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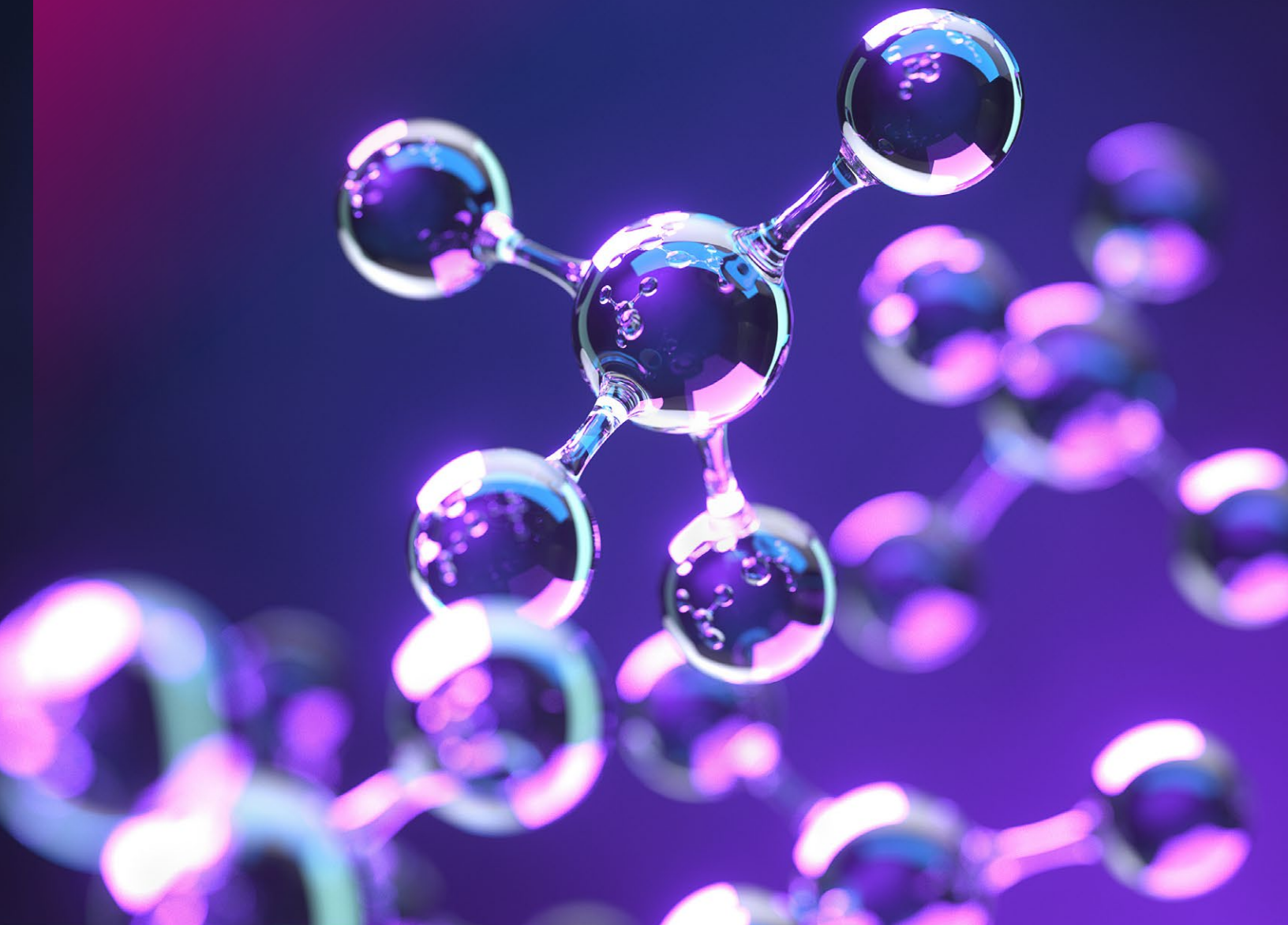
The landscape of available biosimilars



Biosimilars have the potential to deliver significant cost savings across healthcare.

