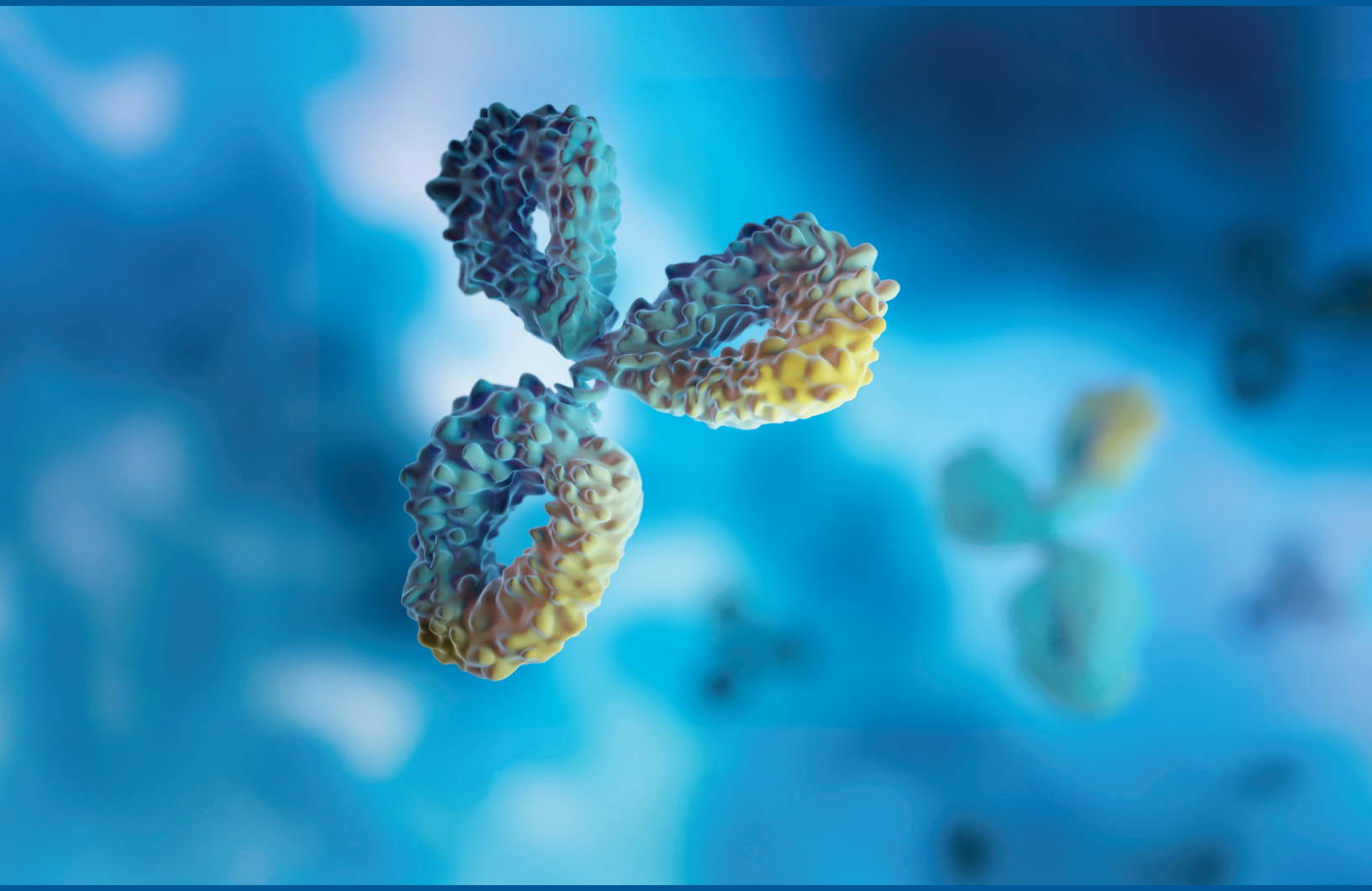
Alosa Health

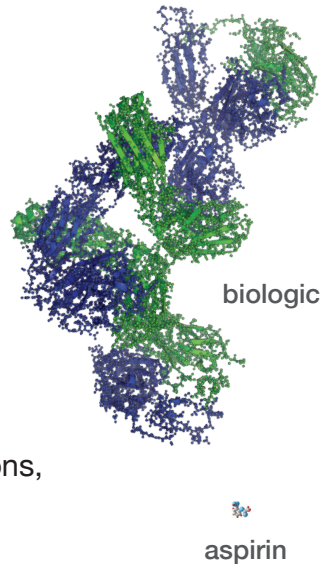
Bringing unbiased evidence to clinical care

