars in the pharmacy benefit face a much harder path to success because many plans are financially motivated to pick a higher cost drug with a higher rebate. When considering higher cost/higher rebate drugs, patient cost-sharing is often based on the higher price without consideration of the rebate. Plans are then able to secure a rebate through their pharmacy benefit manager, which drops the price for the insurer considerably.

The appeal of high cost/high rebate drugs is easier to comprehend by using the example of Medicare Part D, where the plan liability percentage is set by the government. Creating a simplified example of the dollar flow, Table 3, shows a $1,200/month reference product covered under Medicare Part D in 2025. The plan liability will be 65% ($780) and the beneficiary will owe 25% of the $1,200 ($300). The manufacturer picks up the other 10% ($120) from the changes to the Part D benefit design. However, they also provide the plan with a 50% rebate ($600), which means that the net price of the reference product to the plan is $180.

Table 3. Medicare Part D 2025 Example

2025	Reference	Biosimilar
Price of Drug	$1200	$600
Plan Liability (65%)	$780	$390
Beneficiary Liability (25%)	$300	$150
Manufacturer Liability (10%)	$120	$60
Manufacturer Rebate/Discount to Plan	$600	$0
Net Price to Plan	$180	$390
Net Manufacturer Profit	$480	$540

Source: Apteka Analysis

Biosimilar would need to provide additional $210 in rebates for parity, bringing profit to $330

A biosimilar that comes in at $600 (50% discount from the reference product) would create a $390 liability for the plan that would not be offset by additional discounts or rebates. Beneficiaries would see a lower cost-sharing at $150 (25% of $600.)

To create financial equity between the reference and the biosimilar, the biosimilar manufacturer would need to provide an additional $210 in rebates, bringing their net profit to $330 compared to the reference product's $480. The rebate math makes it challenging to have a financially viable biosimilar.

To date, pharmacy benefit biosimilars have been limited to biosimilar insulin and, starting in 2023, adalimumab. Based on experience thus far, Part D patients have not had broad access to biosimilars overall.

Decreasing Cost to Patients

Thus far, biosimilar competition has not yet been systematically associated with lower out-of-pocket (OOP) spending for patients. One study looking at commercially-insured patients found that annual OOP spending for patients that used biosimilars was similar to those using the reference product.[23]

There are several potential reasons why biosimilar competition has not consistently led to OOP savings for patients:

- Patient cost sharing is dependent on insurance benefit design. Patients face distinct phases of the benefit over the course of the plan year -- deductibles, coinsurance and OOP maximums. It is difficult to calculate if a patient is spending less and/or if they hit their OOP maximum - the savings of the biosimilar more directly benefit the payer, not the patient.

- Patient cost-sharing for provider-administered drugs is often a coinsurance rate that is based on payer reimbursement, which varies between Medicare and commercial payer. Medicare reimburses based on an ASP plus a percentage, while commercial payers reimburse providers at a much higher rate than Medicare, thus increasing the OOP coinsurance amount for patients and negating savings.

- Payers might be translating any cost savings from biosimilars into lower premiums, which are difficult to discern.

Most Medicare beneficiaries have seen little difference in their OOP spending. While patient OOP cost-sharing in Part B is 20%, most Medicare beneficiaries have supplemental coverage through Medigap plans which can reduce or even eliminate cost-sharing for Part B drugs regardless of whether it is a biosimilar or a reference product.

In commercial coverage, reference products often offer patient assistance programs which result in lowered OOP spending, negating any savings that the biosimilar might offer.[24]

Until the 2019 passage of the Bipartisan Budget Act (BBA), Medicare Part D patients faced higher cost-sharing for biosimilars compared to reference products, because biosimilars did not offer manufacturer discounts during the coverage gap. The BBA extended manufacturer discounts to biosimilar drugs and increased the discount provided by branded and biosimilar drug manufacturers from 50 percent to 70 percent.[25]

For example, in cases where infliximab was covered under Medicare Part D, the biosimilar was only moderately less expensive (18% less) than the reference product.[26] However, until the passage of the BBA, the biosimilar would have cost the beneficiary more ($1,700.)[26]

Patients in Part D face the same coinsurance obstacles for biosimilars and reference products because plans tend to put specialty products in specialty tiers with high coinsurance (25 – 33%). There may be savings from using a biosimilar, but it is dependent on the plan formulary design.

