

THE PROMISE OF BIOSIMILARS



As more biosimilars reach the marketplace, Amgen expects to see significant savings driven by competition with originator products and between biosimilars.¹ At a time when healthcare costs are rising, potential cost savings from switching from originator biologics to biosimilars is projected to be between \$40-250 billion by 2025 in the U.S., and in Europe, cost savings are already estimated to be more than €10 billion.^{2,3}

WHAT ARE BIOLOGICS?

Biologics are produced in genetically engineered living cells.⁴

Biologic medicines include therapeutic proteins, which replace or augment beneficial human proteins, and monoclonal antibodies.⁴

WHAT ARE BIOSIMILARS?

Biosimilars are biologic medicines that are highly similar to existing licensed biologic products (reference products or originator biologics) with no clinically meaningful differences in terms of safety and efficacy.⁴

Reference product or originator biologic refers to the original biologic medicine, approved based on a full dossier of product-specific preclinical and clinical data, against which a biosimilar is evaluated.⁴

WHY BIOSIMILARS?



Biosimilars may provide patients, physicians, and payers a range of treatment options and a degree of flexibility of choice in therapies that they may not otherwise have.⁴



Over time, meaningful savings can be derived from head-to-head competition – with originator products and between biosimilar products.⁵



Savings could be used to improve the broader healthcare system by allowing more funds to support system-wide improvements in key areas, such as:

- Supporting the adoption of new innovative medicines and technologies;⁶
- Diagnosis and prevention;⁶ and
- Maintaining appropriate healthcare staffing levels.⁶

BIOSIMILARS ARE NOT GENERICS

Generics are small molecule drugs and exact copies of their originator products. They are manufactured using a wholly reproducible process.⁷

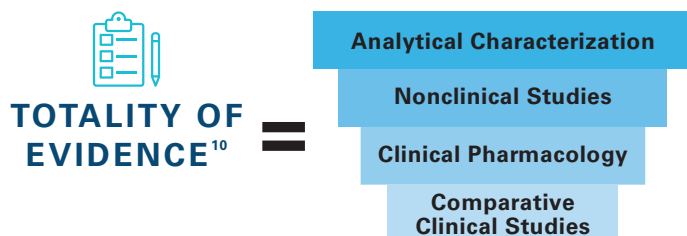
Biologics, including biosimilars, are more structurally complex than generics and can be up to 1,000 times their size.⁸

A biologic molecule is grown in living cells which leads to inherent variability; therefore, a biosimilar is highly similar, though not structurally identical, to an originator product.⁸

Because of these distinct properties, biologics are more complicated to develop than small molecule drugs, and the regulatory pathway for biosimilar approval contains additional scientifically appropriate steps compared with the pathway for generic drugs.⁸

DEMONSTRATING BIOSIMILARITY

For biosimilars, the totality of evidence to demonstrate biosimilarity is necessary to support licensure. No single study or endpoint should be considered “pivotal” in a biosimilar marketing application.⁹



A BIOSIMILAR DEVELOPMENT PROGRAM MUST...

...demonstrate that the biosimilar candidate is highly similar to and has no clinically meaningful differences from its originator product. Physicians and patients can trust that licensed biosimilars have been thoroughly tested and have a similar safety and efficacy profile as the originator product.¹⁰

MANUFACTURING & SAFETY MONITORING: A SENSITIVE MATTER

All biologics, including biosimilars, must be held to the same manufacturing quality standards to support confidence and help to drive uptake of biosimilars.



Biologics are produced through an intricate process, using living cells. Because the manufacturing process for the originator biologic is proprietary, biosimilar manufacturers must independently develop their own process to create a biosimilar candidate, which will lead to some inevitable differences between processes and products.^{8,11}

The manufacturing process involves a number of proprietary steps and conditions, including:

- Cell Line Creation or Expression
- Bioreactor Conditions
- Protein Extraction and Purification
- Formulation and Packaging

It is extremely important to carefully monitor and control all aspects of production.¹²

- A change to any of these manufacturing components can affect the complex structure of the biosimilar, potentially altering one or more critical quality attributes and impacting its biological function.¹²
- In addition, the manufacturing process can lead to variability in structural aspects of the product such as post-translational modifications.^{8,9} Post-translational modifications have the potential to impact the molecule's effects such as biologic activity, efficacy, safety, and immunogenicity.
- As part of its review, regulatory authorities evaluate the manufacturing process and strategy to control potential variations, to ensure manufacturers produce biological products with consistent clinical performance.⁸



The complexity of biologics demands post-approval safety monitoring for all biologics, including biosimilars, to detect post-approval safety signals and potential differences between and among biologics.⁸

THE POTENTIAL TO EXPAND TREATMENT OPTIONS

A European Commission report found that biosimilar competition provided additional treatment options.¹³



Biosimilars may promote competition resulting in savings that allow payers an opportunity to more effectively manage existing healthcare budgets.



Biosimilars have the potential to expand or increase access.¹³



For markets without a reference product available, biosimilars may provide biologic treatment options where none existed.

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