

Frequently Asked Questions

Key Stakeholders

Executive Summary

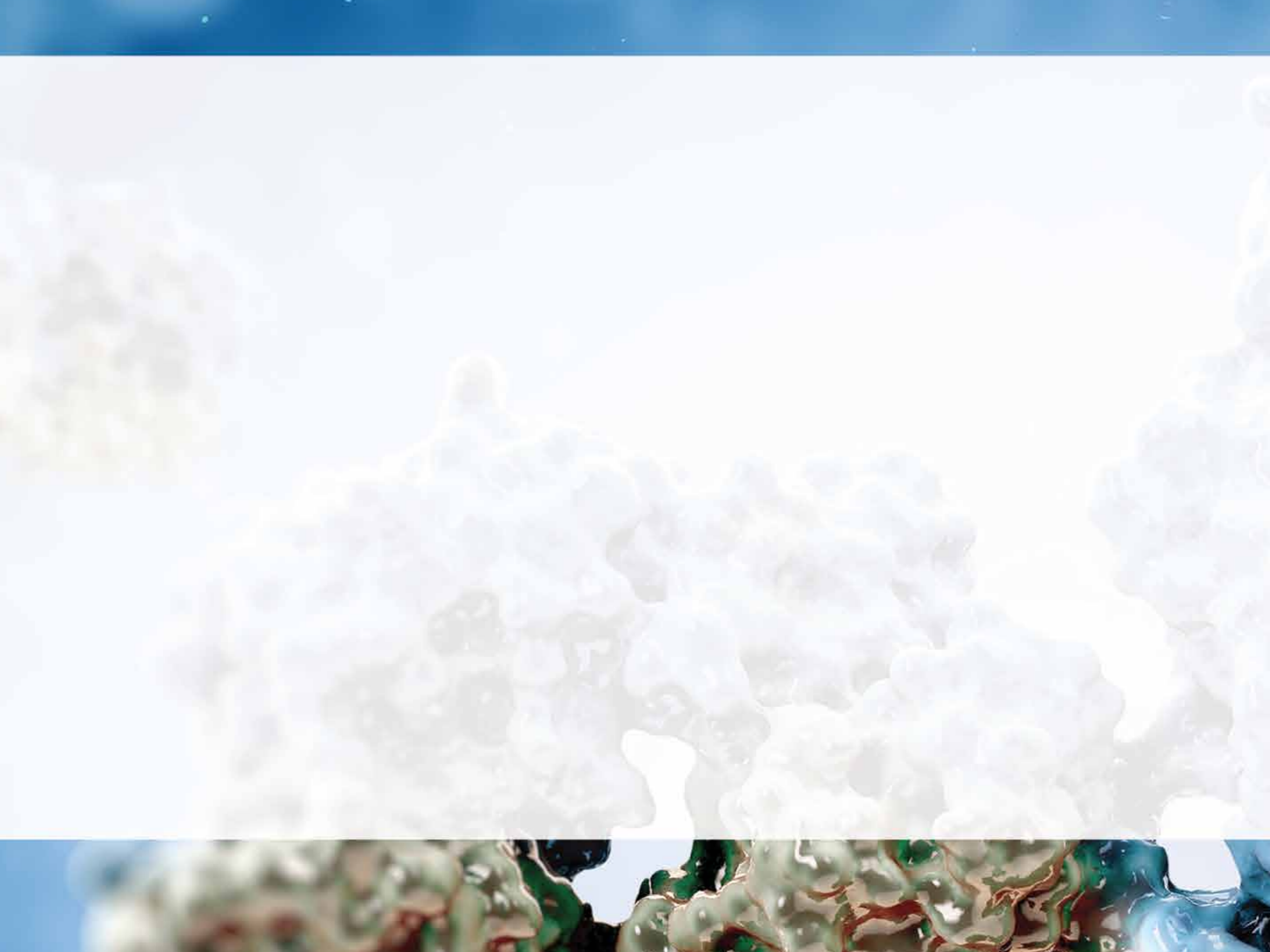
Understanding Biosimilars

Potential Benefits of Biosimilars

TAKE A CLOSER LOOK at Biosimilars

2018 Trends in Biosimilars Report





Dear Colleagues,

The US healthcare system continues to evolve, and for nearly a decade biosimilars have remained a topic of interest for healthcare stakeholders looking to decrease spending while maintaining good patient outcomes.

Biosimilars are expected to play an increasingly prominent role in healthcare by improving patient access to biologics and potentially decreasing patient out-of-pocket costs for these therapies. They offer patients and physicians additional therapeutic options, create headroom to allow the healthcare system to adopt innovative medicines, and enhance competition among existing biologic medicines already in the market. We expect that 2018 will be another opportunity for growth in the use of these products.

At Amgen, we believe our deep experience in biologics development and unparalleled capabilities in biotechnology manufacturing will position us as a leader and the partner of choice in the biosimilars space. Building greater confidence in biosimilars will require buy-in from key stakeholders, including providers, payers, patients, and regulators, each of whom will bring their own perspectives on the adoption, utilization, and reimbursement of biosimilars.

As an active participant in the ongoing national discussion, we are pleased to share with you the fifth edition of our Trends in Biosimilars Report, the content of which was developed based on conversations with various members across the US healthcare community. The report provides an overview of the key issues facing stakeholders in the biosimilar market and represents part of Amgen's commitment to being at the forefront of biosimilar education.



A handwritten signature in black ink, appearing to read 'Claes Hornstrand', written in a cursive style.

Claes Hornstrand
Vice President
US Value and Access, Amgen

Amgen's core focus is to discover, develop, and deliver innovative medicines for patients with serious illnesses. We are inspired every day to engineer robust and differentiated therapeutics. In addition, we are leveraging our extensive biotechnology experience to create high-quality biosimilars and reliably supply them to patients.

Biotechnology provides sophisticated ways to attack disease, and Amgen was among the first companies to recognize the potential of modern biotechnology in developing valuable medicines for patients. Now, nearly 4 decades later, Amgen is leveraging its biotechnology experience to develop biosimilars.

At the heart of Amgen's commitment to biosimilars is our mission to serve patients. High-quality, reliably supplied biosimilars are expected to offer additional treatment options for patients—and we believe that we bring the highest quality science to this new space in healthcare.

Both the development and supply of these complex medicines are expected to be scientifically challenging and capital-intensive. Biosimilar manufacturers like Amgen will benefit from having significant biologics expertise, infrastructure, and investment to successfully bring these medicines to market.

That is why at Amgen we are leveraging our experience and using the same personnel, services, and manufacturing expertise from the company's innovative business to

produce high quality, reliably supplied medicines for some of the most complex diseases, such as those in oncology and inflammation.

We are proud of being a dependable healthcare partner and supplier of our medicines. In fact, ongoing data monitoring of drug shortages by the American Society of Health-System Pharmacists showed that Amgen was one of only 2 manufacturers to have zero drug shortages from 2007 to 2017.¹

At Amgen, we focus on providing experiences that go beyond the medicine itself. We combine our biologic portfolio with appropriate services to offer oncology and inflammation solutions. We are developing relevant services not just for patients, but also for payers, pharmacists, and allied healthcare professionals, where we can provide assistance and make a difference.

As Amgen strives towards the approval and launch of our portfolio of 10 biosimilars,²⁻⁴ we look forward to adding new chapters to our story, while maintaining Amgen's commitment to connecting patients with vital medicines.





Executive Summary

Understanding
Biosimilars



Potential Benefits
of Biosimilars



Considerations for
Key Stakeholders



Other
Considerations



Understanding Biosimilars

Biosimilars are a category of drugs that offer patients the opportunity to access more treatment options at a potentially lower cost. A biosimilar is a biologic that is “highly similar” to an approved biologic (or reference product) that is already being used to treat patients.⁵

The Biologics Price Competition and Innovation Act (BPCIA), signed into law as part of the Affordable Care Act (ACA) in 2010, provided an abbreviated approval pathway for biosimilars.⁶ Prior to that, biosimilars were only available in other parts of the world.

The types of data that are generated for biosimilars (eg, comparative analytical data), and how they are considered by the Food and Drug Administration (FDA), are different than for innovator biologics. For example, the goal of a biosimilar development program is not to re-establish the safety and efficacy of the product, but rather to demonstrate that the biologic product is biosimilar to the reference product.⁷

It is generally understood that there are acceptable variabilities between the biosimilar and the branded reference product, and an approved biosimilar will have no clinically meaningful differences from the reference product in terms of efficacy and safety.

Potential Benefits of Biosimilars

Biosimilars offer benefits to almost every stakeholder in the healthcare system. They can reduce costs by offering a lower-cost treatment option while increasing access to therapies and driving adherence. The 2 factors that primarily drive potential savings from biosimilars include the following:



Lower cost of development
for a biosimilar than for a
reference biologic



Increased competition
in the healthcare system

Due to their prospective lower cost, biosimilars may help expand patients' access to appropriate treatment for conditions managed with biologics, therefore allowing more patients to be treated, at an earlier point, and with an expanded range of therapeutic interventions that were previously restricted due to budget constraints.⁸

Considerations for Key Stakeholders

Employers/Payers



Employers are a prime audience for biosimilars because 157.4 million people (49% of the US population) have employer-sponsored health insurance—more than any other payer type.⁹ As a result, employers command great influence in the healthcare system. How biosimilars are covered and placed on formularies, their potential to decrease costs while maintaining patient access to necessary treatments, whether physicians will be willing to prescribe them, and how to transition patients to biosimilars will be of utmost importance.

In the same vein as employers, payers are looking to biosimilars as an opportunity to control costs and offer more treatment choices.¹⁰ Payers are striving to implement programs to ensure patients are receiving the care they need, while also saving money.



Formulary
Decision Making



Driving Utilization
Through Contracting



Reimbursement



Medicaid



Formulary Decision Making

Third-party drug coverage, benefit designs, and related policies will affect the uptake of biosimilars. Policies may vary, depending on whether the drug falls under the pharmacy or medical benefit. Preferentially positioning biosimilars can provide formulary advantages, and greater differences in copayment amounts and/or coinsurance between the tiers for biosimilars and reference products will help foster biosimilar uptake.



Driving Utilization Through Contracting

An ongoing commitment to driving competition will help create a sustainable US biosimilar market. While the prices of generic drugs can be discounted as much as 90% from their brand equivalents, the prices of biosimilars at launch have not been discounted this much from their reference products—nor were they expected to be.¹¹ The first 2 biosimilars on the US market (for different reference products) had wholesale acquisition costs (WACs) discounted 15% from their reference products, with the discount increasing to nearly 20% for one of them.¹²⁻¹⁴ However, the introduction of a rival biosimilar at a 35% discount resulted in one of the competitor biosimilars also increasing its discount from nearly 20% to an average sales price at 35%.¹⁴