Since March 2015, there have been 40 approvals by the Food and Drug Administration (FDA) for biosimilars for use in the United States and 25 launched as of December 2022.[1] (Note: It is expected that in early July 2023, there will be 41 biosimilar approvals and 37 launches in the U.S. market.) The approvals have led to a market shift for payers, specialty providers, and their patients. The potential biosimilars have in increasing access to life-changing therapies is tremendous. And with dozens of biosimilars awaiting approval,[2] patients will have even more options for promising treatments for cancer, autoimmune conditions like rheumatoid arthritis or inflammatory bowel disease, and diabetes.

What is a biosimilar?

A biosimilar is a biologic that is highly similar to another biologic that's already FDA-approved, which is known as a reference product. Biosimilars have no clinically meaningful differences from their reference product in terms of safety, purity, and potency.[3]

Biologics or biosimilars are typically delivered in a healthcare setting, often as an infusion or injectable.

The differences between generics and biosimilars

Biosimilars are not generics. Generics are exact copies of synthetic pharmaceuticals, and the active ingredients must be the same as a brand name drug. Biosimilars are copies of biologics, which are medications made with living cells. They can have slight differences in clinically inactive components. The important thing to remember is that there is no difference in how a biosimilar and its reference product treat patient conditions.[4]

According to the IQVIA Institute's Report on Biosimilars in the United States 2020-2024, the availability and use of biosimilars have accelerated and are on track to reduce drug costs by $100 billion over the next five years.[5]

Those numbers on cost reduction are dependent on the uptake of approved biosimilars through all sites of care, including community practices. And as more biosimilars are approved and prescribed, patients will have more affordable options to access care, and the reduction in overall drug costs in the United States should be realized.

Approved biosimilars

Approved biosimilars (3/15-12/22) found at: www.fda.gov/drugs/biosimilars/biosimilar-product-information

Biosimilar name	Approval date	Reference product
Idacio (adalimumab-aacf)	12/2022	Humira (adalimumab)
Vegzelma (bevacizumab-adcd)	09/2022	Avastin (bevacizumab)
Stimufend (pegfilgrastim-fpgk)	09/2022	Neulasta (pegfilgrastim)
Cimerli (ranibizumab-eqrn)	08/2022	Lucentis (ranibizumab)
Fylnetra (pegfilgrastim-pbbk)	05/2022	Neulasta (pegfilgrastim)
Alymsys (bevacizumab-maly)	04/2022	Avastin (bevacizumab)
Releuko (filgrastim-ayow)	02/2022	Neupogen (filgrastim)
Yusimry (adalimumab-aqvh)	12/2021	Humira (adalimumab)
Rezvoglar (insulin glargine-aglr)	12/2021	Lantus (insulin glargine)
Byooviz (ranibizumab-nuna)	09/2021	Lucentis (ranibizumab)
Semglee (insulin glargine-yfgn)	07/2021	Lantus (Insulin glargine)
Riabni (rituximab-arrx)	12/2020	Rituxan (rituximab)
Hulio (adalimumab-fkjp)	07/2020	Humira (adalimumab)
Nyvepria (pegfilgrastim-apgf)	06/2020	Neulasta (pegfilgrastim)
Avsola (infliximab-axxq)	12/2019	Remicade (infliximab)
Abrilada (adalimumab-afzb)	11/2019	Humira (adalimumab)
Ziextenzo (pegfilgrastim-bmez)	11/2019	Neulasta (pegfilgrastim)
Hadlima (adalimumab-bwwd)	07/2019	Humira (adalimumab)
Ruxience (rituximab-pvvr)	07/2019	Rituxan (rituximab)
Zirabev (bevacizumab-bvzr)	06/2019	Avastin (bevacizumab)

