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Biosimilar interchangeability: evolving market and treatment landscape

Market Trend Summary

Yashu Malhotra, M.Pharm. | November 2024

Biosimilar Interchangeability

From regulation to acceptance: the journey to key regulatory changes in the U.S market

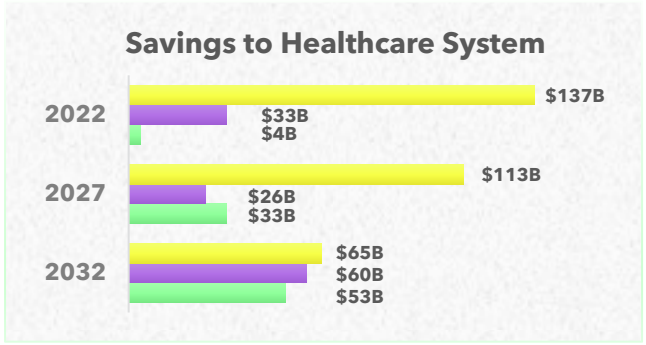
Background

The FDA defines an interchangeable biological product as a biosimilar to the reference product that produce the **same clinical result as the reference product** in any given patient and can be substituted for the reference product at the pharmacy, depending on state pharmacy laws.

The Biologics Price Competition & Innovation Act amended the Public Health Service Act in 2010 easing biosimilar approval via the new abbreviated 351(k) pathway. This pathway was updated in May 2019 to help companies achieve the "interchangeable" designation for their biosimilars by conducting switching studies and confirming similar efficacy and safety with the reference brand.

- However, to align with the policies used by other regulatory agencies, such as the EMA, the U.S. FDA, in its draft guidance published in June 2024, recommends considering biosimilar interchangeability upon approval, thereby eliminating the requirement for conducting switching studies.

Clarivate's latest biosimilars forecast model shows steady growth in the uptake of biosimilars, thereby reducing reference brand sales and saving **$53 billion** to the U.S. healthcare system.



*Note: The data on sales of the reference brand and biosimilars, and the consecutive savings, are taken from Clarivate **Biosimilars | Market Event & Forecast | G7**, published in September 2024.*

Key directives amending biosimilar interchangeability

- **Red Tape Elimination Act, July 2023**

  Originally introduced in November 2022, the act was updated to boost biosimilar competition and remove the need for switching studies. Its goal was to amend the federal code to deem all biosimilars as interchangeable upon approval and require the FDA to brief relevant committee heads if a switching study is mandated.

- **Medicare Advantage and Part D Final Rule 2025, April 2024**

  The CMS issued a final rule revising several Medicare programs and became the **first** to implement biosimilar interchangeability: CMS announced that starting in 2025, biosimilars can be substituted as part of regular formulary maintenance without needing prior approval. This process also allows Part D sponsors to make mid-year substitutions immediately.

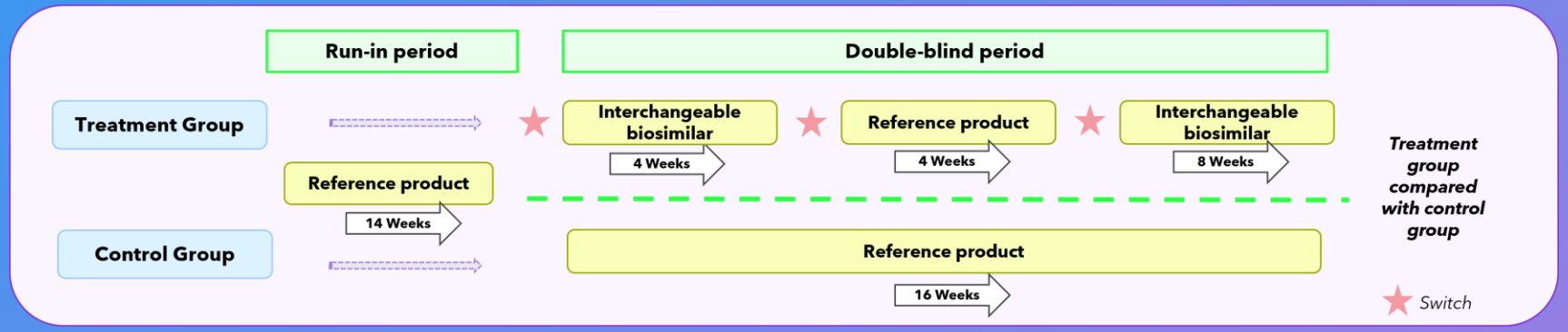
- **U.S. FDA Draft Guidance, June 2024**