Biosimilars in clinical practice

A non-inflammatory approach to the most recent evidence and regulations



Biologics have transformed care for many conditions



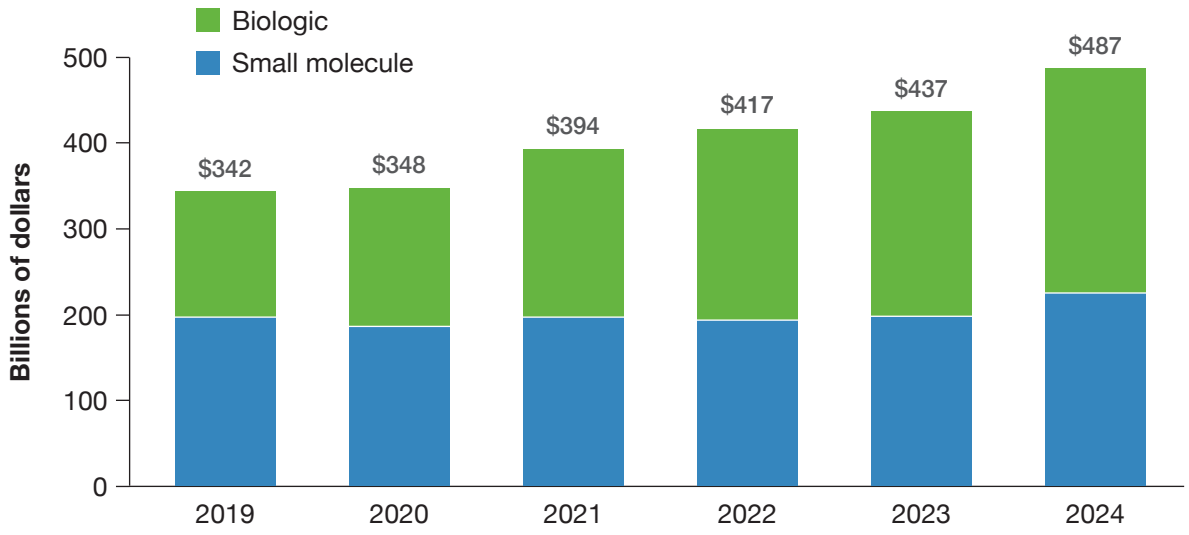
Biologics are large, complex molecules usually derived from living cells.

- Examples include monoclonal antibodies, cellular therapies (e.g., CAR-T), gene therapies, vaccines, and products derived from human blood or plasma (e.g., albumin).
- They have proven extremely useful in treating a wide variety of conditions, including autoimmune diseases and cancer.
- Biologics are more difficult to manufacture than conventional **small-molecule medicines** with simple chemical structures, like aspirin.[1]

Biologics accounted for 1 in 3 new medications in 2024.[2]

Biologics account for half of U.S. prescription medication spending, even though they represent a small fraction of medications.

FIGURE 1. U.S. net spending on biologics grew by 80% between 2019 and 2024, while spending remained steady for small-molecule medicines (both brand name and generic).[3]



Biosimilars are less costly but are underused

The number of biosimilars available in the U.S. is rapidly increasing.[4]

The first biosimilar medication was approved by the U.S. Food and Drug Administration (FDA) in 2015. Since then, the FDA has approved more than **75 biosimilars** for **19 different products.**[5]

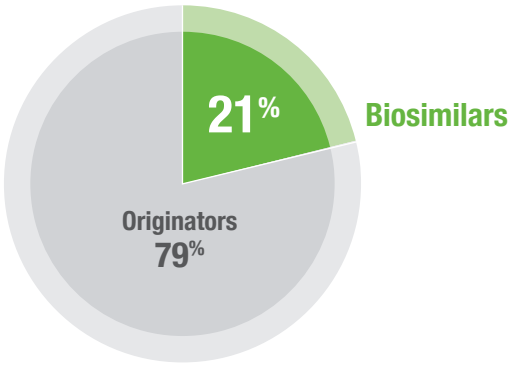
10 **Adalimumab** biosimilars (comparable to Humira)

8 **Ustekinumab** biosimilars (comparable to Stelara)

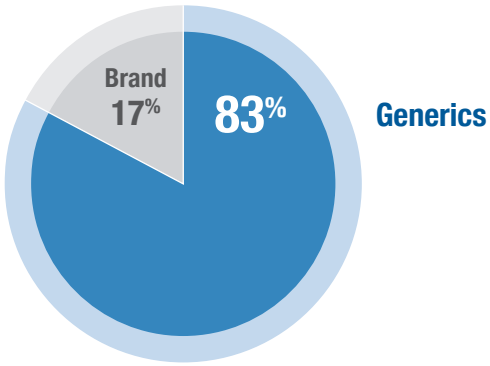
Other monoclonal antibody medications used to treat autoimmune and other diseases with biosimilar versions include eculizumab (Soliris), infliximab (Remicade), rituximab (Rituxan), and tocilizumab (Actemra).