Biosimilar name	Approval date	Reference product
Kanjinti (trastuzumab-anns)	06/2019	Herceptin (trastuzumab)
Eticovo (etanercept-ykro)	04/2019	Enbrel (etanercept)
Trazimera (trastuzumab-qyyp)	03/2019	Herceptin (trastuzumab)
Ontruzant (trastuzumab-dttb)	01/2019	Herceptin (trastuzumab)
Herzuma (trastuzumab-pkrb)	12/2018	Herceptin (trastuzumab)
Truxima (rituximab-abbs)	11/2018	Rituxan (rituximab)
Udenyca (pegfilgrastim-cbqv)	11/2018	Neulasta (pegfilgrastim)
Hyrimoz (adalimumab-adaz)	10/2018	Humira (adalimumab)
Nivestym (filgrastim-aafi)	07/2018	Neupogen (filgrastim)
Fulphila (pegfilgrastim-jmdb)	06/2018	Neluasta (pegfilgrastim)
Retacrit (epoetin alfa-epbx)	05/2018	Epogen (epoetin-alfa)
Ixifi (infliximab-qbtx)	12/2017	Remicade (infliximab)
Ogivri (trastuzumab-dkst)	12/2017	Herceptin (trastuzumab)
Mvasi (bevacizumab-awwb)	09/2017	Avastin (bevacizumab)
Cyltezo (adalimumab-adbm)	08/2017	Humira (adalimumab)
Renflexis (infliximab-abda)	05/2017	Remicade (infliximab)
Amjevita (adalimumab-atto)	09/2016	Humira (adalimumab)
Erelzi (etanercept-szzs)	08/2016	Enbrel (etanercept)
Inflectra (infliximab-dyyb)	04/2016	Remicade (infliximab)
Zarxio (filgrastim-sndz)	03/2015	Neupogen (filgrastim)

The role of the payer in biosimilar access

Addressing the high costs of specialty drugs is one of the core tenets for the Centers for Medicare & Medicaid Services (CMS), which is why the focus of many of their policies around reimbursement have concentrated on value-based payments that are focused on clinical outcomes.

Private payers are following the same path. Some of the key considerations include[6]:

Clinical efficacy: Considering patient outcomes and clinically meaningful differences between products, as well as a known occurrence and predictability of adverse events

Supplier reliability and manufacturing capability: Ensuring the product will be available consistently and the manufacturer has a history of experience and reliance

Cost savings: For both the payer and patient, understanding that there may be associated government intervention, particularly Medicare Part B reimbursement, rebates, and copay assistance programs

Patient adherence: Addressing whether patients would be willing to continue treatment if prices were more affordable and if side effects were manageable

While the FDA launched a curriculum toolkit for healthcare providers,[7] payer policies need to mimic the mindset that with access to these cost-saving treatments, expanding the market and increasing competition would help to further lower costs and potential reimbursements for therapies using biosimilars.[8]

Xcenda completed a survey on managed care trends in September 2022; the survey found that between commercial and government payers, almost all of the organizations reported currently having policies in place that encourage the use of biosimilars.[9] The survey participants also noted that prior authorization and step edits are the formulary management techniques used most frequently to encourage the use of preferred products.[9]

Payers will continue to look for comparable clinical outcomes when utilizing the most cost-efficient biosimilar. Access to data from specialty practices, government agencies, manufacturers, and pharmacy benefit managers will only help to provide patients with effective, lower-cost alternatives.

In the Xcenda survey, participants noted that cost savings and interchangeability are the top factors to drive adoption of biosimilars within organizations, with cost savings being the overwhelming response. Having interchangeability data available (along with real-world evidence) is expected to have a significant impact on adoption, with payers using manufacturers, contacts, materials, and published reports as their top evidence sources in review of biosimilars.[9]

Other potential meaningful changes for reimbursement

Several manufacturers (members of the Biosimilars Forum) presented ideas for potential changes to increase savings with the use of biosimilars. Some of those proposed changes include[10]:

- Reducing Medicare costs, potentially saving up to $5.2B in taxpayer dollars over ten years and a potential for $3.3B in patient out-of-pocket costs with the increased use of biosimilars
- Implementing a shared savings model whereby Medicare savings associated with prescribing a biosimilar, compared to a reference biologic, would be shared with physicians, incentivizing their use (H.R. 2869 and S. 1427)
- Considering legislation that would require the addition of a new quality measure in the Medicare Advantage (MA) and Part D Star Rating system to include assessments of plan benefit and formulary design in encouraging patient access to biosimilars. Patients will learn which MA and Part D plans offer access to lower-cost biosimilars as they select their plans (H.R. 2855)
- Considering a Coverage Gap Discount Program where biosimilars are classified as "applicable drugs" in the program, allowing for a level playing field on Part D formularies with the brand

