Answers to 5 common questions about biosimilars

More biosimilars are coming to the market

As more biosimilars gain regulatory approval, it's helpful to review the chemical, legal, regulatory and market factors that allow biosimilars to drive positive clinical and cost outcomes—both for individuals and employers.

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What are biosimilars?

A biosimilar is a biological agent that has no clinically meaningful differences from an existing biologic drug that has been approved by the U.S. Food and Drug Administration (FDA). These biologic drugs are also known as an "innovator," "reference product" or "originator."

While this seems simple, you still need to account for the underlying complexity of any biologic drug. Conventional, small molecule drugs are chemically synthesized with well-defined molecular structures. In contrast, biologics are produced from living systems. As a result, they are much larger and are far more complex at the molecular level.

This complexity also means manufacturing processes for biologic drugs differ greatly from those for small molecule drugs. Unlike generics, minor differences between the reference product and the proposed biosimilar product in clinically inactive molecular components are acceptable.

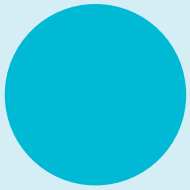
One primary difference between biosimilars and traditional generics is complexity of the drugs they are based on.

Biosimilars and generics — a comparison

Here's an example of the molecular composition of a monoclonal antibody (common large molecule biologic drug) versus aspirin (common small molecule drug).[1]

Biologic and biosimilar medications

Monoclonal antibody, large molecule, difficult to make



Brand and generic medications

Aspirin (acetylsalicylic acid), small molecule, easy to make

*Graphic is for illustrative purposes only.

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Why now?

Biologics are in development for many therapy areas. The list now includes conditions historically treated by small molecule drugs. Many drug classes—from insulins to monoclonal antibodies to vaccines—are biological drugs.

Biologics represent the cutting edge of pharmacy. Some of the most promising new drug classes, including gene and cell therapies, are biologic in origin. These therapies may offer valuable means to treat a variety of diseases currently lacking effective treatment options.

Accordingly, biologic drugs are heavily represented in the drug pipeline. About 1 in 4 new drugs are biologic.

Given this increasing influx of biologic drugs, interest in biosimilar options has been growing. The FDA created an abbreviated regulatory pathway for biosimilars in 2010. However, the first approved biosimilar did not hit the U.S. market until 2015. Since then, the FDA has approved 33 biosimilar products for 11 different innovators. In 2021–2022 alone, 6 new biosimilar products were approved.[4] And more are on the way, both in the short- and long-term.

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global best selling drugs in 2021 are biologics[2]

14

of 50 new FDA-approved drugs are biologics[3]

3

What took biosimilars so long to arrive?

Biosimilars are complex to manufacture, so it takes a long time before they arrive in the market. To make a biosimilar, a drug maker must essentially reverse engineer the reference product and then identify an appropriate “cellular factory” to make the biosimilar.[5]

In addition to patents covering the active ingredients in a biologic, originator product makers also obtain patents for formulations and specific manufacturing processes. Thus, biosimilar manufacturers need to show that their drug has no clinically meaningful differences from the originator biologic and was made via different manufacturing method.

Subsequently, a biosimilar manufacturer must test to make sure that their drug closely replicates the reference product. They must then find the methods needed to manufacture safely and consistently at scale. Biosimilar manufacturers must also confirm their findings in a clinical trial. Patient recruitment for clinical trials can be difficult given that patients with serious conditions such as cancer may be reluctant to test a biosimilar when an existing biologic is already available.[6]

It is only after these considerable hurdles are cleared that a new biosimilar can be submitted for regulatory approval. In all, this process can take 5–10 years and requires an investment of $100 million–$250 million. By comparison, developing a conventional generic usually takes about 2 years and $1 million–$10 million.[7] As a result, few companies have the technical and financial resources to make biosimilars.

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What is the potential financial effect of biosimilars?

Although biologics account for only 2% of overall prescription volume, they make up 43% of overall drug spending.[8] The final cost savings attributable to biosimilars will be influenced by a variety of factors.

One consideration is that the upfront and ongoing manufacturing complexity may limit their savings potential. The biosimilars currently available are typically priced 10% to 30% lower than originator products.[9] In contrast, generic competition for a small molecule drug can drive prices down as much as 95% when 6 or more generic options are available.[10] Likewise, having multiple biosimilars in market for a biologic drug may be a prerequisite for substantial cost savings.

The savings potential of biosimilars also varies according to drug class. For example, launches of biosimilar insulins for diabetes have been relatively rare, despite high spending on the class. In contrast, the cancer medication Herceptin® has 5 biosimilar products now available in the marketplace.[11]

Yet, the availability of a biosimilar is only part of a potential cost-saving equation. Patients may be reluctant to accept a biosimilar over an established biologic that is already part of their routine.

There are also barriers to biosimilar acceptance among physicians. They may be reluctant to swap a biosimilar for a patient already being treated with the innovator. A study of rheumatologists found that 73% were likely or very likely to initiate a biosimilar therapy for a patient who had not yet taken a biologic. But only 35% said they were likely or very likely to do so for a patient already doing well on the original innovator. Also, some providers may have negotiated favorable pricing for an innovator that helps promote its continued use, despite biosimilar alternatives.

One factor that may significantly influence uptake of biosimilars going forward is the FDA designation of interchangeable biosimilars. Generic medications are routinely substituted for brand name medications. Similarly, a biosimilar product with the FDA interchangeable designation may be substituted by the dispensing pharmacy, if permissible by state law, without any intervention of the provider who prescribed the reference product.

In addition to showing the product is expected to produce the same clinical result as the reference product, a manufacturer of a proposed interchangeable product needs to meet additional requirements. This includes showing that switching back and forth between the reference product and the biosimilar causes no additional safety or efficacy risks to the patient.[12] To date, only 2 biosimilars have achieved an interchangeable designation from the FDA.[13]

Despite this multitude of variables, there is optimism that savings due to biosimilars will grow as more come to market. One study estimates biosimilars will reduce spending on their reference products by $42 billion between 2022 and 2026.[14] However, this landscape is constantly evolving.

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Are biosimilars the best choice?

While biosimilars may help reduce prices in the aggregate, this may not always be the case at an individual drug level for employers and employees.

"Biosimilars add value by helping lower costs through competition," says Susan Maddux, chief pharmacy officer at UnitedHealthcare. "As more biosimilars launch, especially those used to treat chronic conditions, there will be more opportunities to impact a broader patient population."

UnitedHealthcare offers management strategies that support better employee health at the lowest net cost. Each innovator and its biosimilar(s) are evaluated1 by 1; when it's financially supportable, we prefer or cover the biosimilar. Biosimilars are preferred over innovators that treat select cancers, inflammatory conditions and anemia.

Employers save **up to 60%** with UnitedHealthcare biosimilar management strategies.[15]

Biosimilars are available and preferred for:

Neupogen® – Cancer support
Remicade® – Inflammatory
Epogen/Procrit® – Anemia
Neulasta® – Cancer support
Avastin® – Cancer
Herceptin® – Cancer
Rituxan® – Cancer

Contact your UnitedHealthcare representative for more information

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[15] Average savings is 41%. UnitedHealthcare 2020 commercial book of business data. Savings may vary.