So far, biosimilars have saved about $56 billion for U.S. patients and payers, including Medicaid and Medicare.[6]

Compared to generic medicines, biosimilars are underutilized.



Adalimumab biosimilars account for **1 in 5 prescriptions** within 2 years of becoming available.[6]



On average, **generic medications account for 4 in 5 prescriptions** within 2 years of becoming available.[7]

This may be changing. Because biosimilars can be so much less costly, some insurance plans have started preferring biosimilars and, in some cases, choosing to not cover the originator biologic.

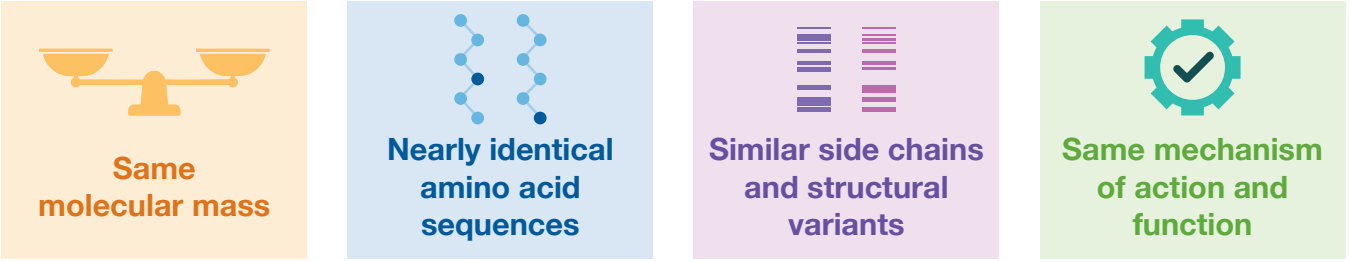
But how similar are biosimilars?

For biologics, there's no such thing as exactly the same.

- Complex manufacturing processes using living cells can cause **small variations between batches** of any biologic, including originator biologic products.
- The FDA requires **regular testing and tightly regulates this variation** to ensure that the differences do not change the safety or effectiveness of both original biologics and biosimilars.

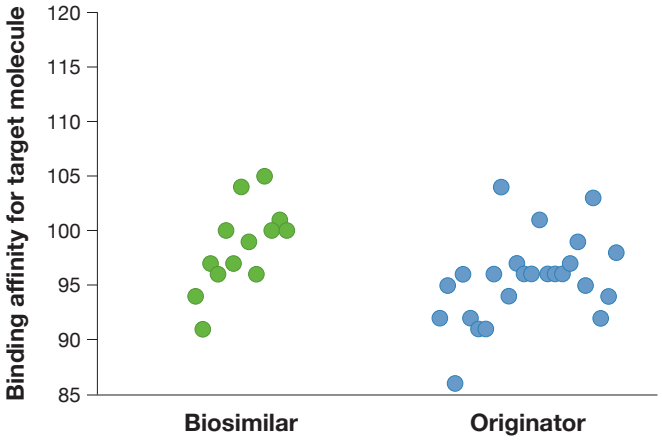
The FDA requires proof that biosimilars are "highly similar" to the original biologic medication.

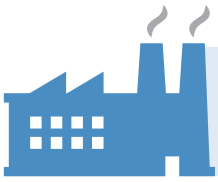
FIGURE 2. Rigorous testing is done to make sure that biosimilars do not show any meaningful differences from the reference biologic[8,9]:



Any differences between biosimilars and the original are no greater than the variation between different batches of the original biologic.

FIGURE 3. Variation in the biologic medication's activity measured by bioassay of a single batch is similar for the original biologic and biosimilars.[10]



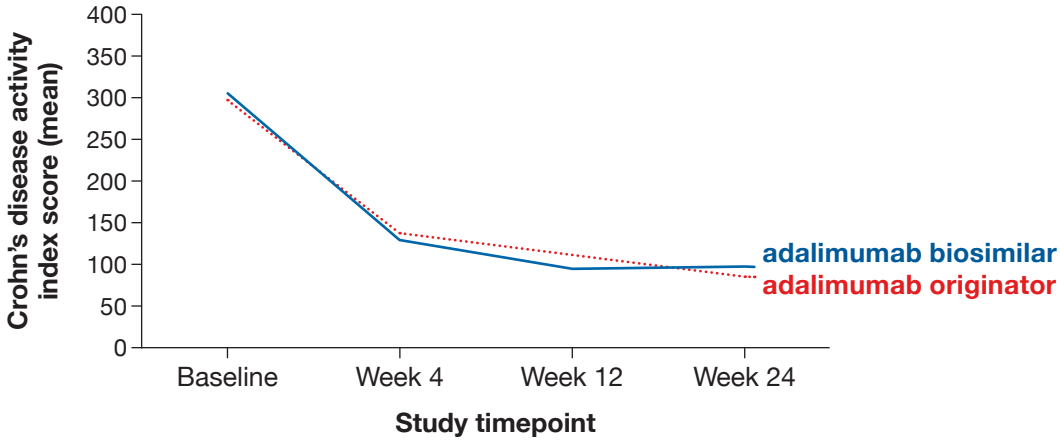


Many biosimilars are manufactured in the same facilities used to make other originator biologic medications.[11,12]