After nine years, the success of biosimilars in terms of decreasing costs, increasing patient access, and decreasing patient costs sums up as "it depends" and "sort of." The path forward was gaining momentum and seemed positive. However, this may be changing as more biosimilars are covered under the pharmacy benefit.

As explained below, gaps between the reality and the potential of biosimilars were exposed, and the challenges of pharmacy benefit management and payer preferences were realized.

Understanding the Gaps between Reality and Potential

Expected biosimilar launches and uptake are likely to increase overall spending on biosimilars to $20–$49B in 2027 and cumulative sales of $129B over the next five years. Thus, there is a need to understand the delta between the current landscape and the potential of biosimilars.[4]

The biosimilar landscape had been evolving, mostly concentrated on provider-administered, medical benefit biologics. That is until January 2023, when the first adalimumab biosimilar was launched. From January to October 2023, adalimumab biosimilars were launched with list-price discounts generally between 55% and 85%, based on the reference product's WAC of $3,461 per 40-mg pen.[5] Despite launching at these discounts, adalimumab biosimilars have not been given preferred formulary positioning in most cases, and have thus gained only 3% of market share through 2023.[5]

This lack of early uptake is caused by plan choice, and plans often prefer high-cost, high-rebate products. Reference products can increase their rebates to approximate the net price of biosimilars.[5] This was the case with adalimumab, which saw volume remain relatively stable over the first year although net sales had decreased due to rebates.[27] Payers and pharmacy benefit managers chose the reference product rebates over biosimilar discounts.[5]

86%

Of eligible brand biologics do not have a biosimilar under development

The failure of biosimilars to garner market share despite significant discounts and even having interchangeable products approved, has called into question the viability of the biosimilar marketplace. That is, until April 2024, when CVS took adalimumab off its formulary and favored a biosimilar that was comarketed with one of their wholly owned subsidiaries.[28] Within three weeks, CVS was able to switch more users to their preferred biosimilar than had been on any of the biosimilars in the previous 15 months. Even with over 13,000 fills on the biosimilar, the reference product is still dominating the market.[29]

Another critical note, the current biosimilar landscape is not as robust as needed; 86% of brand biologics that are eligible for biosimilar competition do not have a biosimilar under development.[4] To understand the obstacles to a more robust biosimilar landscape, it helps to think of the issues in two buckets – barriers to entry and barriers to utilization.

Barriers to Entry

Regulatory uncertainties and intellectual property barriers can stifle biosimilar development. It takes six to nine years and costs between $100 million and $300 million to get a biosimilar approved and on the market.[7] Over half of that time and spending is consumed by clinical trials.[30] This is not just a problem in the U.S., recent analysis suggests that resources required for biosimilar development are affecting launches in European markets, and are expected to hinder future launches there too.[31]

$100 - $300M

Cost to get a biosimilar to market in the U.S.

To obtain higher utilization, an interchangeable designation might help; pharmacists and patients must view pharmacy benefit biosimilars as effective as the reference product. In 2022, the European Medicines Agency gave all approved biosimilars interchangeable designation automatically. In contrast, the FDA currently requires additional multiple switching studies before a biosimilar can be given an interchangeable designation which requires additional time and expense for biosimlars.[11]

There is growing clinical evidence to suggest that switching from a reference product to a biosimilar is safe, particularly in the scenario of a single switch from a reference product to a biosimilar.[8] The U.S. may be walking toward a chage in policy.

In early 2024, the Medicare Part D program suggested a potential shift in the way that the Department of Health and Human Services (HHS), the agency that runs both the Medicare program and the FDA, thinks about interchangeability.