Impact of the Inflation Reduction Act

The Inflation Reduction Act (IRA) will have both positive and negative impacts on the use of biosimilars. The IRA provides a temporary incentive for increased Medicare reimbursement (see page 7 for specifics). Negatively, a biologic's selection for price negotiation can be delayed if the Secretary of the Department of Health and Human Services (HHS) determines there is a "high likelihood" a biosimilar will be licensed and marketed within the two years after which a drug is eligible for negotiation.

For example, if launched outside of the two-year window, a biosimilar would compete against the reference product that has already been affected by price competition. The biosimilar will have to launch at a deeper discount than originally planned, so the impact to manufacturers on production of the biosimilar may not make financial sense.

Biosimilars will be subject to the same rebate penalties as reference products, which means manufacturers will have to pay a rebate to the federal government if prices increase at a rate greater than the rate of inflation.[11]

Reimbursement for providers – a temporary incentive

While payers continue to review data on clinical outcomes, providers have an incentive to offer biosimilars to their patients. CMS has implemented a temporary payment increase for qualifying biosimilars under Medicare Part B. Section 11403 of the IRA includes a temporary increase of 2.0 percent in Medicare Part B payment for certain biosimilars. Beginning on October 1, 2022, existing qualifying biosimilars are being paid based on average sales price (ASP) plus eight percent of the reference biological product's ASP, up from six percent in previous years. The temporary payment increase remains in effect for five years on biosimilars that are less expensive than the reference product.[12]

The policy change with the temporary add-on payment for providers is to "increase access to biosimilars, as well as to encourage competition between biosimilars and reference biological products, which may, over time, lower drug costs and lead to savings to beneficiaries and Medicare."[12] This change was successfully passed under H.R. 2815.

What drives reimbursement challenges with biosimilars for payers?

Formulary management is the biggest challenge to the adoption of biosimilars. Several respondents to the Xcenda survey[9] noted responses like:

> Most pharmacy products have rebates on brands, there were no rebates for most of medical drugs.

> Copay assistance that has been available for reference products and that may not be available for biosims. This will slow patient adoption.

> Plan designs that do not incentivize biosims for patients.

While practices may understand the implications for patients who are prescribed a biosimilar, there may be different requirements for billing. Educating staff with necessary documentation and payers with data on clinical outcomes will support prior authorization decisions and reimbursements for the use of a biosimilar.[13]

Complexity with interchangeability

What is interchangeability?

Interchangeable therapies have been available in the European Union (EU) for several years. The European Medicines Agency and the Heads of Medicines Agencies recently noted that "Interchangeability refers to the possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect."[14] The agencies' scientific rationale is based on their review and monitoring of safety on numerous approved biosimilars over the past 15 years.

It wasn't until July 2021 that the first interchangeable biosimilar for insulin was approved by the FDA,[15] yet the FDA notes that an approval for a biosimilar is not sufficient for interchangeability designation.[16]

The FDA noted (in a draft guidance) that to support a demonstration of interchangeability, the data and information submitted must show that a proposed interchangeable product is biosimilar to the reference product and that it can be expected to produce the same clinical results as the reference product in any given patient.[17]

Interchangeability is not automatic. The FDA will not approve a product as interchangeable unless a biopharmaceutical company specifically seeks the interchangeability determination. For that determination, the agency requires additional data and information to support the designation, often with a "switching study" – a study that analyzes data for safety and efficacy when a patient switches from one biosimilar to another.[16]

Once approved, the "interchangeable" designation allows a biosimilar to be substituted for its reference product at the pharmacy, without additional approvals from the prescribing physician, state law permitting.

The FDA's rigorous process for interchangeability designation is intended to reassure providers and patients that "for products that will be administered more than once, the data and information must show that switching a patient back and forth between the reference product and the proposed interchangeable product presents no greater risk to the patient in terms of safety or diminished efficacy when compared to treating them with the reference product continuously."[17]

What is the value of interchangeability?