Biosimilars have “no clinically meaningful differences” from the original biologic

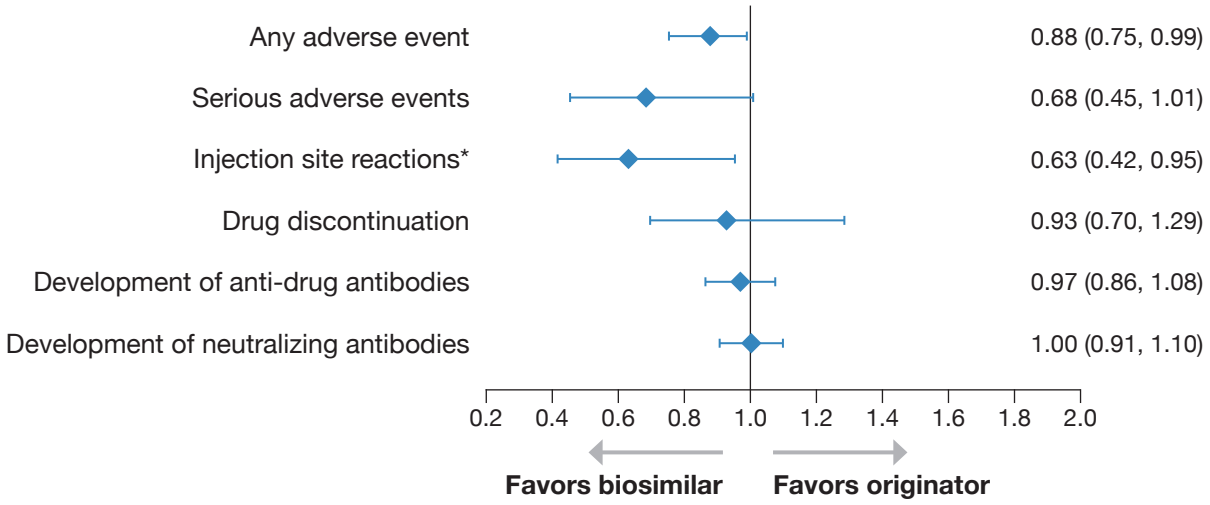
The effectiveness of biosimilars is usually tested in randomized, head-to-head trials, comparing them to the originator biologic.

FIGURE 4. Patients with Crohn’s disease treated with a biosimilar of adalimumab did just as well as those treated with the originator biologic medication.[13]



Biosimilars are also as safe as the original biologic.

FIGURE 5. In 11 clinical trials, patients taking adalimumab biosimilars for rheumatoid arthritis (RA) had similar or lower adverse events rates as those who took the originator biologic.[14]



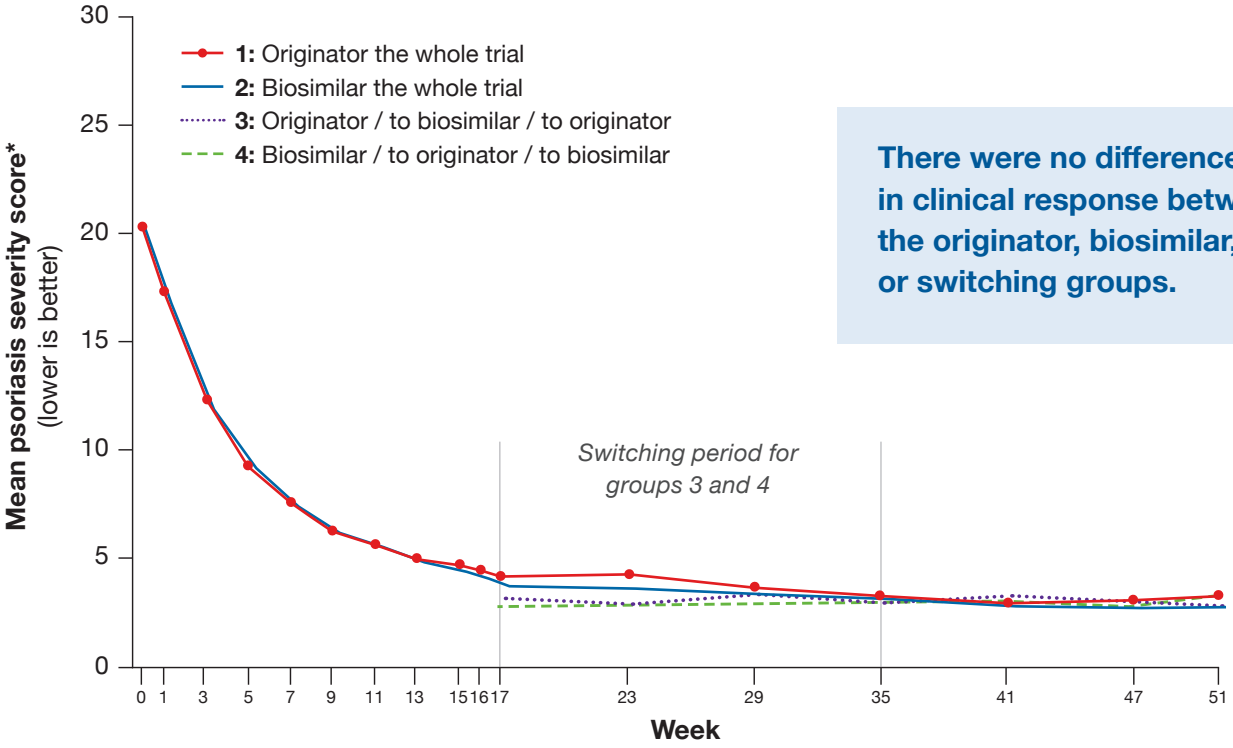
*This lower risk may be due to comparison of adalimumab biosimilar versions that were citrate-free to the originator version containing citrate.