  The FDA's new draft guidance titled "Considerations in Demonstrating Interchangeability with a Reference Product" **recommends** removing the switching study to demonstrate biosimilar interchangeability; instead, the FDA shall accept an assessment of comparative analytical and clinical data in the application or supplement meeting the switching standard outlined in section 351(k)(4)(B) of the PHS Act. Applicants with a pending BLA for a proposed biosimilar can submit an amendment with this assessment for interchangeability review.

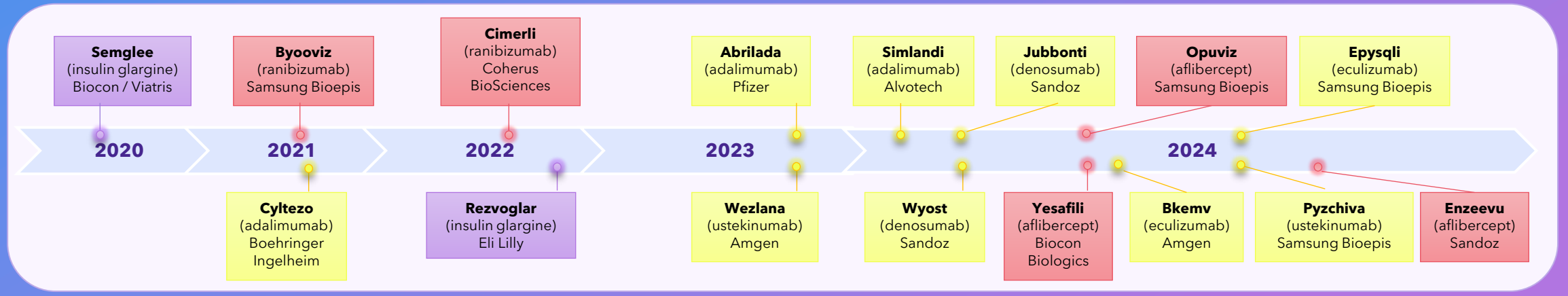
BLA: Biologics License Application; CMS: Centers for Medicare and Medicaid Services; EMA: European Medicines Agency; FDA: Food and Drug Administration

Interchangeable designation is unique to the U.S. market

A switching study to achieve interchangeable designation involves two phases: a **lead-in period** in which patients receive the reference product, followed by a **switching period** in which patients are randomly either switched to the biosimilar or continue with the reference product. The primary endpoints focus on pharmacokinetic parameters (**Cmax**, **Tmax**, **Ctrough**, and **AUCt**), while secondary endpoints assess **safety**, **efficacy**, and **immunogenicity**. The study results should demonstrate that switching does not reduce effectiveness or increase safety risks.



2024 saw a significant increase in approved interchangeable biosimilars



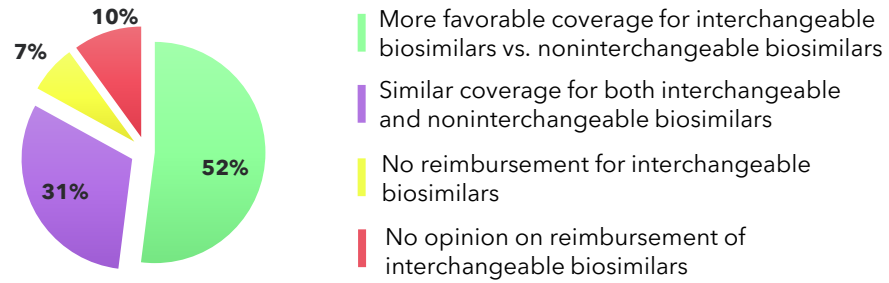
Key Takeaways

Lower costs and easy substitution will boost biosimilars, but regulatory and perception challenges remain.