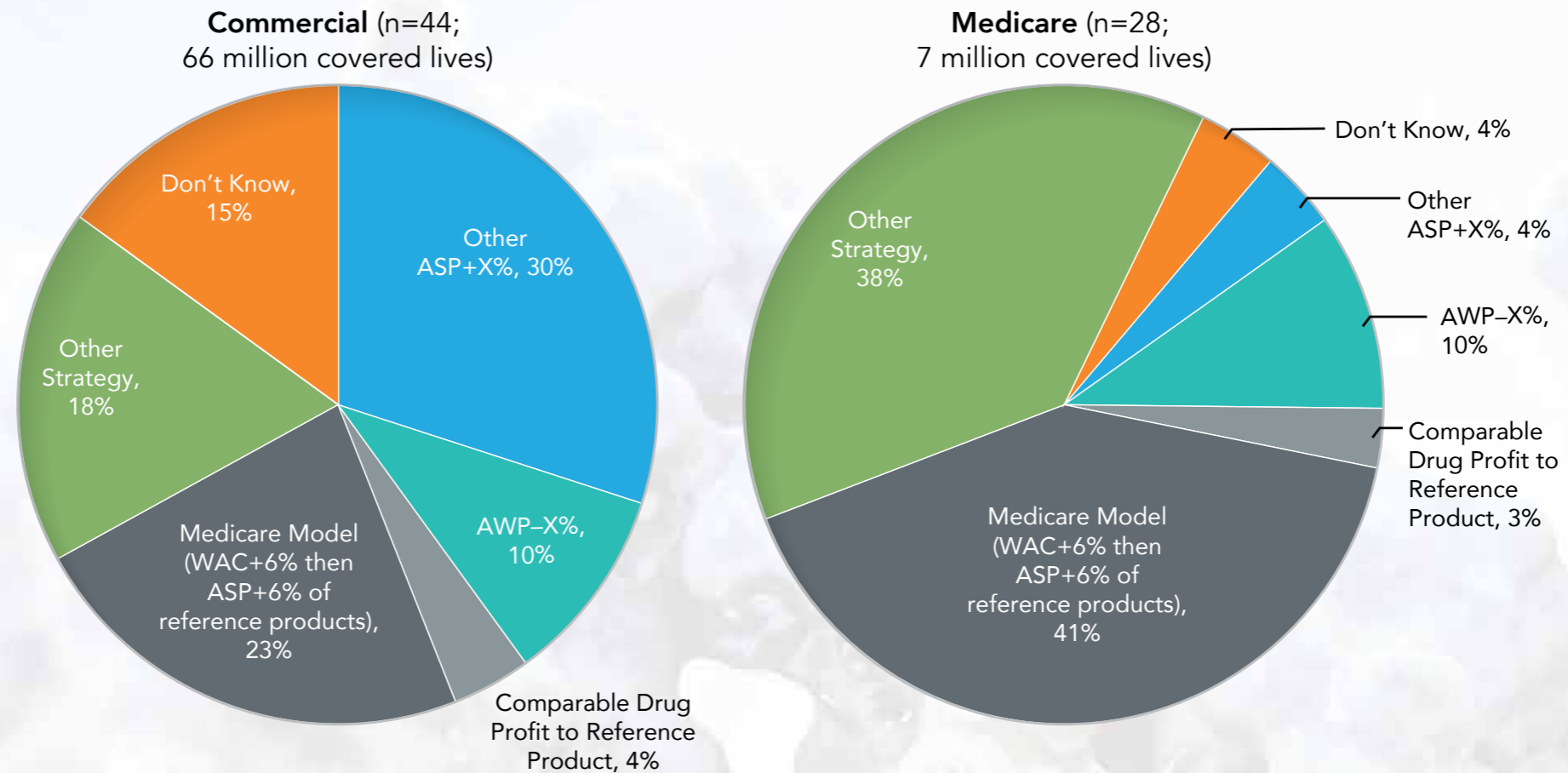
Rebate agreements for biosimilars are likely to be similar to those for the brand market, rather than the generic market. Biosimilar manufacturers will likely need to negotiate with payers to secure a favored formulary position compared to the reference product.



Reimbursement

So far, payers seem to be taking a traditional, fee-for-service approach to reimbursing for physician-administered biosimilars. The 2 figures below show the breakdown of reimbursement methodologies for 44 commercial payers covering 66 million lives and 28 Medicare payers covering 7 million lives, as reported by Magellan Rx Management in 2017¹⁵:

2017 Biosimilar Reimbursement Methodology (% of lives)



Key: ASP – average sales price; AWP – average wholesale price; WAC – wholesale acquisition cost.

Coverage for these products primarily under the pharmacy benefit has not yet been seen; however, under Medicare Part D, biosimilars will be treated as branded drugs as of January 1, 2019.¹⁶ This means that the manufacturers will provide a 70% coverage gap discount that counts toward patients' out-of-pocket spending and allows them to move into catastrophic coverage sooner (where their copayment is reduced to 5%). Until January 1, 2019, patients obtaining biosimilars under Part D will not receive manufacturer assistance, and biosimilars will be treated as generic products (In 2018, Part D plan pays 56% of the drug and the beneficiary pays 44%).¹⁷



Medicaid

The generic-like treatment of biosimilars by Centers for Medicare and Medicaid Services (CMS) in certain parts of Medicare does not cross over into Medicaid. In late December 2016, CMS issued a notice reinforcing its position that biosimilars do not qualify as authorized generic drugs for the purpose of the Medicaid Drug Rebate program and are subject to brand-level rebates.¹⁸

Healthcare Professionals



Healthcare professionals, including physicians, physician assistants, nurse practitioners, and pharmacists, are an extremely important group that can help increase the adoption of biosimilars and educate patients on this new product category. Therefore, it is imperative they have a comprehensive understanding of biosimilars, including the clinical, regulatory, and financial characteristics. Patients are likely to be relatively uninformed about biosimilars, and they will look to their providers for information and clarification.



Need for Physician
Education



Medicare
Part B



Need for Physician Education

Nearly 3 years after the FDA approved the first biosimilar in the US,¹⁹ physicians across specialties still need significant education on biosimilars. In late 2015 and early 2016, the Biosimilars Forum commissioned SERMO to conduct a 19-question survey of 1,201 US physicians across specialties that are high prescribers of biologics, including dermatologists, gastroenterologists, hematologist-oncologists, medical oncologists, nephrologists, and rheumatologists. The survey identified 5 major knowledge gaps:

1. Defining biologics, biosimilars, and biosimilarity
2. Understanding the approval process and use of “totality of evidence” to evaluate biosimilars
3. Understanding that the safety and immunogenicity of a biosimilar are comparable to the originator biologic (reference product)
4. Understanding the rationale for extrapolation of indications
5. Defining interchangeability and the related rules regarding pharmacy-level substitution²⁰

The survey also found that peer-reviewed literature was, by far, the most trusted and preferred information source for biosimilars among physicians.



Medicare Part B

Under Medicare Part B, biosimilars are reimbursed at the biosimilar's average sales price (ASP) plus 6% (4.3% after sequestration) of the reference biologic's ASP.^{21,22} This biosimilar payment model is designed to create a financial incentive for physicians to prescribe a lower-cost biosimilar; the 6% add-on payment (4.3% after sequestration) of the reference product would, consequently, offer a payment boost for prescribers of biosimilars.²³

Medicare Outpatient Prospective Payment System Considerations, Including the 340B Drug Pricing Program

Sites within a healthcare system that qualify as 340B entities can obtain federally mandated "ceiling price" discounts for covered outpatient drugs, while other sites that are not 340B-eligible pay a higher net price.²⁴ In 2018, CMS changed the Medicare Part B payment methodology for 340B drugs without pass-through status, reimbursing at ASP minus 22.5% instead of ASP plus 6%.²⁵ Biosimilars with pass-through payment status will be exempt from Medicare's alternative payment methodology for 340B drugs (ie, ASP minus 22.5%), and will be paid at ASP plus 6% of the reference product. However, biosimilars not on pass-through status, or those with pass-through status expiring, will be paid at the new 340B program rate of ASP minus 22.5% of the reference product.²⁶

Patients



Patient understanding of biosimilar products, including their safety and efficacy, will be key to the utilization of these drugs. Education surrounding what a biosimilar is and the potential for cost savings will be of paramount importance to encourage their utilization. Patients should understand the following points:



What is a biosimilar? Is it safe and effective?



Do biosimilars undergo the same clinical trial process as other FDA-approved products? If not, is that okay?



How much will a biosimilar cost me, and why are they cheaper products? Are there patient assistance programs for biosimilars to help me with these costs?



If there is an FDA-approved biosimilar for the biologic I am taking, is it worth me switching to it?

Other Considerations



Alternative Payment Models

The aim of the ACA to contain healthcare costs while improving quality and outcomes is in line with a more general shift in priorities from volume to value.⁸ The ACA and other subsequent healthcare legislation introduced a variety of value-based programs. Value-based approaches reward providers who deliver treatments that achieve the best outcomes at the lowest cost. Consequently, providers are incentivized to seek the drug with the best value that effectively addresses a patient's condition. Lower-cost biosimilars have an inherent advantage in these scenarios.



Reliable Supply — Avoiding Drug Shortages

To avoid treatment delays and unplanned switching between biologics during the course of treatment, it is important to consider a manufacturer's history of shortages and recalls related to quality concerns and evaluate its capability to maintain adequate production and stock to support demand. It is also important to consider the robustness of the manufacturer's supply chain when evaluating biosimilars.²⁷



2018 Biosimilars Trends Report: Understanding Biosimilars

Understanding
Biosimilars



US FDA Approval Pathway
for Biosimilars



Key Considerations
Checklist



Understanding Biosimilars

Biosimilars are a category of drugs that can offer patients the opportunity to access more treatment options at a lower cost.

What Are Biologics?

Biologics can be composed of sugars, proteins, nucleic acids, or complex combinations of these substances; they may also be living entities, such as cells and tissues. Biologics are isolated from a variety of natural sources—human, animal, or microorganism—and may be produced using biotechnology methods and other cutting-edge technologies.²⁸

What are biosimilars?

- A biologic that is “highly similar” to an approved biologic (reference product) already being used to treat patients is known as a “biosimilar.”⁵
- To achieve a biosimilar designation from the FDA, the biologic must have no clinically meaningful differences in terms of safety and effectiveness from the original biologic, known as the reference product.⁵

Biosimilars are not generics

While it might seem logical to compare biosimilars to generic drugs, there are fundamental differences in their complexity and development.

Compared to small-molecule drugs and generic medicines, biologics and biosimilars are:

- 200 to 1,000 times larger
- Far more structurally complex
- Manufactured in living cells instead of via chemical synthesis²⁹

Biosimilars are biologic drugs, which are much larger and more complex molecules than chemically synthesized drugs. For example, aspirin, a chemically synthesized drug, weighs only 180 daltons (D) and contains has 21 atoms. A biologic, such as an immunoglobulin G antibody, can contain more than 20,000 atoms and weigh more than 150,000 D, which is approximately 800 to 900 times larger.³⁰

Biologics are protein-based therapeutics that are produced using unique cell lines and are manufactured from natural resources such as human and animal cells, yeast, and bacteria.³¹

Because of their complexity and manufacturing processes using different living materials, biosimilars are not exact copies, but rather variants of innovator biologics. It is not currently possible to use 2 different cell lines to produce exactly the same product; thus, the term used is “biosimilar” and not generic.³⁰

While biosimilars have been available in other parts of the world for over a decade,³² they were not available in the US until 2015,³³ as there was no legal pathway allowing the FDA to review them for safety and efficacy in an abbreviated fashion. The Biologics Price Competition and Innovation Act (BPCIA), signed into law as part of the ACA in 2010, provided that abbreviated pathway.³⁴ The biosimilars’ approval process is similar to the abbreviated approach the FDA uses to approve generic equivalents of brand-name drugs.³⁵ Without the BPCIA, manufacturers would have had to seek FDA approval via a Biologics License Application (BLA), a much more costly and time consuming process that would make it extremely difficult to price the product competitively compared to competitor biologics.

For the purposes of licensing drugs, the federal government has specific definitions of various biological products discussed in this report³⁶:

- **“Biologics”** is an umbrella term, and the FDA describes them as “large, complex molecules” used “to diagnose, prevent, treat, and cure diseases and medical conditions.”
- A **“reference product”** is a single biological product approved by the FDA against which a proposed biosimilar product is compared.
- A **“biosimilar product”** is a biologic that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.
- An **“interchangeable product”** is a biosimilar that meets additional requirements outlined by the BPCIA. An interchangeable product may be substituted for the reference product without the involvement of the prescriber—much like how generic drugs that have been deemed “therapeutically equivalent” can be substituted for their brand drugs by a pharmacist.