"If every adalimumab biosimilar had an interchangeability designation, the United States could save additional $765 million annually, according to calculations from three biosimilar experts."

The brand for adalimumab (Humira) generated more than $15 billion in 2021. Experts investigated that if only 63% of the brand prescriptions were substituted (as a lack of interchangeability could lead to abandonment), it would result in a differential of approximately $765 million in economic value of interchangeability.[18]

Clinical confidence in interchangeability

FDA guidance on interchangeability shows providers that there is little reason to expect altered pharmacokinetics, heightened immunogenicity response, increased safety risk, or improved or diminished efficacy in patients who switch back and forth from a reference product to the corresponding biosimilar[20]; these outcomes would hopefully increase providers' confidence in interchangeability with their decisions.

In the Xcenda study, providers ranked real-world evidence on switching and effectiveness as some of the best solutions to overcome barriers to adoption and that interchangeability data will most impact adoption of specific pharmacy benefit biosimilars. In addition, those who participated in the survey do not expect to manage biosimilars differently between those under the pharmacy benefit versus those under the medical benefit.[9]

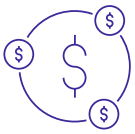
Guidance continues to evolve for interchangeability, with the FDA creating research pilot programs to look at the capability of analytical data and potentially developing alternatives or reducing the size of studies involving human subjects (under the Biosimilar User Fee Act III Regulatory Research Pilot Program).[21]

How is HHS preparing to help improve access to biosimilar therapy, particularly around interchangeability?

As part of a proposed rule released by CMS late in 2022, Medicare Part D plans would, beginning in 2024, be permitted to substitute interchangeable biosimilars as soon as they are available, without waiting for the beginning of the next benefit year, under their Improving Drug Affordability and Access in Part D.[22]

"When it approves a biosimilar, the FDA certifies that it is as safe and effective as the original biologic and that it has been rigorously evaluated. But the FDA does not give it automatic interchangeable status, meaning pharmacists would be free to substitute the biosimilar with a reference product without informing the physician."[9]

What are the challenges faced by providers with adoption of biosimilars?



Pricing structure for biosimilars

In simple terms, biosimilars offer cost savings for patients and, potentially, a greater chance of more affordable access to treatment and greater adherence. The competitive pricing environment based on the increased number of approved biosimilars and potential for interchangeability over the next few months and years should give providers the chance to offer increased options for patients.[23]

To date, almost 80 percent of the biosimilars being developed were from smaller biopharmaceutical companies, many of which do not have the needed resources to adequately market their products. Part of that marketing and distribution model, where the providers are the managers, leads to a significant difference in uptake.[24]

Payers and pharmacy benefit managers

With formulary management, it is expected that payers and pharmacy benefit managers will drive utilization to the lowest net cost. As noted in the Xcenda survey, providers are looking to manufacturer contacts and materials, as well as published literature, as sources of evidence.[9]

It is imperative the providers are diligent in their work with payers to ensure that patients are getting the authorized product at the point of administration, especially as formularies tend to be updated at least annually.

Education for providers and payers

Biopharmaceutical companies are tasked with investing in education for both providers and payers to increase adoption. Clinicians need to have confidence in the effectiveness and safety of specific products; they also need to have companies address those knowledge gaps, including an understanding around the science behind biosimilars and interchangeability.[24]

Summary

Biosimilars have the potential to deliver significant cost savings across healthcare to all stakeholders. Patients can benefit with more affordable treatment options, and with expanded access to all patients, better overall health outcomes could be generated.

As more biosimilars are approved, additional clinical outcomes data are made available, and manufacturers sharpen their wrap-around services for patients, providers, and pharmacies; thus the projected savings will reach into the billions.

Boosting the adoption of biosimilars rests on each stakeholder – manufacturers to provide additional clinical education and services for providers and patients (including patient assistance programs), payers to review clinical data and add more biosimilars to their formularies, and patients to understand that biosimilars offer them more options for treatment.

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