Meta-analyses of over 15,000 patients with RA and psoriasis in randomized trials of TNF-alpha inhibitors **found biosimilars were as safe and effective as originators.**[14,15]

There is a great deal of evidence that switching from a biologic to a biosimilar is safe

Many biosimilar makers conduct randomized switching studies that show no concerns about safety and effectiveness.

FIGURE 6. In a double-blind trial, patients with psoriasis switched four times between originator and biosimilar adalimumab versus staying on their original biologic, with no difference in clinical response.[16]



There were no differences in clinical response between the originator, biosimilar, or switching groups.

*Disease severity was measured by the Psoriasis Area and Severity Index (PASI).

Similar biosimilar switching studies have been conducted in patients with rheumatoid arthritis and Crohn's disease.

Two studies (VOLTAIR-RA and VOLTAIR-CD) found that switching between a biosimilar and original adalimumab caused **no change in the proportion of patients responding to treatment,** as measured by the American College of Rheumatology improvement index (ACR20) or Crohn's Disease Activity Index (CDAI), respectively.[13,17]

The data from switching studies are clear

In a meta-analysis of over 5,200 patients across 21 different biosimilars, patients who switch from the originator biologic to a biosimilar showed **no differences in adverse events or effectiveness** compared to patients who stayed on the same version continuously.[18]

Switching to biosimilars does not increase anti-drug antibodies.

- Some patients develop antibodies to biologic medications that can diminish their effectiveness.
- Despite earlier theoretical concerns, clinical trials of thousands of patients switching to biosimilars have found **no increase in the development of anti-drug antibodies.**[18,19]

Unlike generics, switching to biosimilars may require additional steps by the prescribing clinician.

The FDA has separate standards for biosimilars to be deemed **"interchangeable" with the original biologic,** requiring clinical trials of patients switching between the originator and biosimilar. This designation is needed for patients to be switched to a biosimilar automatically by their pharmacy, as is commonly done for generic medicines. Rules for pharmacy generics and biosimilar substitution differ by state.[20]

All biosimilars must show that they are as safe as the original, even those without an "interchangeable" designation by the FDA.

In 2024, the **FDA announced that it would make it easier for biosimilars to be designated as interchangeable** by eliminating the requirement for switching studies.[21] This likely means that more biosimilars will have this designation going forward, which could make it easier for patients to switch.

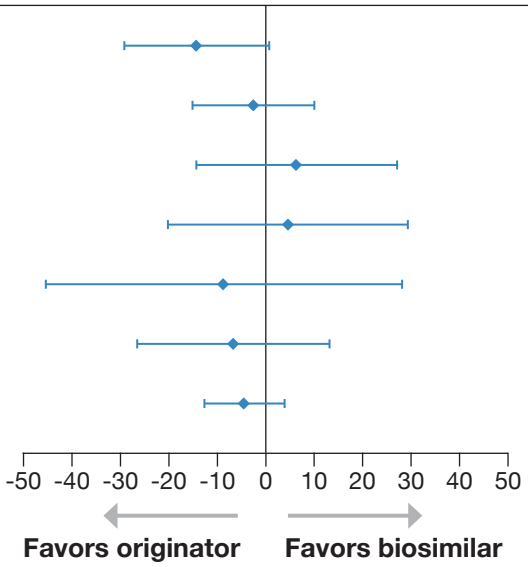
The safety of biosimilars is similar across many indications

- For biologics that are used to treat several different conditions, biosimilars are usually tested in clinical trials for just one or a few of these diagnoses.
- The FDA allows **extrapolation** of biosimilars' safety and effectiveness to other conditions, as long as:[22]
  - this is scientifically justified by the biologic's mechanism of action
  - there are no differences between the biosimilar and the reference biologic that could affect its safety and effectiveness across different indications

Switching studies have included patients with a variety of diagnoses.