In April, the Medicare Part D program moved ahead with its proposal to allow plans to substitute any biosimilar to be substituted for their reference product, regardless of interchangeable designation, as a “maintenance change.” Midyear formulary substitutions of biosimilars for their reference products would apply to all enrollees (including those already taking the reference product prior to the effective date of the change). Interchangeable biosimilars and branded biosimilars could be substituted immediately; all others could be substituted following a 30-day advance notice to affected enrollees.[32]

In June, the FDA put out guidance for comments on interchangeability. This guidance seeks comment on switching studies and if they are needed to demonstrate interchangeability.[10] As pressure mounts to weaken the interchangeability standard, FDA must continue to play a significant role permitting what may and may not be switched and for what indications.

There are also intellectual property barriers that hinder the introduction of biosimilars. In the U.S., patent thickets make launching a biosimilar riskier than it is in other countries.

Patent thickets are a series of patents that overlap and block competitors from entering the market. While the BPCIA grants 12 years of market exclusivity, patents can run parallel to market exclusivity and prevent competitors from entering the market. One study found market launches for 50% of biosimilars in the U.S. have been significantly delayed, not necessarily due to the originator patent but subsequent patents.[33]

Patents can cover things like the biologic molecule itself, the formulations, manufacturing processes, devices for administering the product and packaging. Small tweaks can extend the patent life of a product and make it difficult for a biosimilar to come to market.

Barriers to Utilization

After a biosimilar is approved and enters the market, it can face an uphill battle to gain utilization and market share. Uptake depends on physician prescribing which is influenced by their own judgement, understanding of the medicine and payer reimbursement.

One of the long-standing questions when it comes to biosimilars is would providers be comfortable with them. Unlike in the early days of U.S. approval of biosimilars, it appears that physicians and pharmacists now understand the FDA definition of biosimilars and believe them to be safe and efficacious compared to the approved reference product.[34]

Only **16%** of surveyed doctors and **13.4%** of pharmacists said they felt "very prepared" to talk with patients about biosimilars

Yet, more needs to be done in some specialties. Research among retina specialists found that found that 98% of these providers were at least moderately familiar with biosimilars, but only 61% had prescribed them. Similarly, another study found that only 16% of doctors and 13.4% of pharmacists said they felt "very prepared" to talk with patients about biosimilars. Only 13.3% of doctors would give a biosimilar to a patient already using a biologic, and 18.1% of pharmacists would suggest a biosimilar for a patient already stable on a biologic treatment.[35]

This points to another hurdle in increasing biosimilar utilization – making providers comfortable with switching patients from reference products or even from one biosimilar to another. It is especially hard for a biosimilar to capture significant market share if it is a drug that treats a long-term chronic condition. For chronic diseases like rheumatoid arthritis, the rate of patients new to a given biologic therapy is less than 20% of the total patients taking that drug each year, with the rest being stable and well-maintained on the therapy and therefore unlikely to switch.[36] By contrast, oncology has faster patient turnover and may be more amenable to biosimilar uptake.

A survey of physicians found that 84% disapproved of nonmedical switching (i.e., changing treatment for a stable patient because of cost or availability or insurance formulary) in stable patients.[34] Over time this hesitation may decrease, especially if the FDA expands the qualification for interchangeability and providers gain education, experience and comfort with biosimilars. As it stands now, the existence of interchangeability designation may create the impression that not all biosimilars are as effective as the reference product.

As interchangeability becomes more prevalent, pharmacist education on biosimilars will be more important as well. Overall, about 90% of the pharmacists surveyed knew that a biosimilar had equivalent efficacy and safety, respectively, to its reference but only 20% understood that a pharmacist can substitute an FDA-approved interchangeable without the approval of a prescriber.[37]

The biggest barrier to creating a long-term market for biosimilars, particularly as the landscape shifts to more pharmacy benefit biosimilars, will be reimbursement. The path forward for biosimilars, while similar, is a little different depending on whether a pharmacy dispenses, or provider administers the biosimilar.

Biosimilars have had stronger uptake in the medical benefit buy-and-bill system, where physicians have incentive to select one product over another compared to the pharmacy benefit where rebates motivate payers' coverage decisions.[4]

For provider-administered drugs, Medicare sets the benchmark for most biologic payment. For biosimilars, Medicare Part B pays ASP plus 8% of the reference product's ASP. The idea is that providers will be less disincentivized to provide a biosimilar if they are able to receive the add-on payment that reflects the, often higher, reference product's price. The add-on payment had been 6% of the reference product's ASP but increased as part of the Inflation Reduction Act with a goal of increasing access to biosimilars and encouraging competition between biosimilars and reference products. But it might not be enough to drive a preference for biosimilars compared to reference products depending on provider purchase price (especially if purchasing at the 340B rate) and rebates.