US FDA Approval Pathway for Biosimilars

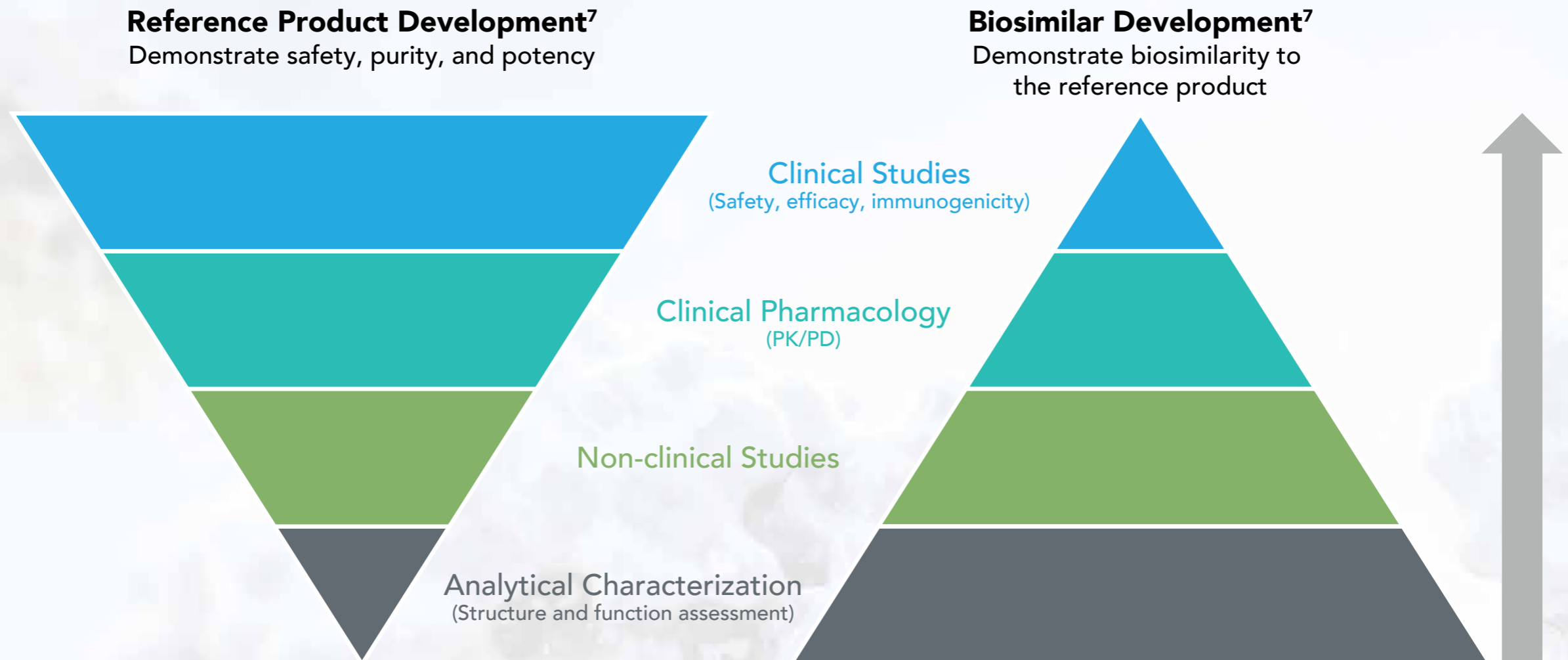
Because biologics contain active substances derived from living cells or organisms, the development of a biosimilar is much more complex than the process for developing a generic drug. A biosimilar requires the creation of a new manufacturing process and a custom cell line, since the reference product's manufacturing process is proprietary and not publicly available.³⁰ Due to the complex nature and production methods of biologics and biosimilars, relatively minor changes in manufacturing processes may significantly affect product quality and/or safety, or the criteria by which similarity is determined.^{37,38}

Small-molecule drugs, by contrast, are chemical entities that tend to be relatively easy to synthesize, so manufacturers can make exact copies of the originators. These generic versions perform predictably in humans, because the active molecules are exact copies.³⁹

When the BPCIA was signed into law as part of the ACA in 2010, it established an abbreviated approval pathway for biosimilars in the US; however, to give manufacturers an incentive to continue developing innovative biologics, the BPCIA also granted biologics 12 years of marketing exclusivity, during which rivals may not launch biosimilars.⁶

Based on the provisions in the BPCIA, the FDA recommends a stepwise biosimilar development approach that should begin with extensive comparative analytical studies and proceed to animal and clinical studies. At each step in development, the applicant should identify any differences between the reference and biosimilar products, what residual uncertainty remains based on the potential impact of the observed difference, and then design subsequent studies to address the remaining residual uncertainty.^{7,40}

As illustrated below, while a biosimilar may need fewer clinical trials and clinical pharmacology studies than its reference product to attain FDA approval, it may also require a greater preponderance of analytical characterization and nonclinical studies.



The types of data that are generated for biosimilars (eg, comparative analytical data) and how they are considered by the FDA are different than for innovator biologics. For example, the goal of a biosimilar development program is not to re-establish the safety and efficacy of the reference product, but rather to demonstrate that the biologic product is biosimilar to the reference product.^{7,40} No single study is considered “pivotal” to a biosimilar application; rather, the totality of data and information submitted to the FDA support the demonstration of biosimilarity.⁷

Currently, the FDA does not require comparative analytical or clinical studies between biosimilars, meaning biosimilar candidates will be evaluated only against the designated reference product.⁴⁰

It is generally understood that there are acceptable variabilities between a biosimilar and its branded reference product, and an approved biosimilar will have no clinically meaningful differences from the reference product in terms of efficacy and safety. However, it is important to note that there may be some nonclinical differences between the biosimilar and the reference product, such as delivery device, packaging or distribution channels, which could have potential implications for payers, healthcare providers, and patients.⁶

The BPCIA’s abbreviated licensure pathway is not a lower approval standard for biosimilar biologic products compared to reference biologics. Rather, the abbreviated pathway allows for reliance on the FDA’s previous finding of safety and effectiveness for the reference product, promoting a potentially shorter, or abbreviated, and less costly development program.⁷

Extrapolation of Indications

While reference products with multiple indications have undergone clinical studies to prove safety and efficacy for each indication, biosimilars are not required to be evaluated against every indication held by the reference product; instead, the FDA may consider the “extrapolation” of efficacy and safety data from one indication to another. In fact, the FDA has stated that extrapolation is critical to improving access and options at a potentially lower cost.³⁴

Extrapolation is the approval of a biosimilar for use in an indication held by the reference product, not directly studied in a comparative clinical trial with the biosimilar.³⁴

Extrapolation is not an assumption that the data from one directly studied indication or population alone is sufficient to support approval in a different non-studied indication or population. The biosimilar manufacturer must provide scientific justification to support extrapolation, which may include knowledge of the mechanism(s) of action, pharmacokinetics, pharmacodynamics, efficacy, safety, and immunogenicity of the reference product in each of its approved indications.⁴⁰

Some indications, however, may be initially excluded from an approved biosimilar’s label due to FDA-established exclusivity periods. The FDA provides 7 years of exclusivity for orphan indications (diseases or conditions that affect fewer than 200,000 patients in the US) to encourage the development of drugs to meet the needs of patients with rare diseases.⁴¹ A biosimilar may not be licensed by FDA for the protected orphan indication until after the expiration of the 7-year orphan drug exclusivity period or the 12-year reference product exclusivity, whichever is later.⁴²

Determination of Interchangeability

Biosimilar biological products are, by definition, not interchangeable, and are not substitutable without a new prescription. While generic drugs can be substituted by a pharmacist for their brand equivalents, the same is not true for a biosimilar. Only biosimilars that have undergone additional analysis and, subsequently, have been determined by the FDA to be “interchangeable” can be readily substituted by a pharmacist. So far, the FDA has not designated any biosimilar to be interchangeable to its reference product.^{36,43}

A manufacturer of a proposed **interchangeable** product must show the product is biosimilar to a reference product **and** that it can be expected to produce the same clinical result as the reference product in any given patient.⁴³

The FDA has issued draft guidance for demonstrating interchangeability; the agency requires a “dedicated switching study” design, in which patients start with the reference product and are randomly assigned to switch to the biosimilar or continue using the reference product. The “switching” group would be expected to incorporate at least 3 switches between the reference and biosimilar products.⁴³

In the absence of the FDA or a state permitting the automatic substitution of products, hospitals, health plans, and pharmacy benefit managers (PBMs) may consider the use of “therapeutic interchange” as the mechanism to substitute a biosimilar for its reference product. Therapeutic interchange is the process of substituting one product for another, when both products are expected to produce similar clinical effects and outcomes based on scientific evidence. Many health systems today use therapeutic interchange for a variety of drugs and biologics to lower costs.⁴⁴

As of March 1, 2018, 38 states and Puerto Rico have passed laws stating that any biological product under consideration for substitution must first be approved as interchangeable by the FDA.⁴⁵

Pharmacovigilance and Naming

Pharmacovigilance, the monitoring, and tracking of drug safety over time is important to detect any emerging safety signals.⁴⁶ To help facilitate pharmacovigilance, the FDA released final guidance on the nonproprietary naming of biological products in January 2017.⁴⁷

Under this guidance, each originator biologic, related biologic, and biosimilar will be assigned a nonproprietary name consisting of a core name and a hyphenated distinguishing suffix made up of 4 lowercase letters.

The FDA believes that this naming convention will help ensure accurate identification of products and their associated manufacturers, while also minimizing the inadvertent substitution of biologics not deemed to be interchangeable.

Generic drugs and brand drugs share the same nonproprietary name because they are chemically identical. However, reference biologics and biosimilars are not chemically or biologically identical, so the FDA issued guidance on the nonproprietary naming of all biological products (not just biosimilars).

The examples below show the difference between the non-proprietary names of a reference product and its biosimilar:

Reference Product	Biosimilar
SameCoreName-	abcd
SameCoreName-	efgh

Key Considerations Checklist – Understanding Biosimilars

- Biosimilars are “biologic” drugs, which are much larger and more complex molecules than chemically synthesized drugs, and are produced from living cells.
- The BPCIA was signed into law as part of the ACA in 2010, establishing an abbreviated approval pathway for biosimilars in the US.
- The BPCIA’s abbreviated licensure pathway is not a lower approval standard for biosimilars.
- The goal of a biosimilar development program is not to re-establish the safety and efficacy of the product, but rather to demonstrate that the biologic product is biosimilar to the reference product.
- It is generally understood that acceptable variabilities exist between the biosimilar and the branded reference product.
- Extrapolation is the approval of a biosimilar for use in an indication (or indications) held by the reference product not directly studied in a comparative clinical trial with the biosimilar.
- To be designated “interchangeable,” a manufacturer must show the product is biosimilar to a reference product and that it can be expected to produce the same clinical result as the reference product in any given patient. No product has yet been deemed interchangeable by the FDA.
- Each originator biologic, related biologic, and biosimilar will be assigned a nonproprietary name consisting of a core name and a hyphenated distinguishing suffix made up of 4 lowercase letters.

Notes





Potential Benefits of Biosimilars

System-wide Cost
Savings and Opportunity



Improved Patient
Outcomes



Summary of
Potential Benefits



Key Considerations
Checklist



Biosimilars offer benefits to almost every stakeholder in the healthcare system. They can reduce costs by offering a lower-cost treatment option and can potentially improve patient outcomes by increasing access to therapies and driving adherence. Either result can be beneficial. Indeed, the competition fostered by the introduction of biosimilars in the market can benefit patients by providing high-quality products at more affordable prices.

System-wide Cost Savings and Opportunity

The introduction of biosimilars creates opportunities for cost savings for payers, employers, state and federal governments, and patients compared to the reference products. Two factors primarily drive these savings:

Developing a biosimilar costs less than a reference biologic

Biosimilars are expected to take 8 to 10 years to develop, at a cost between \$100 and \$200 million,⁴⁸ compared to an estimate of \$2.6 billion for developing a new drug.³⁰ As a result, manufacturers have fewer expenses to recoup, which theoretically allows for biosimilars to build upon the innovation of the reference product and have lower list prices.

Biosimilars introduce competition into the healthcare system

As the number of treatment choices increases for a particular disease or condition, manufacturers are incentivized to lower the prices of their products to maintain or increase market share.

The introduction of competition from biosimilars may also create downward pressure on reference-product prices—leading to even greater spending reductions.⁸

Biosimilars will save money by being less expensive to develop than reference biologics, increasing competition, and improving patient outcomes.^{8,30}

Expanded Patient Access

Due to their lower cost, biosimilars may help expand patients' access to appropriate treatment for conditions managed with biologics, therefore allowing more patients to be treated, at an earlier point, and with an expanded range of therapeutic interventions that were previously restricted due to budget constraints.⁸

Summary of Potential Benefits

Manufacturers can build on their heritage of innovative cures and treatment of chronic disease by improving patient access through the development of biosimilars, thus demonstrating commitment to their patient community. Biosimilars are yet another way that manufacturers are helping patients save money and realize better care.

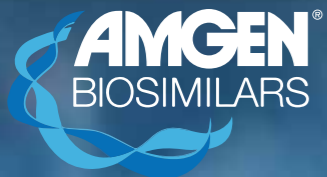
In the absence of information, physicians and patients may be skeptical and unwilling to make the switch to a biosimilar, and payers may hesitate to develop policies that support the broader use of biosimilars. To provide such information for stakeholders, manufacturers should generate data demonstrating how long-term use of the biosimilar and switching between the branded and biosimilar agent affects efficacy and safety.⁴⁹

Key Considerations Checklist – Potential Benefits of Biosimilars

- The introduction of biosimilars creates opportunities for cost savings.
- Two factors primarily drive potential savings from biosimilars:
 - 1) Developing a biosimilar costs less than a reference biologic, and
 - 2) Biosimilars introduce competition into the healthcare system.
- The adoption of lower-cost biosimilars could allow payers, safety-net entities, and patients to reallocate their healthcare resources to expand patient access to therapies.
- Biosimilars can potentially expand patient access to therapies and drive adherence.