FIGURE 7. In a trial of patients taking infliximab for different indications, those randomized to switch to a **biosimilar*** had the same rates of relapse as those who remained on the reference biologic.[23]

	1-year risk of relapse (%)	
	Originator n=202	**Biosimilar** n=206
Crohn's disease	21%	37%
Ulcerative colitis	9%	12%
Spondyloarthritis	40%	33%
Rheumatoid arthritis	37%	30%
Psoriatic arthritis	54%	62%
Psoriasis	6%	13%
Overall	**26%**	**30%**



***This biosimilar** was approved on the basis of trials in rheumatoid arthritis and ankylosing spondylitis.[23]

Professional societies have reviewed the evidence on biosimilars and endorse their use.

These recommendations apply to all FDA-approved biosimilar products.[24-26]

ACR American College of Rheumatology

aga American Gastroenterological Association

AAD American Academy of Dermatology Association

Practical points to consider

Patients' costs for biosimilars depend on their insurance.

Patients' out-of-pocket costs depend on their insurance coverage. In many cases, patients pay a **deductible** (100% of costs until they reach a certain amount of spending) or **coinsurance** (percent of medication cost), and in these cases patients may pay less if they use a lower-priced biosimilar medication.

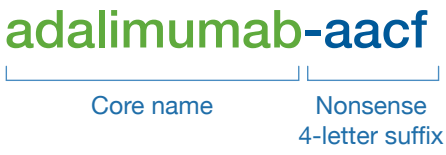
For patients who use manufacturer copay cards or assistance programs, they will need to check if similar programs are available from the biosimilar maker.

Patient administration may vary.

- **All biosimilars of adalimumab have a citrate-free version.**
  - Citrate-free formulations reduce injection site discomfort.[27] Originator adalimumab and all biosimilars also have citrate-free options.
  - For the originator adalimumab, the citrate-free version has a higher concentration (e.g., 40 mg in 0.4 mL) than the non-citrate-free version (e.g., 40 mg in 0.8 mL). This is not necessarily true for biosimilars; some have a lower concentration and are citrate-free.
- **Autoinjector devices may vary slightly** in their mechanism of use.

Biosimilar names can be confusing.

FDA-approved biologics include a 4-letter suffix at the end of the core name, to identify which manufacturer made the biologic.[28] An example:

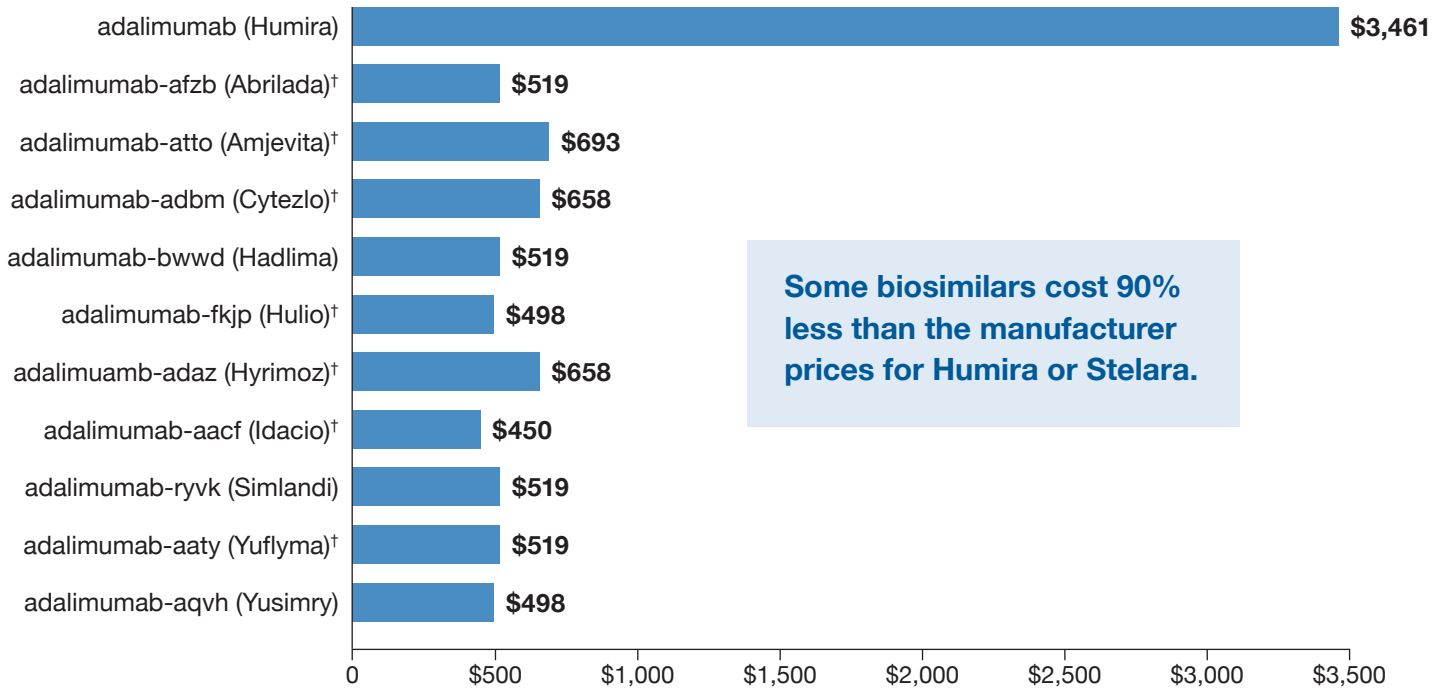


All new originator and biosimilars are assigned this 4-letter suffix, such as Skyrizi (risankizumab-rzaa), but biologics approved before 2017 do not have the suffix (e.g., Humira is adalimumab with no suffix). **Many biosimilars also have their own proprietary (or brand) names.**

Biosimilars are much less costly

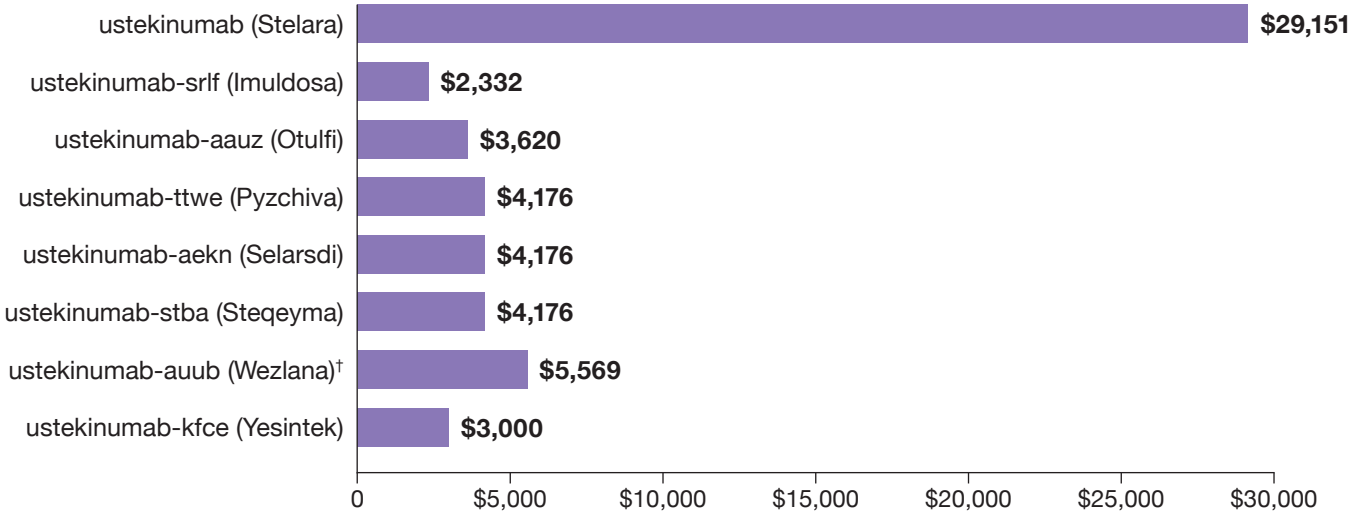
FIGURE 8. Wholesale acquisition costs* per treatment for originator biologic and its biosimilars.

Adalimumab 40 mg



Some biosimilars cost 90% less than the manufacturer prices for Humira or Stelara.

Ustekinumab 90 mg¥



*These prices are a guide; patient costs will be subject to copays, discounts, and other incentives. Current as of July 29, 2025.
†Product is also sold as a higher-priced version that presumably has confidential discounts.
¥The price for ustekinumab-hmny (Starjemza) was unavailable.

Key points

- **Biosimilars are lower-cost alternatives** to biologics that are increasingly available and, in some cases, preferred by insurance companies over the costlier originator biologics.
- **Biosimilars are "highly similar" to the original;** small structural variations between biosimilars and originators are similar to the variation expected between different batches of the original biologic.
- Rigorous testing including head-to-head clinical trials provides confidence that **biosimilars are as safe and effective as the original biologic.**
- There is ample evidence that **patients can be switched to biosimilars from biologics** without any safety concerns or diminished effectiveness.