Clarivate's 2024 primary market research indicates that key stakeholders (payers and physicians) are inclined to use and accept biosimilar interchangeability.

- Our research shows that more than half of surveyed U.S. payers (N = 60) foresee more favorable coverage for interchangeable biosimilars compared with noninterchangeable biosimilars.

Formulary coverage of interchangeable biosimilars by U.S. payers



*Note: The data on formulary coverage are taken from **Biosimilars | Access & Reimbursement | US | Payer Insights** by Clarivate, published in August 2024.*

- More than one-third of surveyed endocrinologists (N = 30) are willing to prescribe interchangeable biosimilars to their patients.
- **Lower cost to patients** and **lower net cost versus the brand** are the key factors for choosing interchangeable biosimilars over noninterchangeable biosimilars, according to surveyed physicians.

Strengths

Cost effective: Lower development costs compared with originator biologics, leading to potential healthcare savings.

Pharmacy-level substitution: Interchangeable biosimilars can be substituted at the pharmacy without the prescriber's intervention, like generics.

Regulatory confidence: Interchangeability designation by the FDA indicates high confidence in a biosimilar's safety and efficacy.

Shorter development timelines compared with originator biologics.

Weaknesses

Limited interchangeable approvals: Not all biosimilars are deemed interchangeable, limiting their use in some settings.

State law variability: State pharmacy laws can impact substitution of interchangeable biosimilars, causing usage inconsistencies.

Complex manufacturing: The complex and costly manufacturing limits the number of high-quality biosimilar producers.

Lack of trust: Some stakeholders, such as certain physicians and payers, may have low confidence in biosimilars.

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Opportunities

Enhanced market penetration: Interchangeable biosimilars can capture a larger market share owing to the ease of pharmacy substitution.

Increased trust and adoption: Successful use of interchangeable biosimilars will increase trust and lead to broader adoption.

Market competition: Interchangeable biosimilars foster competition, lowering prices for both biosimilars and original biologics.

Regulatory support: The FDA's aim to streamline the biosimilar approval process for inter-changeability may speed up market entry and create broader availability.

Threats

Regulatory challenges: Gaining interchangeability status is rigorous and costly, requiring extensive studies to ensure safe and effective switching.

Perceptions challenges: Some healthcare providers and patients may be skeptical about safety and efficacy of switching between biosimilars and reference products.

Competition from innovator companies: Unbranded biologics and authorized generics can compete with interchangeable biosimilars at low cost.

IP issues: Patent and intellectual property legal battles can pose significant obstacles.

Clarivate Coverage of Biosimilars

- **Biosimilars | Market Event & Forecast | G7**, assessing the **current events** and **market sizing for biosimilars** across six therapeutic areas: Oncology, Immunology, Endocrinology, Ophthalmology, Respiratory, and Nephrology.
- **Biosimilars | Current Treatment | US/EU**, offering comprehensive insights into **physicians' perceptions and attitudes** toward biosimilars across various specialties.
- **Biosimilars | Access & Reimbursement | Global**, analyzes the implications of **regulatory changes concerning biosimilars** in the **G7** and major **ex-G7** markets.
- **Biosimilars | Access & Reimbursement | US/EU**, provides in-depth knowledge of **payers' attitude toward biosimilars** and management of formularies.
- **Clarivate | Emerging Biosimilars | Global**, provides up-to-date **pipeline analysis** and **launch predictions** of biosimilars in the G7 markets.
- **Clarivate | Corporate Strategies | Global**, provides in-depth knowledge of **strategies** employed by reference brand and biosimilar developer companies to **defend the competition** in the market.
- **Clarivate | China-In Depth | China**, covers the landscape of biosimilars in the China market.

About the author

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