Notes





Key Stakeholders: Employers/Payers

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Through Contracting

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Reimbursement

The Part D
Donut Hole
for Biosimilars

Key Considerations
Checklist

Key Stakeholders: Employers/Payers

Employers are a prime audience for biosimilars because 157.4 million people (49% of the US population) have employer-sponsored insurance—more than any other payer type.⁹ As a result, employers command great influence in the healthcare system. Employers also have a vested interest in controlling and containing healthcare costs, not only for themselves but also for their employees, who are absorbing a greater percentage of healthcare costs each year.

Escalating healthcare costs, historically low interest rates, and an aging workforce have made employee benefits a significant line item for employers over the last 10 years. The cost of providing employee benefits in the US increased 24% between 2001 and 2015, fueled largely by a doubling in healthcare benefit costs.⁵⁰ Additionally, though insurers' medical cost trends (ie, cost increases for medical products or services, combined with utilization of products and services) have moderated in recent years, they still ranged between 6% and 7.5% per year since 2013—thereby outpacing economic growth and inflation.⁵¹

Sometimes employers dictate coverage, sometimes they do not

In the US, most people are covered by private insurance, which is often sponsored by their employer. Sometimes employers are self-insured and dictate coverage. Other times, employers are the payer, but coverage policies are administered through an insurance company.

How biosimilars are covered and placed on formularies, their potential to decrease costs while maintaining patient access to necessary treatments, whether physicians will be willing to prescribe them, and how to switch patients to biosimilars will be important considerations for employers and payers.

In the same vein as employers, payers are looking to biosimilars as an opportunity to control costs and offer more treatment choices.¹⁰ Payers are striving to implement programs to ensure patients are receiving the care they need, while also saving money.

Key healthcare decision makers believe that biosimilars can help restrain drug spending, but the products are not expected to provide immediate substantial budget impact. A 2016 survey by *Managed Healthcare Executive*, in partnership with Access Market Intelligence and the National Institute of Collaborative Healthcare, of 228 US executives at medical practices, hospitals, large healthcare systems, benefit management organizations, health plans, long-term care organizations, and group purchasing consulting firms showed that the majority of respondents felt biosimilars hold great promise in reducing the specialty drug spend, but only 8.5% of survey respondents foresaw this happening in 2017, while 21.4% of respondents expected to see reduction in 2018, 13.4% in 2019, and 25% in 2020.⁵²

Formulary Decision Making

Third-party drug coverage, benefit designs, and related policies will affect the uptake of biosimilars. Policies may vary, depending on whether the drug falls under the pharmacy or medical benefit. Speciality drugs such as biologics may be covered under the medical benefit, the pharmacy benefit, or both.⁵³ Self-administered medicines (often delivered by a specialty pharmacy) are typically covered under the pharmacy benefit, while those injected or infused under the supervision of a physician are typically paid for as medical benefits.⁵⁴ As of December 2017, none of the biosimilars marketed in the US are covered primarily under the pharmacy benefit by most insurers.

Preferentially positioning biosimilars can provide formulary advantages, and greater differences in copayment amounts and/or coinsurance between the tiers for biosimilars and reference products will help foster biosimilar uptake.

Approximately 3 years after the FDA approved the first biosimilar, commercial payers appear to have become comfortable with the products, as reported by Avalere Health in their 2017 survey of 45 US health plans; 81% of plans reported they are covering a biosimilar product. Nearly all payers indicated that a biosimilar's cost relative to its reference product is a key decision-making factor for determining coverage. In addition to costs compared to the reference product, health insurers cited the efficacy and safety of the biosimilar as important factors for coverage decisions.⁵⁵

Table 1. Scenarios for Formulary Placement of Biosimilars

	Impact	Challenges
<p>Scenario 1: Biosimilar: Preferred Tier</p> <p>Reference Product: Non-preferred/Specialty Tier</p>	<ul style="list-style-type: none"> • Lower out-of-pocket costs for patients choosing the biosimilar • Still maintains relatively unfettered access to the reference biologic 	<ul style="list-style-type: none"> • More patient friendly, but may not drive biosimilar utilization as much as Scenario 2
<p>Scenario 2: Biosimilar: On Formulary</p> <p>Reference Product: Off Formulary</p>	<ul style="list-style-type: none"> • Drive greater utilization of biosimilar • Enables plan to replace the reference product with a biosimilar on a more expensive tier 	<ul style="list-style-type: none"> • Potentially greater out-of-pocket costs for patients • Patient access to the reference product would comparatively be much more limited, perhaps requiring prior authorization

Of course, payers must become very knowledgeable about a biosimilar before adjusting any formulary structure that positions a biosimilar preferentially compared to its reference product. According to Avalere Health’s research, approximately 2 years after its launch, the first FDA-approved biosimilar was covered by 94% of employer-sponsored insurance plans, with over 40% of employer plans covering the biosimilar in the preferred brand tier.⁵⁵ Compare that scenario to the coverage profile of the second FDA-approved biosimilar: 7 months after being on the market, only 42% of employer plans covered it.



Healthcare providers, however, may react differently to biosimilars replacing reference products on formularies. A report by Spherix Global Insights in 2017 surveying 103 US gastroenterologists showed a significant decline since 2016 in their ulcerative colitis patients treated with an injectable reference biologic.⁵⁴ The decline was attributed to the adoption of biosimilars and the use of a different originator biologic, potentially indicating that physicians were changing their prescribing patterns to avoid insurance mandates for biosimilar use. Over one-third of the surveyed physicians agreed that if a pharmacy or managed care plan advised them to use a biosimilar over its reference product, they were more likely to choose a different agent altogether.⁵⁶

This reticence might be a specialty-by-specialty issue, though. A 2017 survey by Cardinal Health of 200 oncologists, who represented a mix of US community and hospital-based practices, found that when it came to treating breast cancer, 73% of participating oncologists were open to prescribing a biosimilar to treat both adjuvant and metastatic patients, while only 10% indicated they would not prescribe a biosimilar.⁵⁷

As a demonstration of commercial payers' acceptance of some biosimilars as therapeutic substitutes to their reference products, they have started replacing reference biologics with biosimilars. In 2016, the largest pharmacy benefit manager (PBM) and the largest health insurer replaced a reference biologic with the first FDA-approved biosimilar on their 2017 national formularies.^{58,59} In 2017, the second-largest PBM also replaced a reference biologic with the first FDA-approved biosimilar on its 2018 national formulary.⁶⁰

Biosimilars may also be good candidates for outcomes-based contracts or risk sharing between manufacturers and payers, as those opportunities could demonstrate their equivalent effectiveness while lowering costs, which could justify a preferred formulary position compared to their reference products.

Driving Utilization Through Contracting

A typical consequence of a robust, competitive marketplace is that prices for goods or services decrease as more competitors enter the market.⁶¹ An ongoing commitment to driving competition will help create a sustainable US biosimilar market. A 2016 report from the IMS Institute for Healthcare Informatics (now IQVIA) notes that biosimilars enable stakeholders—including payers, physicians, and patients—to benefit from increased choice in therapeutic options.⁶² Competition lies at the center of the biosimilar value proposition, driving pharmaceutical innovation and affirming healthcare system sustainability.

While the prices of generic drugs can be discounted as much as 90% from their brand equivalents, the prices of biosimilars at launch have not been discounted that much from their reference products—nor were they expected to be.¹¹

In some situations, group purchasing organizations (GPOs) may select preferred agents to represent the vast majority of provider and member needs, and then work to raise member awareness to optimize contract performance. In this way, GPOs may play an important role in building and maintaining the market for biosimilars.⁴⁶

What is a GPO?

A GPO is an entity that helps healthcare providers – such as hospitals, nursing homes and home health agencies – realize savings and efficiencies by aggregating purchasing volume and using that leverage to negotiate discounts with manufacturers, distributors and other vendors.⁶³

The first two biosimilars on the US market (for different reference products) had wholesale acquisition costs (WACs) discounted 15% from their reference products, with the discount increasing to 20% for one of them.^{12,13} However, the introduction of a rival biosimilar at a 35% discount resulted in the competitor biosimilar also increasing its discount from nearly 20% to an average sales price at 35%.¹⁴

A pharmaceutical purchase or discount agreement for an individual biosimilar may also be negotiated across a manufacturer's product portfolio. Given that biosimilar manufacturers' portfolios vary, this could be a differentiating point when negotiating contracts with various manufacturers.

Rebate agreements for biosimilars are likely to be similar to those in the brand market, rather than the generic market. Biosimilar manufacturers will likely need to negotiate with payers to secure a favored formulary position compared to the reference product.

Although competitive bidding (or tendering) for pharmaceutical products is often employed by various countries in the EU, it is not typically seen in the US; however, competitive bidding (or choosing to utilize only one brand for a product) may be considered a type of payer management strategy. In considering competitive bidding-type contracting for reference products and their biosimilars, it is important for payers to consider the following:

Choosing a single-source supplier may limit the initial number of suppliers or cause a reduction in the number of suppliers in the market over time

A single-source supplier may increase the risk of product supply issues, and securing a new source in these instances is time-consuming and disruptive to treatment

Initial choice of a single-source supplier and any subsequent changes in the supplier may lead to increases in switching costs for health systems

Patients and physicians may be concerned about a lack of choice in therapies and the potential consequences of being forced to switch between therapeutic options that are not designated as interchangeable⁶⁴

Information Technology

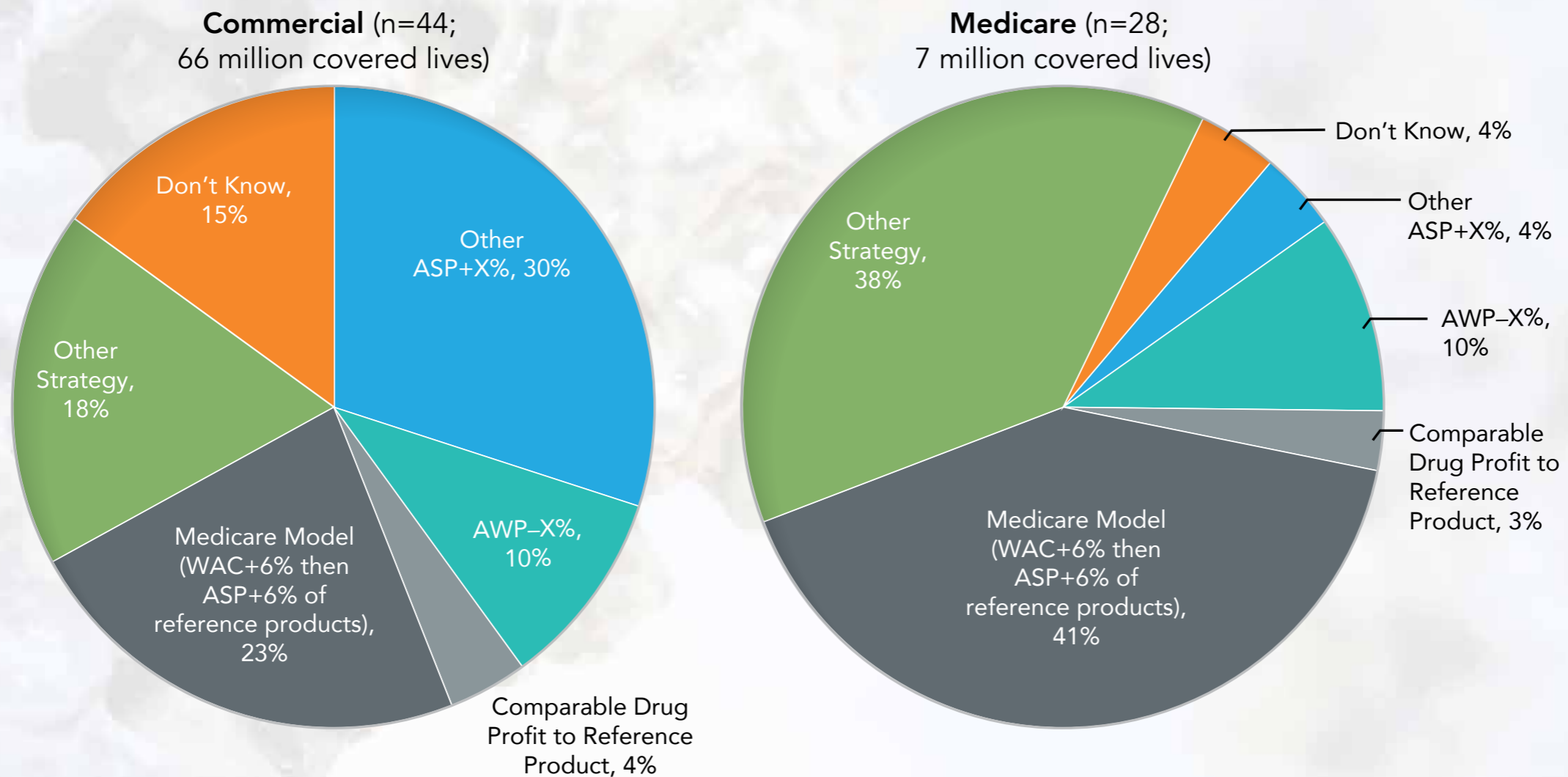
Another consideration for payer and provider organizations is the need to adapt their information technology (IT) systems to accurately manage and track biosimilars. This process will likely involve changes to ensure capabilities of distinguishing between multiple versions of biologic products and biosimilars. The system must be able to accurately track and trace product preference, conversions, utilization, and reported adverse events, as well as identify specific products for reimbursement and rebate tracking.⁶⁵