See **www.AlosaHealth.org/Biosimilars** for information for patients on the safety and efficacy of biosimilars.

References:

(1) U.S. Food and Drug Administration. Biological Products Definitions. https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf. Accessed Sept 9, 2025. **(2)** Center for Drug Evaluation and Research. *Advancing Health Through Innovation: New Drug Therapy Approvals 2024.* Silver Spring, MD: U.S. Food and Drug Administration;2025. **(3)** IQVIA Institute for Human Data Science. *Understanding the Use of Medicines in the U.S. 2025: Evolving Standards of Care, Patient Access, and Spending.* April 2025. www.iqviainstitute.org. **(4)** Drugs@FDA: FDA-Approved Drugs. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed Sept 10, 2025. **(5)** U.S. Food and Drug Administration. Biosimilar Product Information. Sept 4, 2025; https://www.fda.gov/drugs/biosimilars/biosimilar-product-information. Accessed Sept 15, 2025. **(6)** Association for Accessible Medicines. *The U.S. Generic & Biosimilar Medicines Savings Report.* September 2025. **(7)** Rome BN, et al. *Value in Health.* 2021;24(6):804-811. **(8)** U.S. Food and Drug Administration. Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. 2015; https://www.fda.gov/regulatory-information/search-fda-guidance-documents/scientific-considerations-demonstrating-biosimilarity-reference-product. Accessed Aug 28, 2025. **(9)** U.S. Food and Drug Administration. Biosimilars Info Sheet. https://www.fda.gov/media/154915/download. Accessed Sept 22, 2025. **(10)** U.S. Food and Drug Administration. FDA Briefing Document. Oncologic Drug Advisory Committee. *ABP215, a proposed biosimilar to Avastin (bevacizumab) BLA 761028.* July 13, 2017; https://www.fda.gov/files/advisory%20committees/published/FDA-Briefing-Information-for-the-July-13--2017-Meeting-of-the-Oncologic-Drugs-Advisory-Committee-%28AM-Session%29.pdf. Accessed Sept 11, 2025. **(11)** Spencer D. 5 Top Pharma Manufacturers in Puerto Rico. September 26, 2019; https://pharmaboardroom.com/articles/5-top-pharma-manufacturers-in-puerto-rico. Accessed Sept 11, 2025. **(12)** U.S. Food and Drug Administration. BLA 761024: BLA Approval. September 23, 2016; https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2016/761024orig1s000ltr.pdf. **(13)** Hanauer S, et al. *Lancet Gastroenterol Hepatol.* 2021;6(10):816-825. **(14)** Ascef BdO, et al. *JAMA Netw Open.* 2023;6(5):e2315872. **(15)** Phan DB, et al. *JAMA Dermatol.* 2023;159(7):763-771. **(16)** Blauvelt A, et al. *Br J Dermatol.* 2018;179(3):623-631. **(17)** Cohen SB, et al. *Ann Rheum Dis.* 2018;77(6):914-921. **(18)** Herndon TM, et al. *PLoS One.* 2023;18(10):e0292231. **(19)** Cheng CA, et al. *Clin Pharmacol Ther.* 2023;114(6):1274-1284. **(20)** Sacks CA, et al. *JAMA Intern Med.* 2021;181(1):16-22. **(21)** U.S. Food and Drug Administration. Considerations in Demonstrating Interchangeability With a Reference Product: Update. June 20, 2024; https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-update. Accessed Sept 29, 2025. **(22)** U.S. Food and Drug Administration. Biosimilar Product Regulatory Review and Approval. https://www.fda.gov/files/drugs/published/Biosimilar-Product-Regulatory-Review-and-Approval.pdf. Accessed Sept 29, 2025. **(23)** Jørgensen KK, et al. *Lancet.* 2017;389(10086):2304-2316. **(24)** Fraenkel L, et al. *Arthritis Rheumatol.* 2021;73(7):1108-1123. **(25)** Menter A, et al. *J Am Acad Dermatol.* 2019;80(4):1029-1072. **(26)** Singh S, et al. *Gastroenterology.* 2024;167(7):1307-1343. **(27)** Nash P, et al. *Rheumatol Ther.* 2016;3(2):257-270. **(28)** U.S. Food and Drug Administration. Nonproprietary Naming of Biological Products: Guidance for Industry. January 2017; https://www.fda.gov/regulatory-information/search-fda-guidance-documents/nonproprietary-naming-biological-products-guidance-industry. Accessed Sept 11, 2025. **(29)** Samsung Bioepis. Biosimilar Market Report. 2025; https://m.samsungbioepis.com/upload/attach/SB+Biosimilar+Market+Report+Q3+2025.pdf. Accessed Sept 16, 2025.

About this publication

These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition. More detailed information on this topic is provided in a longer evidence document at AlosaHealth.org.

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