Provider economics have historically driven the provider-administered biosimilar market, but payers are starting to play a stronger role in management of provider-administered drugs and certainly define the set of products on formulary for pharmacy benefit drugs.

Commercial payers negotiate directly with providers and the payment can vary dramatically based on the market power of the provider. In one recent study, markups at hospitals eligible for 340B discounts were 6.59 times higher than those in independent physician practices, and price markups at noneligible hospitals were 4.34 times higher than those in physician practices.[38] As discussed previously, hospitals eligible for 340B prefer the reference product because they can purchase the product at highly discounted rate and get reimbursement at the commercial rate to secure a generous profit.

Biosimilar utilization in 340B evidence suggests that discount percentages are larger for reference products than for biosimilars. This means that 340B hospitals would have weaker financial incentives to use biosimilars compared with non-340B providers. Given the substantial proportion of hospitals participating in the 340B program, it could be a factor that has meaningfully reduced overall biosimilar use in the US.[39] One study found that biosimilar use for noneligible hospitals was 34.7% while 340B eligible hospitals had a biosimilar utilization rate of 11.8%.[39]

However, increased utilization of biosimilars could reduce the income of most providers who treat commercially insured patients since biosimilars' lower prices will generate lower provider markups and gross revenue compared with biologics. The perverse incentive suggests a need for alternative reimbursement methodologies.

As demonstrated in the previous section, for pharmacy benefit drugs, the U.S. supply chain thrives on high cost, high rebate products. A study of 1,335 U.S. branded prescription drugs found that between 2015 and 2018, the average rebate nearly doubled. Each additional dollar of rebate was associated with a $1.17 increase in list price.[36] The more expensive a product, the larger the administrative fees that pharmacy benefit managers can collect.

High cost, high rebate drives stakeholder revenue

It is challenging for biosimilars to enter the market and quickly gain enough momentum to gain the scale necessary to be able to compete with established reference products that may be willing to dramatically increase rebates to be competitive with biosimilars. This "cat and mouse" game sets a barrier to market entry for biosimilars, and it discourages biosimilar manufacturers from making the necessary investments to be able to launch a biosimilar.[36]

Rebates can incentivize payers to prefer reference products and payers will push reference products to provide rebates until the price drops so low that it makes little financial sense to offer the biosimilar when the reference product is the same price.

And, as said earlier, patients have little incentive to pick biosimilars over reference products. To drive utilization in the biosimilar market, patients should share in the savings from use of biosimilars over reference products. Although some studies have suggested that enrollment in plans that were highly managed (like Health Maintenance Organizations) was associated with the use of a biosimilar, while enrollment in a high-flexibility plans (like preferred provider organizations (PPO) and point-of- service (POS) plans was associated with a lower probability of switching and starting treatment with a biosimilar.[40]

Changing health policy can also add uncertainty to biosimilar development. For example, the Inflation Reduction Act increased biosimilar reimbursement in Medicare but it also introduced government price drug negotiation. Medicare stops or postpones the negotiation if a biosimilar is expected within two years, but that requires a biosimilar company to self-identify to the government and does not cover situations where a biologic has been on the market for 13 years and eligible for negotiation but has patents that extend for several more years.

If Medicare negotiates a reference biologic and then a biosimilar enters the market and wants to compete, it is unclear if there will be enough of a profit margin to create a return on investment for a new product that does not have market share.

Inflation Reduction Act Case Study

Ustekinumab was selected as one of the first ten drugs subject to the Inflation Reduction Act's price negotiations. These prices will be in effect as of January 1, 2026. However, because of the way the timelines have worked, Ustekinumab will have multiple biosimilars (six as of December 2024) on the market as of early 2025. The reference product will continue to be subject to the government negotiated price until the end of 2026.