Systems may need to be reprogrammed to support various coding and pricing schemes and to account for new insurance authorizations for different Healthcare Common Procedure Coding System (HCPCS) codes.^{46,66} Evaluation of the potential costs associated with making the necessary IT system changes, in addition to the total cost of full formulary conversion to a biosimilar, may be compared to potential savings to help determine if a change will be beneficial in the short-term and long-term.⁶⁵

Reimbursement

So far, payers seem to be taking a traditional, fee-for-service approach to reimbursing for physician-administered biosimilars. The figures below show the breakdown of reimbursement methodologies for 44 commercial payers covering 66 million lives and 28 Medicare payers covering 7 million lives, as reported by Magellan Rx Management in 2017¹⁵:

2017 Biosimilar Reimbursement Methodology (% of lives)



Key: ASP – average sales price; AWP – average wholesale price; WAC – wholesale acquisition cost.

Key Stakeholders: Employers/Payers

Certain payment methodologies have advantages over the others. For example, Medicare Part B reimburses non-340B biosimilars at the biosimilar's ASP plus 6% (4.3% after sequestration) of the reference biologic's ASP.⁶⁷ The Medicare reimbursement methodology is designed to eliminate a disincentive to providers for prescribing biosimilars by providing the add on payment based on the higher-priced reference product.

This environment creates an inherent financial advantage for providers to favor higher-cost biologics, as the higher ASP translates directly to higher reimbursement.⁶⁸

The study recognized 2 scenarios in which using a biosimilar in place of the reference product is financially beneficial for both payers and providers:

Fixed reimbursement model

Under this model, payers "capitate" the cost of the drug by paying a fixed amount regardless of whether the reference product or biosimilar was administered, thereby eliminating the financial incentive for providers to use the more expensive reference product. In this case, providers realize the value of lowering their acquisition cost, while payers reduce their drug spend by reimbursing less than they currently pay for the reference product.

Differential reimbursement model

Like Medicare's approach, a differential model offers an opportunity for an add-on payment for the biosimilar (eg, equivalent to the add-on payment for the reference product) that is larger than under a straightforward ASP methodology, which can incentivize biosimilar product choice by providers.

The study argued that for either reimbursement model to be a viable option, there must be a middle ground for payers and providers, where payers realize cost savings while still providing financial incentives for providers to adopt biosimilars.

Revising reimbursement models for biosimilars, perhaps along the lines of the differential reimbursement model, may help incentivize providers to adopt the lower-priced products—or, at least, remove incentives to prescribe higher-priced alternatives that drive up healthcare costs for the entire system. A biosimilar with an equivalent add-on payment as its reference product would still be less expensive, since its ASP is lower.

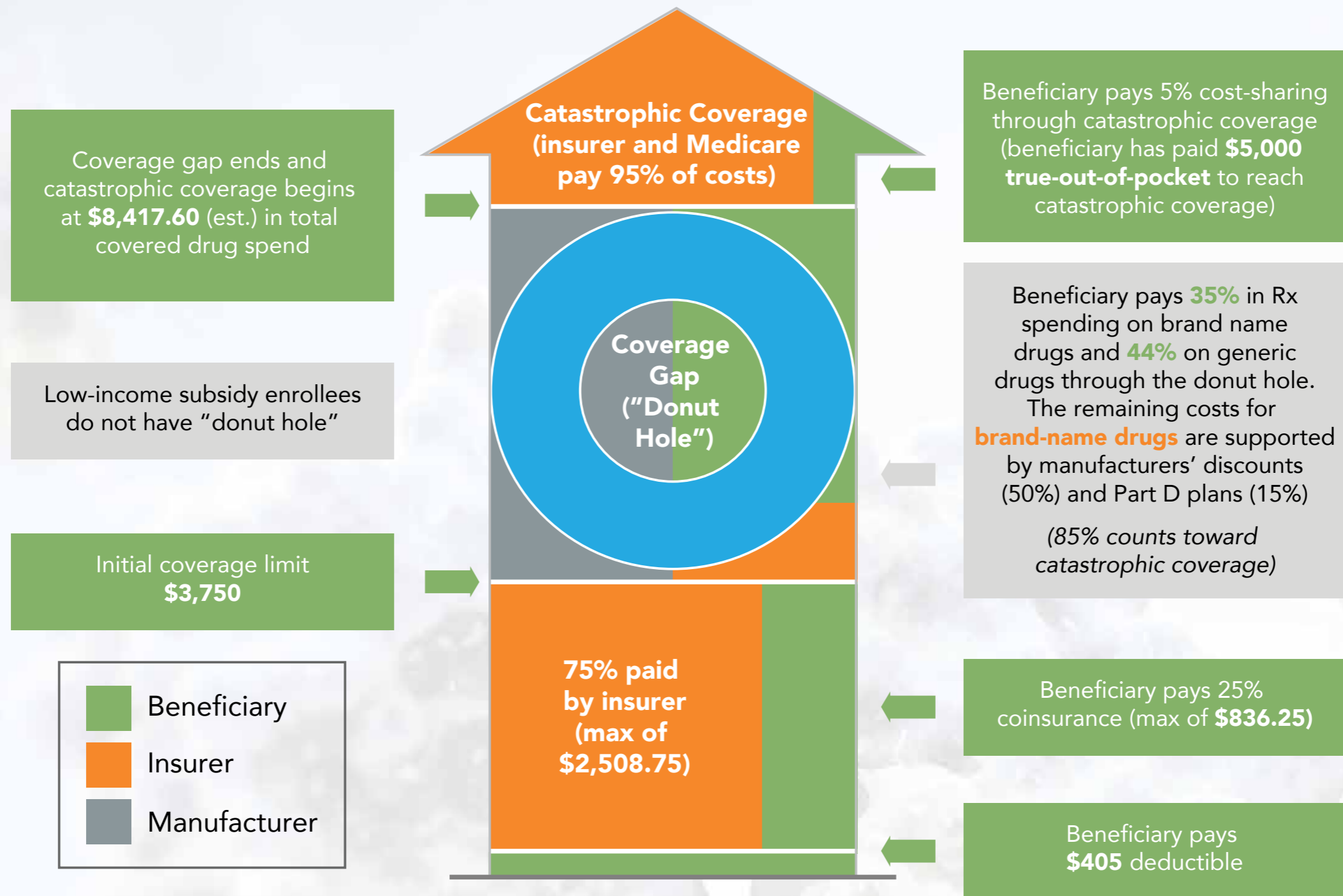
The Part D Donut Hole for Biosimilars

The standard Medicare Part D benefit is divided into 4 phases of coverage: deductible, initial coverage, coverage gap (“donut hole”), and catastrophic coverage. Before the ACA, patients were responsible for 100% of costs while they were in the coverage gap. Once beneficiaries’ “true out-of-pocket” spend fulfills the coverage-gap requirement, he or she enters the catastrophic phase of coverage, where the patient pays no more than 5% of costs. At this point, the Part D plan is responsible for 15% of the cost and Medicare pays the other 80%.⁶⁹

To limit patient out-of-pocket costs, Congress created the Coverage Gap Discount Program as part of the ACA, which aimed to eliminate the coverage gap so that once beneficiaries satisfied their deductible, they would have a 25% copayment until they reached catastrophic coverage.⁷⁰ The Coverage Gap Discount Program manages subsidies differently for brand and generic drugs. For 2018, Part D enrollees receive a 50% discount on the total cost of their brand-name drugs while in the donut hole, which is paid by pharmaceutical manufacturers. For generic drugs, patients pay 44% for generics, and the Part D plan pays the remaining 56%.⁷¹

Part D plan contributions while beneficiaries are in the coverage gap do not count toward fulfilling beneficiaries’ requirements for reaching catastrophic coverage, while the payments made by pharmaceutical manufacturers do count.⁷¹

2018 Part D Benefit Design^{69,72}



In February 2018, Congress passed legislation for Part D plans to be contributing 5% in the donut hole starting in 2019. Starting January 1, 2019, pharmaceutical manufacturers will be contributing 70% of the total cost of brand-name drugs while patients are in the donut hole.¹⁶

One other significant change from Congress is that manufacturers of biosimilars will provide discounts in the coverage gap starting in plan year 2019. To date, biosimilar manufacturers are not eligible to pay the 50% manufacturer coverage-gap discounts, leaving patients and Part D plans to pick up the cost differential. Biosimilar manufacturers will join brand-name pharmaceutical manufacturers in contributing 70% to patients' donut-hole expenses.¹⁶

While this policy will change in 2019, Medicare Part D beneficiaries may end up paying higher coinsurance amounts for biosimilars while they are in the coverage gap in 2018, since they do not have the benefit of the manufacturer paying 70% of the costs. Biosimilars being more expensive for patients in the coverage gap may lead to a preference to use the reference products, which could actually end up costing patients more in the long run.

Additionally, CMS has proposed to modify the definition of generic drugs, for the purposes of non-low-income subsidy (LIS) catastrophic and LIS cost-sharing, to include biosimilar therapies. As a result, instead of LIS Medicare beneficiaries paying a \$3.70 or \$8.35 brand copayment (depending on their income level) for biosimilars in 2018, they would pay a \$1.25 or \$3.35 generic copayment (depending on their income level) for biosimilars. Instead of non-LIS beneficiaries in catastrophic coverage paying the greater of 5% coinsurance or a \$8.35 brand copayment for biosimilars in 2018, they would pay the greater of 5% coinsurance or a \$3.35 generic copayment.⁷² Given Congress' change for biosimilars, CMS' ultimate decision on this matter is still unknown.

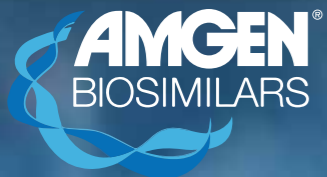
Key Considerations Checklist – Employers/Payers

- Employers are a critical group for biosimilars because 157.4 million people (49% of the US population) have employer-sponsored insurance—more than any other payer type.
- An important issue for employers and payers will be how biosimilars affect formularies, and their potential to decrease costs while maintaining patient access to necessary treatments.
- Stakeholders believe biosimilars can help hold down drug spending, but the substantial effect on costs is not expected to be immediate.
- Third-party drug coverage, benefit designs, and related policies will affect the uptake of biosimilars.
- Preferentially positioning biosimilars will provide formulary advantages, and greater differences in copayment amounts and/or coinsurance between the tiers for biosimilars and reference products will help foster biosimilar uptake.
- Payers have a couple of scenarios for formulary placement of biosimilars: 1) place the lower-cost biosimilar on a preferred formulary tier and the reference product on a non-preferred or specialty tier; and 2) include the biosimilar on the formulary, but exclude the reference product.
- In one survey, nearly all payers indicated that a biosimilar's cost relative to its reference product is a key decision-making factor for determining coverage.

- Major payers and PBMs have started replacing reference biologics with their biosimilars on their formularies.
- Many purchasers and providers consider biosimilars to be branded products available as an alternative to reference products.
- While the prices of generic drugs can be discounted as much as 90% from their brand equivalents, the prices of biosimilars at launch have not been discounted that much from their reference products—nor were they expected to be.
- Another consideration for payer and provider organizations is the need to adapt their IT systems to accurately manage and track biosimilars.
- Payers seem to be taking a traditional, fee-for-service approach to reimbursing for biosimilars.
- Reimbursing for all biologics, including biosimilars, via their own ASPs creates an inherent financial advantage for providers to favor higher-cost biologics, as a higher ASP translates directly to higher reimbursement.
- In 2018, patients in the Part D coverage gap face significant barriers to access for biosimilar options. However, this will change in 2019 given legislation passed by Congress in February 2018.

Notes





Key Stakeholders: Healthcare Professionals

Need for
Physician
Education

Medicare
Part B

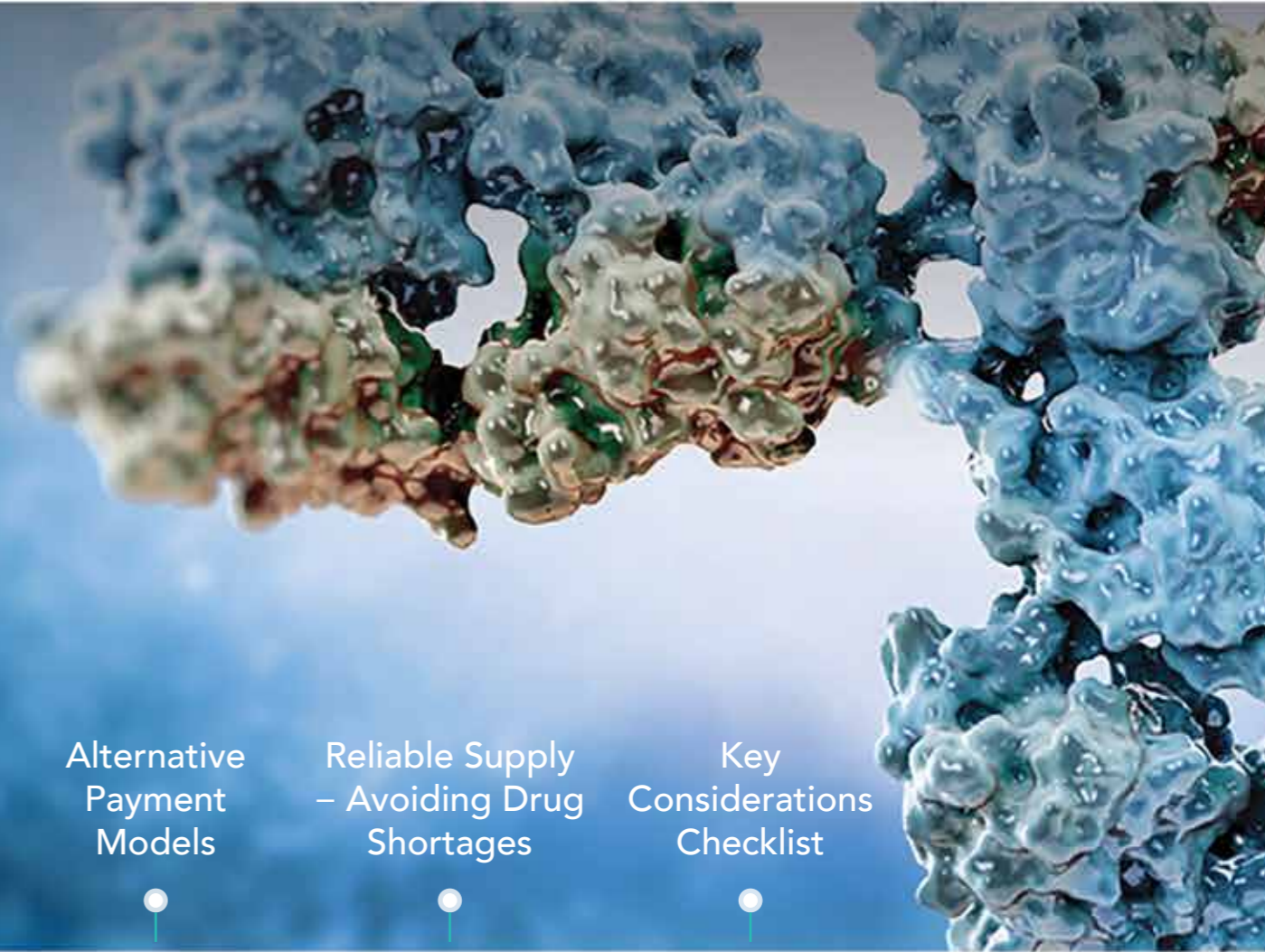
Commercial
Payers

Medicaid

Alternative
Payment
Models

Reliable Supply
– Avoiding Drug
Shortages

Key
Considerations
Checklist



Healthcare professionals, including physicians, physician assistants, nurse practitioners, and pharmacists, are an extremely important group that can help to increase the adoption of biosimilars and educate patients on this new product category. Therefore, it is imperative they have a comprehensive understanding of biosimilars, including the clinical, regulatory, and financial characteristics. Patients are likely to be relatively uninformed about biosimilars, and they will look to their providers for information and clarification.

Need for Physician Education



Nearly 3 years after the FDA approved the first biosimilar,¹⁹ physicians across specialties still need significant education on biosimilars. In late 2015 and early 2016, the Biosimilars Forum commissioned SERMO to conduct a 19-question survey of 1,201 US physicians across specialties who are high prescribers of biologics, including dermatologists, gastroenterologists, hematologist-oncologists, medical oncologists, nephrologists, and rheumatologists. The survey results showed the specialty physicians' actual knowledge of the fundamentals of biosimilars was low; the portion of respondents answering correctly rarely surpassed 50% for questions that focused on key aspects of these therapies.²⁰

The survey of high prescribers of biologics identified 5 major knowledge gaps:

1. Defining biologics, biosimilars, and biosimilarity
2. Understanding the approval process and use of "totality of evidence" to evaluate biosimilars
3. Understanding that the safety and immunogenicity of a biosimilar are comparable to the originator biologic (reference product)
4. Understanding the rationale for extrapolation of indications
5. Defining interchangeability and the related rules regarding pharmacy-level substitution

The survey also reported that peer-reviewed literature was, by far, the most trusted and preferred information source for biosimilars among physicians.

One area that needs to be emphasized is that the focus of clinical studies for biosimilars is not to establish the clinical effectiveness of the biosimilar product; rather, it is to demonstrate similar clinical efficacy between the biosimilar and the branded product.^{7,40}

Some manufacturers develop larger, more thorough studies to demonstrate clinical differentiation of their biosimilars. Though the additional detail is not necessarily needed to obtain FDA approval, it can equip clinicians in making treatment decisions and to help instill patient confidence.

Despite their need for additional education about biosimilars, more physicians are becoming comfortable with prescribing biosimilars for their patients, but they are also weighing more factors into their choice of prescribing biosimilars at all. In September 2016, a tracking report developed by InCrowd including responses from 150 US-based, board-certified physicians in specialties where biologics prescribing is significant (dermatology, endocrinology, gastroenterology, oncology and rheumatology) found that 84% of physicians said they intend to prescribe biosimilars in the coming 3 years.⁷³ However, fewer said they would allow pharmacy-level substitution of these drugs for their patients than when asked 6 months before (17% vs 28%).

This reticence might be a specialist-by-specialist issue. Another recent survey of 200 oncologists found that when it came to treating breast cancer, 73% of participating oncologists (N=184) would be open to prescribing a biosimilar to treat both adjuvant and metastatic patients, while only 10% indicated they would not prescribe a biosimilar.⁵⁵

Medicare Part B



The ACA includes language to help incentivize provider utilization of biosimilars by requiring Medicare to reimburse physicians at the biosimilar's ASP plus 6% (4.3% after sequestration) of the reference biologic's ASP.^{21,22} This biosimilar payment model is designed to create a financial incentive for physicians to prescribe a lower-cost biosimilar; the 6% add-on payment (4.3% after sequestration) of the reference product would, consequently, offer a payment boost for prescribers of biosimilars.²³

A primer on sequestration for Medicare

The Budget Control Act of 2011 required, among other things, mandatory across-the-board reductions in federal spending, also known as “sequestration.”

In general, Medicare fee-for-service claims on or after April 1, 2013, will incur a 2% reduction from the Medicare program.

Beneficiary payments for deductibles and coinsurance are not subject to the 2% payment reduction—their payment obligations to providers are not reduced and remain the same.⁷⁴

Sequestration thus reduces the total Medicare payment providers receive for Part B drugs from 106% of ASP to 104.3% of ASP.⁷⁵

As of January 2018, CMS assigns each biosimilar a unique HCPCS code, and its ASP will not be combined with other biosimilars’ ASPs.⁶⁷ This is a change from previous billing and coding policy that grouped biosimilars with a common reference product in the same HCPCS code.²¹

For the 2 US-marketed biosimilars currently sharing a billing code, CMS will be releasing guidance soon about how it will bring the situation into compliance with its new policy.

On the next page are hypothetical examples of physician office/community clinic and outpatient payments for a biosimilar under Medicare Part B.⁷⁶

Medicare Part B: Community Clinics, Hospitals, and Health Systems

Table 2. Payment Methodology for Biosimilars Under Medicare Part B^{67,76}

Biologic Product	Reference	Biosimilar A	Biosimilar B
WAC (List Price)	\$1,000.00	\$800.00	\$700.00
ASP ^a	\$800.00	\$640.00	\$560.00
6% of Reference Product's ASP		\$48.00	
Payment Rate (ASP + 6%) (before sequestration)	\$848.00	\$688.00	\$608.00
Payment Rate (ASP + 4.3%) (after sequestration)	\$831.40	\$674.24	\$595.84
Patient Cost-share (20%) ^b	\$169.60	\$137.60	\$121.60

^a Note: This hypothetical example assumes that the biologics' (both reference and biosimilar) ASPs are 20% less than the WAC based on rebates over time.

^b Sequestration lowers the 80% Medicare payment to physicians by 2%, but the beneficiary copayment remains at 20% of the original payment rate of ASP+6%.

Key: ASP – average sales price; WAC – wholesale acquisition cost.

Medicare Outpatient Prospective Payment System Considerations, Including the 340B Drug Pricing Program

The 340B program requires drug manufacturers to sell outpatient drugs at a discount to providers serving high numbers of low-income Medicare, Medicaid and Supplemental Security Insurance patients. Sites within a healthcare system that qualify as 340B entities can obtain federally mandated “ceiling price” discounts for covered outpatient drugs, while other sites that are not 340B-eligible pay a higher net price.²⁴ Ceiling prices for 340B drugs are not publicly disclosed, but it has been estimated that 340B entities save 15% to 60% on prescription drug costs through this program.^{77,78}

Before January 1, 2018, Medicare paid both 340B and non-340B entities at the same rate for certain 340B treatments, such as biologic drugs, even though 340B entities can obtain those treatments at a discount.⁷⁷ Effective January 1, 2018, however, CMS changed the Medicare Part B payment methodology for 340B drugs. Medicare adopted a policy to pay for separately payable, non-pass-through drugs and biologicals (other than vaccines) purchased through the 340B program at ASP minus 22.5%.²⁵ CMS assigns pass-through status to qualifying new drugs and biologicals each year, which lasts for at least 2 years, but not more than 3 years.⁷⁹

Additionally, CMS adopted a policy that any biosimilar with pass-through payment status will be exempt from Medicare’s alternative payment methodology for 340B drugs (ie, ASP minus 22.5%). Biosimilars with pass-through payment status will continue to be paid at ASP plus 6% of the reference product. However, biosimilars not on pass-through status, or those with pass-through status expiring, will be paid at the new 340B program rate of ASP minus 22.5% of the reference product.⁸⁰

Biosimilars with pass-through payment status = ASP plus 6% of the reference product’s ASP

Biosimilars without pass-through payment status = ASP minus 22.5% of the reference product’s ASP

Medicare Outpatient Prospective Payment System Considerations, Including the 340B Drug Pricing Program (continued)

Table 3. Hospital Outpatient Department Payment Methodology for 340B Reference Biologics and 340B Biosimilars in Medicare Part B

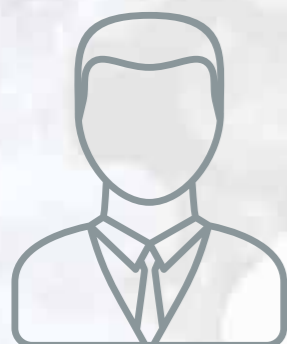
Biologic Product	Reference	Biosimilar A, <u>with</u> pass-through status	Biosimilar A, <u>without</u> pass-through status
WAC (List Price)	\$1,000.00	\$800.00	\$800.00
ASP ^a	\$800.00	\$640.00	\$640.00
6% of Reference Product's ASP	N/A	\$48.00	N/A
22.5% of Reference Product's ASP	\$180.00	N/A	\$180.00
Hospital Outpatient Payment Rate (before sequestration)	\$620.00	\$688.00	\$460.00
Hospital Outpatient Payment Rate (after sequestration)	\$610.08	\$676.99	\$452.64
Patient Cost-share (20%)	\$124.00	\$137.60	\$92.00

^a Note: This hypothetical example assumes that the biologics' (both reference and biosimilar) ASPs are 20% less than the WAC based on rebates over time.
Key: ASP – average sales price; WAC – wholesale acquisition cost.