For companies pursuing a biosimilar this is uncharted territory. It is unknown what the government negotiated rate will be, but biosimilar manufacturers of Ustekinumab will need to price their drugs lower to have any potential success. It is unclear if it is possible to make an adequate return on investment for a new biosimilar.

While negotiated rates are beneficial to patients, the failure of the biosimilar market long term may have greater costs.

There is also the $2,000 OOP cap for Medicare Part D beneficiaries. If a beneficiary expects to hit the annual cap regardless of whether they take a biosimilar or a reference product, they may not be motivated to seek a lower cost medicine.There is also concern that state policy efforts like prescription drug affordability boards (PDABs) could negotiate upper payment limits for reference products that limit the viability of future biosimilars.

One last concern is pharmacy access to biosimilars. While pharmacies may stock a brand drug, it is not reasonable to expect them to maintain inventory of nine different biosimilars. This issue will be more relevant as pharmacy-based biosimilars enter the market.

Securing the Biosimilar Market

Given the healthcare system spending on biologics, it is critical that the biosimilar market thrive. If biosimilars leave the market, originator reference products will lose the incentive to reduce prices and reverse any savings gained with biosimilars. As Stacie Dusetzina, a health policy professor at Vanderbilt University said, "It's not clear to me there's any incentive at all for companies to spend their time and money creating biosimilars. And if no one will, then the price of the brand would never come down."[29]

Long-term sustainability should be the goal of policy solutions so that, one day, the success of biosimilars mirrors that of generics in the U.S. **A sustainable biosimilar system will consider the needs of manufacturers who need to take the risk to invest in developing and marketing biosimilars, payers who need to see savings over the long term, providers who have incentives to switch to biosimilars and patients that have increased access and reduced costs when they take biosimilars.**

TACKLE MISPERCEPTIONS ABOUT BIOSIMILARS

- While the FDA does have resources on biosimilars for providers, physicians and pharmacists need more biosimilar education.
- Specific payment codes could be used to pay to spend time educating patients on biosimilars.
- Changes in interchangeability standards and requirements could make switching between products more common, reinforcing that biosimilars are highly similar to their reference product leading to lower levels of concern.

INCENTIVIZE USE OF BIOSIMILARS

- The add-on fee of 8% of the reference product's ASP is likely helpful, but it may not be enough to incentivize provider use of biosimilars because it uses average provider acquisition rates which may not reflect an individual provider's reality.
- The federal government, through Medicare and/or Medicaid, could incentivize providers through quality measures, to use biosimilars. In many countries the originator and biosimilar are subject to reference pricing which levels the playing field quickly.[41]
- Continue to review 340B utilization of reference products over biosimilars and consider Medicare changes to reimbursement that would incentivize use of biosimilars.

- Hospital outpatient departments typically have large volume and can negotiate higher reimbursement from commercial payers. To get them to switch to biosimilars, which will have reduced reimbursement and thus reduced margins, payers and providers could work toward a shared savings arrangement that compensates hospital outpatient departments for additional utilization of biosimilars.[42]

- While now expired, OCM practices noted that utilizing lower cost biosimilars was a relatively easy method for reducing costs per treatment.[4] The Centers for Medicare & Medicaid Services (CMS) could directly call out and financially encourage the use of biosimilars through direct provider administration or through prescriptions in their Center for Medicare and Medicaid Innovation (CMMI) models like the Enhancing Oncology Model or the Accountable Care Model.

- Currently there is little to no difference in Medicare patient OOP between biosimilar and reference products. CMS could institute reduced cost-sharing for biosimilars to incentivize patients to use them.

- Continue efforts to push transparency into pharmacy benefit manager dealings and preference for rebates so that employers and patients can get the benefit of lower spending due to biosimilars.

As we look ahead, we must recognize the progress biosimilars have made. Biosimilars have saved almost $25 billion dollars over nine years with no reduction in quality. Their uptake, particularly with provider-administered biosimilars, has grown more quickly with each drug launched. Yet the fragility of the market was demonstrated with the pharmacy benefit biosimilars. In order to achieve long-term savings for the healthcare system and patients, stakeholders need to encourage and protect this new market or it could disappear.

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