As Table 3 shows, the Medicare payment amounts for products under the 340B Drug Pricing Program change quite a bit, depending on the product's pass-through payment status. Starting in 2018, both the provider's payment and the patient's cost-share will vary appreciably depending on the biological product being prescribed and administered under the 340B Drug Pricing Program.

Decision makers in hospitals and health systems should ensure awareness of any differences between a biosimilar and its reference product, as well as biosimilars with and without pass-through payment status, with respect to the 340B Drug Pricing Program.

Commercial Payers



Biologics may be covered under the medical benefit or the pharmacy benefit.⁵³ Self-administered medicines (often delivered by a specialty pharmacy) are typically covered under the pharmacy benefit, while those injected or infused under the supervision of a physician are typically paid for as medical benefits.⁵⁴ As of December 2017, none of the biosimilars marketed in the US are covered primarily under the pharmacy benefit by most insurers.

Third-party drug coverage, benefit designs, and related policies will affect the uptake of biosimilars. Policies may vary, depending on whether the drug falls under the pharmacy or medical benefit. As discussed, biosimilars are expected to be less expensive than their reference products. The extent to which this cost difference will influence patients will depend on whether and how the products are covered by payers, as well as the configuration of patients' benefit designs. Preferentially positioning biosimilars will provide biosimilars with formulary advantages, and greater differences in copayment amounts and/or coinsurance between the tiers for biosimilars and reference products will help foster biosimilar uptake.

Payers have a couple of scenarios for formulary placement of biosimilars. One option is to have the lower-cost biosimilar on a preferred formulary tier and the reference product on a non preferred or specialty tier. This would result in lower out-of-pocket costs for patients choosing the biosimilar, but would still offer relatively unfettered access to the reference biologic.

Payers may need to become familiar with biosimilars before placing them preferentially on the formulary compared to the reference product. According to Avalere Health's 2017 survey of 45 US health plans, approximately 2 years after its launch, the first FDA-approved biosimilar was covered by 94% percent of employer-sponsored insurance plans, with over 40% of employer plans covering the biosimilar in the preferred brand tier. Compare that coverage to the coverage scenario for the second FDA-approved biosimilar: 7 months after being on the market, only 42% of employer plans covered it.⁵⁵

Another formulary scenario is to include the biosimilar but exclude the reference product. This design would enable the plan to place the biosimilar on a more expensive tier, potentially resulting in greater out-of-pocket costs for patients. Accessing the reference product would comparatively be much more difficult, perhaps requiring a prior authorization.

Approximately 3 years after the FDA approved the first biosimilar, commercial payers appear to have become comfortable with the products, as Avalere Health's survey found 81% of plans reported they are covering a biosimilar product. Nearly all payers indicated that a biosimilar's cost relative to its reference product is a key decision-making factor for determining coverage. In addition to costs compared to the reference product, health insurers cited the efficacy and safety of the biosimilar as important factors for coverage decisions.⁵⁵

As a demonstration of commercial payers' acceptance of some biosimilars as therapeutic substitutes to their reference products, they have started replacing reference biologics with their biosimilars. In 2016, the largest pharmacy benefit manager (PBM) and the largest health insurer replaced a reference biologic with the first FDA-approved biosimilar on their 2017 national formularies.^{58,59} In 2017, the second-largest PBM also replaced a reference biologic with the first FDA-approved biosimilar on its 2018 national formulary.⁶⁰

Healthcare providers, however, may react differently to biosimilars replacing reference products on formularies. Spherix Global Insights' 2017 report surveying 103 US gastroenterologists showed a significant decline since 2016 in their ulcerative colitis patients treated with an injectable reference biologic. The decline was attributed to the adoption of biosimilars and the use of a self-injectable reference product, potentially indicating that physicians were changing their prescribing patterns to avoid insurance mandates for biosimilar use. Over one-third of the surveyed physicians agreed that if a pharmacy or managed care plan advised them to use a biosimilar over its reference product, they were more likely to choose a different agent altogether.⁵⁶



This reticence might be a specialty-by-specialty issue, though. A 2017 survey by Cardinal Health of 200 oncologists representing a mix of US community and hospital-based practices found that when it came to treating breast cancer, 73% of participating oncologists were open to prescribing a biosimilar to treat both adjuvant and metastatic patients, while only 10% indicated they would not prescribe a biosimilar.⁵⁷

As biosimilars continue to gain acceptance by the payer community, it will only become more necessary for providers to verify their patients' benefits to determine if reference biologics and/or biosimilars are preferred on the health plans' formularies.

Medicaid



The generic-like treatment of biosimilars by Centers for Medicare and Medicaid Services (CMS) in certain parts of Medicare does not cross over into Medicaid. In late December 2016, CMS issued a notice reinforcing its position that biosimilars do not qualify as authorized generic drugs for the purpose of the Medicaid Drug Rebate program and are subject to brand-level rebates. The notice adds that the "best price of the reference biologic and the biosimilar biologic should be determined separately as the lowest price available from each manufacturer."¹⁸

Alternative Payment Models



CMS Programs and Initiatives to Pay for Value and/or Quality in Which Lower-cost Biosimilars May Help Providers Achieve Goals

- **Quality Payment Program (via MACRA), consisting of 2 tracks:**
 - **Merit-based Incentive Payment System (MIPS):** Allows participating providers to earn a performance based payment adjustment, based on demonstrating providing high-quality and cost-efficient care. MIPS replaces the Physician Quality Reporting System (PQRS), value-based modifier, and Electronic Health Records Incentive Program (also called “meaningful use”), and adds a new category for Improvement Activities.⁸¹
 - **Advanced Alternative Payment Models (APMs):** Specific programs that add incentive payments to provide high-quality and cost-efficient care. APMs can apply to a specific clinical condition, a care episode, or a population.⁸²
- **Oncology Care Model (OCM),** which utilizes appropriately aligned financial incentives to enable improved care coordination, appropriateness of care, and access to care for beneficiaries undergoing chemotherapy. The OCM encourages participating practices to improve care and lower costs through an episode-based payment model that financially incentivizes high-quality, coordinated care.⁸³

- **Physician Compare**, which helps patients find and compare Medicare providers so they can make informed decisions about their healthcare. It shows participation in quality activities, performance information against various healthcare categories, and patient survey scores.^{84,85}
- **Shared Savings Program**, which creates a new type of healthcare entity, an Accountable Care Organization (ACO). An ACO agrees to be held accountable for the quality, cost, and experience of care of an assigned Medicare fee-for-service beneficiary population.⁸⁶ Each ACO is accountable for the total cost of care for their assigned beneficiaries. If an ACO's spending for the beneficiaries is below the benchmark, then the ACO may share in the cost savings.⁸⁷

The ACA, which became US law in 2010, attempts to help solve long-standing challenges the US healthcare system has faced related to access, affordability, and quality of care.⁸⁸ The aim of the ACA to contain healthcare costs while improving quality and outcomes is in line with a more general shift in priorities from volume to value.⁸

The ACA and other subsequent healthcare legislation introduced a variety of value-based programs, such as the Medicare Shared Savings Program and the Advanced Alternative Payment Model in the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), in which providers are accountable for the total cost of care for a set of services.^{82,86,87}

These value-based approaches reward providers who give treatments that achieve the best outcomes at the lowest cost. Consequently, they incentivize providers to seek the drug with the best value that effectively addresses a patient's condition. Lower-cost biosimilars have an inherent advantage in these scenarios.

Reliable Supply — Avoiding Drug Shortages



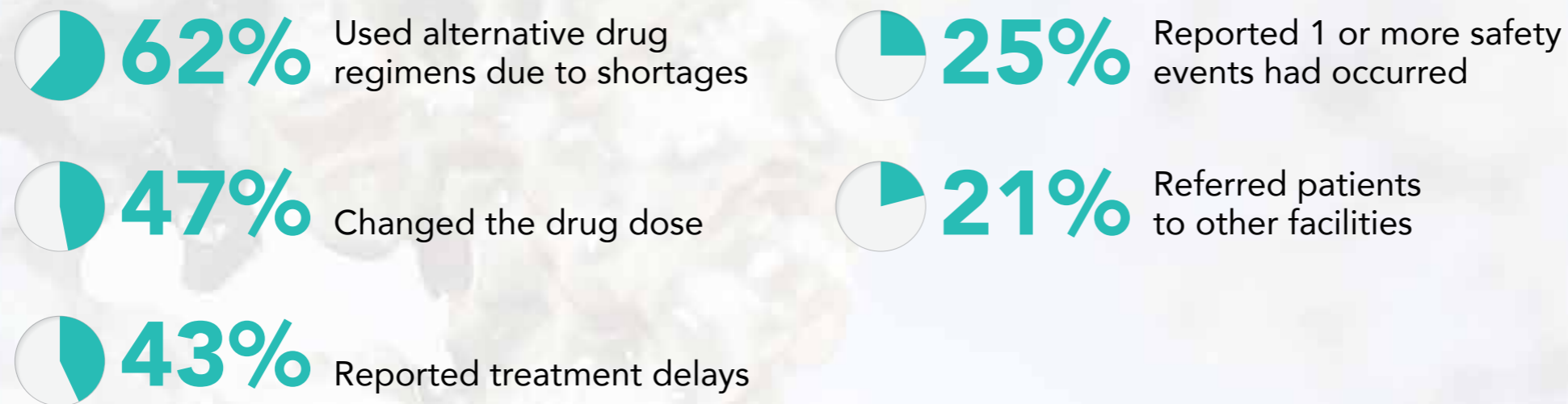
Unfortunately, drug shortages are common and have been the subject of numerous articles in recent years.^{46,89} Due to their highly specialized manufacturing process, sterile injectables make up a large percentage of these shortages.⁹⁰ The number of new shortages has decreased overall since 2011. However, the number of ongoing shortages remains high (see figure below and Table 4 on next page).⁹¹

Number of Drug Shortages From January 2010 Through December 2015⁹¹



In one survey, 98% of pharmacy directors reported at least 1 oncologic drug shortage during the prior year, with the following consequences⁹²:

Table 4. Consequences of Oncologic Drug Shortages and Percentage of Respondents Reporting a Resulting Issue



A 2010 survey of 353 pharmacy directors conducted by the American Society of Health-System Pharmacists found that the time and labor their staff spends managing drug shortages are significant, and the information available to manage drug shortages was suboptimal.⁹³

To avoid treatment delays and unplanned switching between biologics during the course of treatment, it is important to consider a manufacturer's history of shortages and recalls related to quality concerns and evaluate its capability to maintain adequate production and stock to support demand. It is also important to consider the robustness of the manufacturer's supply chain when evaluating biosimilars.²⁷

Key Considerations Checklist – Healthcare Professionals

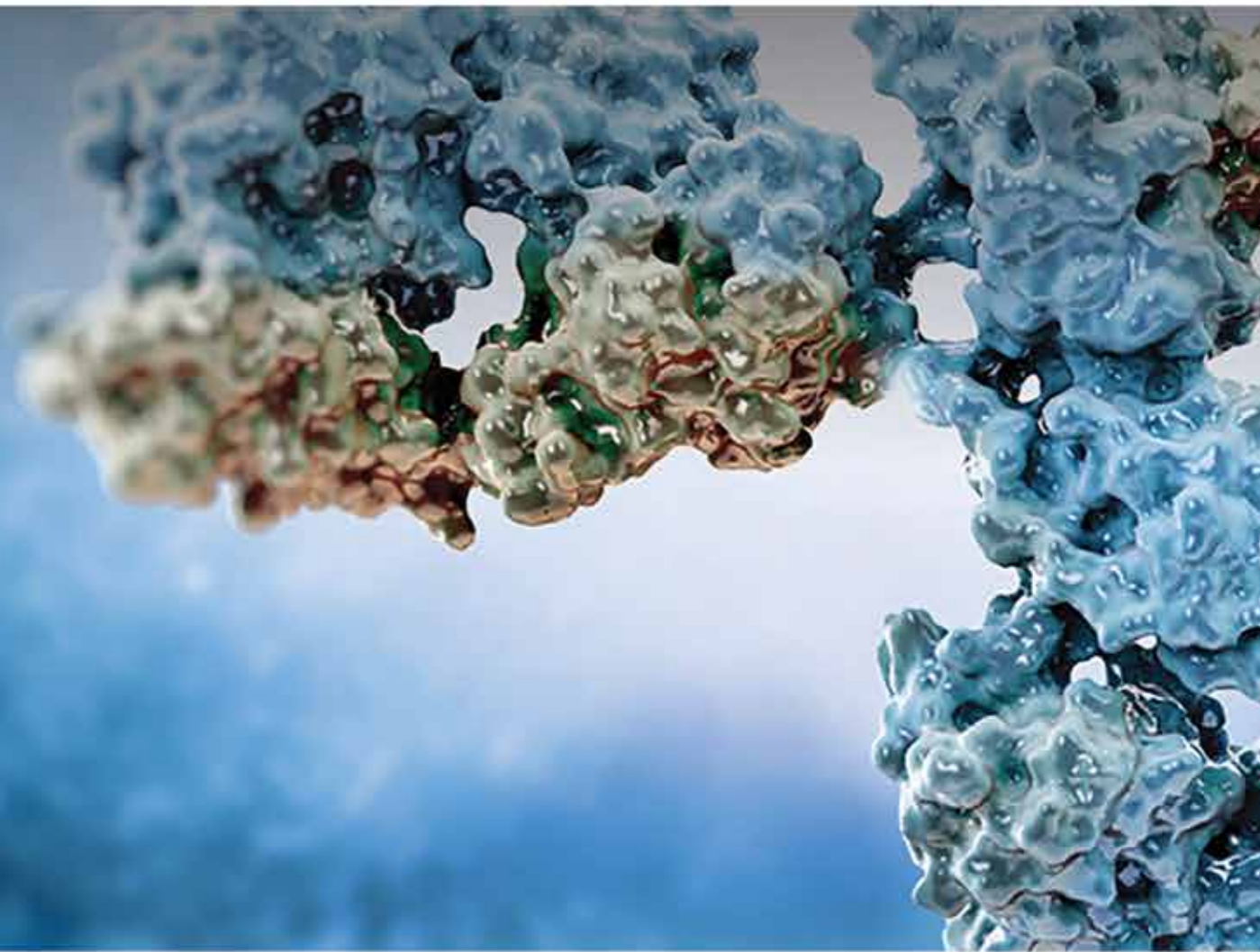
- Healthcare professionals are an extremely important group that can help to increase the adoption of biosimilars and educate patients on this new product category, as patients are likely to be relatively uninformed about biosimilars and will look to their providers for information and clarification.
- Approximately 3 years after the FDA approved the first biosimilar, physicians across specialties still need significant education on biosimilars.
- Peer-reviewed literature was reported as the most trusted and preferred information source, by far, for biosimilars among physicians.
- More physicians are becoming comfortable with prescribing biosimilars for their patients.
- The ACA includes language to help incentivize provider utilization of biosimilars by requiring Medicare to reimburse physicians at the biosimilar's ASP plus 6% (4.3% after sequestration) of the reference biologic's ASP.
- CMS will assign each biosimilar a unique HCPCS code, and its ASP will not be combined with other biosimilars' ASPs.
- Decision makers in hospitals and health systems should ensure awareness of any differences between a biosimilar and its reference product, as well as biosimilars with and without pass-through payment status, with respect to the 340B Drug Pricing Program.

- CMS adopted a policy that any biosimilar with pass-through payment status will be exempt from Medicare's alternative payment methodology for 340B drugs (ie, ASP minus 22.5%). Biosimilars with pass-through payment status will continue to be paid at ASP plus 6% of the reference product. However, biosimilars without pass-through payment status will be paid at the new 340B program rate of ASP minus 22.5% of the reference product's ASP.
- In 2018, patients in the Part D coverage gap face significant barriers to access for biosimilar options. However, this will change in 2019 given legislation passed by Congress in February 2018.
- Physicians need to be well-educated on the financial implications of biosimilar prescribing under Medicare Part D in order to counsel their patients appropriately.
- Third-party drug coverage, benefit designs, and related policies will affect the uptake of biosimilars.
- Payers have a couple of scenarios for formulary placement of biosimilars: 1) place the lower-cost biosimilar on a preferred formulary tier and the reference product on a non-preferred or specialty tier; and 2) include the biosimilar on the formulary, but exclude the reference product.
- Major payers and PBMs have started replacing reference biologics with their biosimilars on their formularies.
- While the prices of generic drugs can be discounted as much as 90% from their brand equivalents, the prices of biosimilars at launch have not been discounted that much from their reference products—nor were they expected to be.

- Payers seem to be taking a traditional, fee-for-service approach to reimbursing for biosimilars.
- Reimbursing for biosimilars via their ASP creates an inherent financial advantage for providers to favor higher-cost biologics, as a higher ASP translates directly to higher reimbursement.
- The ACA and other subsequent healthcare legislation introduced a variety of value based programs in which providers are accountable for the total cost of care for a set of services.
- Value-based programs incentivize providers to seek the drug with the best value that effectively addresses a patient's condition. Lower-cost biosimilars have an inherent advantage in these scenarios.
- To avoid treatment delays and unplanned switching between biologics during the course of treatment, it is important to consider a manufacturer's history of shortages and recalls related to quality concerns and evaluate its capability to maintain adequate production and stock to support demand.



Patients – Frequently Asked Questions



Patients – Frequently Asked Questions

What Is a Biologic?

Biologics are typically much larger molecules than those found in conventional pharmaceuticals, and in many cases their exact composition is unknown (or even unknowable). You're unlikely to find biologic drugs in tablet form—they tend to be delicate molecules that exist in liquid solutions, which is why most of them are injected or infused.⁹⁴

A substance that is made from a living organism or its products and is used in the prevention, diagnosis, or treatment of cancer and other diseases. Biological drugs include antibodies, interleukins, and vaccines.⁹⁵

What Is a Biosimilar?

A biosimilar approved by the FDA is highly similar to and has no clinically meaningful differences in terms of safety and effectiveness from an FDA-approved biological product, which is known as the “reference product.” Biosimilars are not the same as generic drugs—but like generics, biosimilars may offer more affordable treatment options to patients.⁹⁶

Are Biosimilars Safe and Effective?

All FDA-approved biological products, including reference products and biosimilar products, undergo a rigorous evaluation so that patients can be assured of the efficacy, safety, and quality of these products.³⁴

What Are the Benefits of Using a Biosimilar?

An increase in market competition for biological products may lead to reduced costs for both patients and our healthcare system. Similar to how the introduction of generic drugs in the US has led to significant cost savings, biosimilars have the potential to save our healthcare system billions of dollars over the coming years.⁹⁶



Will Biosimilars Make Me Feel Better?

Biosimilars undergo rigorous testing to ensure that they are as effective as the reference biologics you may be using now.⁴⁰ If your current treatment makes you feel better, the FDA has ensured its biosimilar will perform just as well.

Will There Be Support Available for Patients on Biosimilars?

Just like pharmaceutical manufacturers provide assistance to patients for many brand drugs, some manufacturers are expected to provide many of the same types of support for biosimilars. Examples of assistance include copayment assistance, free product, and educational resources that describe their biosimilars in easy-to-understand language. The methods of assistance do not work with all types of insurance.

Charity organizations are also expected to provide replacement products for individuals on Medicare.

Checklist of Questions to Ask Your Doctor

What is a biosimilar?

Are biosimilars safe?

Are biosimilars effective?



Will a biosimilar make me feel better?

How much will a biosimilar cost me?

Why are biosimilars cheaper?

Do biosimilars undergo the same clinical-trial process as other FDA-approved products?

If not, is that okay?

If I have been on the same therapy for a long time, is there a reason I should switch?

Is there an FDA-approved biosimilar for the biologic I am taking?

If so, is it available on the market?

Is it on my health plan's formulary?

If so, which tier?

What is the out-of-pocket difference between it and the biologic I am taking?

Are there any patient support programs for the biosimilar, in case I have questions or need assistance?

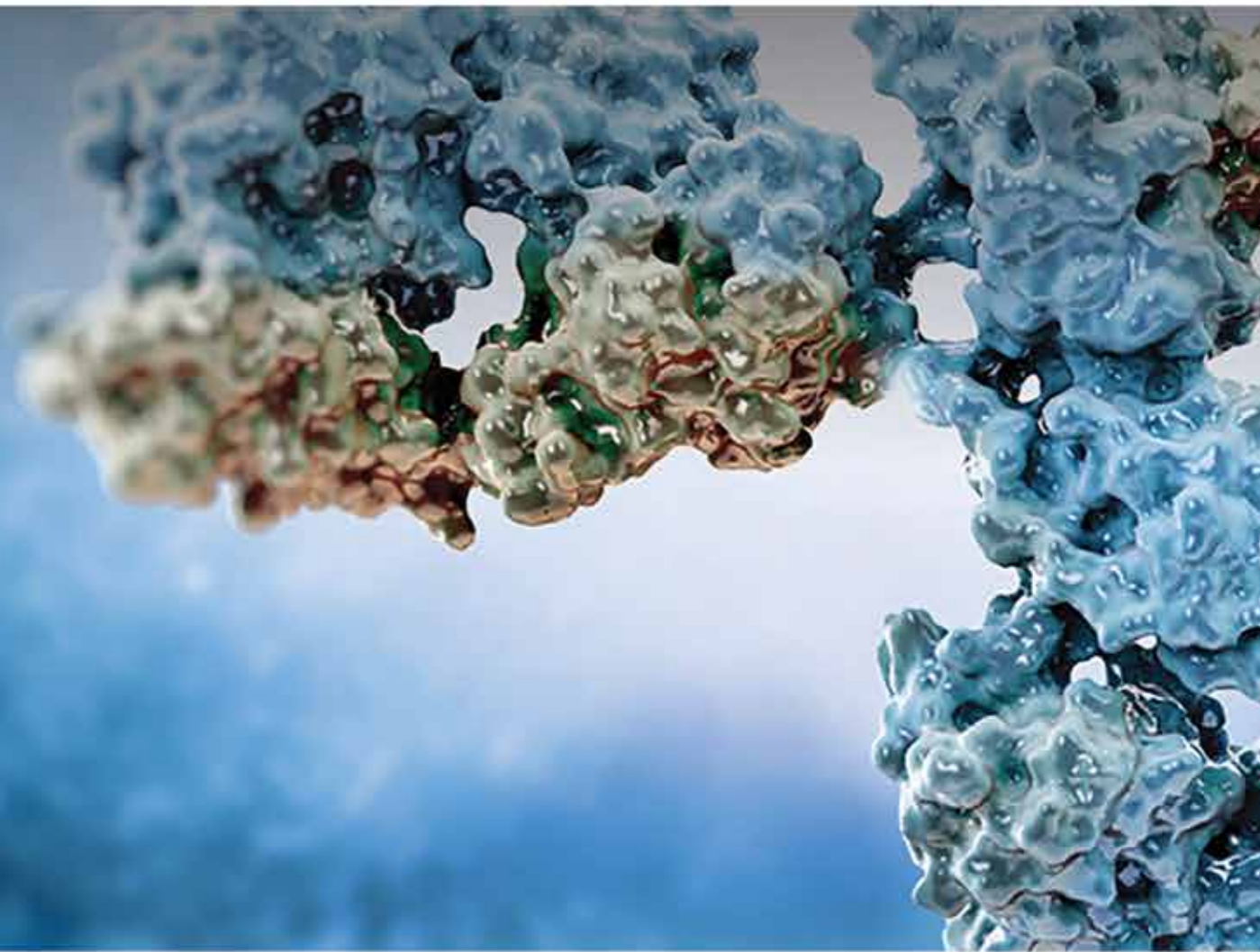
Is there a biosimilar available for my condition, even if it is different from the biologic I am taking?

If there is not a biosimilar for me, do you know if there are any in development?





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