Important Facts
Health Care Professionals
Should Know
About Biosimilars
Biosimilars: Defining Characteristics

Biosimilars are highly similar versions of reference biologics, with no clinically meaningful differences in terms of safety, purity, and potency.¹

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Biologics, including biosimilars, are much more complex than small molecules²⁻⁵

While small molecule generics are chemically synthesized, biosimilars (and reference biologics) are created in living cells and require significant expertise and state-of-the-art technology.²,⁴

Development of Biosimilars

Extensive analytical, nonclinical, and clinical studies are part of development¹

The goal of biosimilar development is to demonstrate that there are no clinically meaningful differences between the proposed biosimilar and the reference biologic based on the totality of evidence.¹,⁶⁻⁸

Developmental Pathways

Standard Biologics

Clinical studies

Clinical pharmacology PK/PD

Nonclinical

Analytical

Biosimilars

Comparative clinical studies

Bioequivalence in healthy volunteers

Comparative clinical pharmacology PK/PD

Nonclinical

Analytical

PK, pharmacokinetics; PD, pharmacodynamics.

Biosimilar development does not independently reestablish the clinical benefit of the reference biologic.¹
Potential of Biosimilars

Projected growth in prescription drug spending creates a need for efficiencies within health care systems\(^9,10\)

As possible alternatives to existing biologics, biosimilars have the opportunity to address growing market demands and potentially expand access for patients with life-threatening and chronic diseases\(^{10-13}\):

- Biologics accounted for nearly half of approximately $85 billion spent on the top 15 drugs in 2015\(^{14}\)
- 7 of 15 highest expenditure drugs were biologics, accounting for $39.5 billion in spending in 2015\(^{14}\)
- Globally, biologic sales continue to grow as a proportion of total pharmaceutical sales including small molecules\(^{15}\)

Biosimilars may offer a number of potential benefits to patients, payers, and providers in addition to cost savings to the health care systems\(^{10-13}\)

- Offer a variety of therapeutic options
- Possible savings and efficiencies to the health care system
- Additional treatment choices at a lower cost to the health care system
- Increase access to biologics, which may lead to improved health outcomes overall
Biosimilars may be approved through an abbreviated licensure pathway if similarity with a reference biologic has been established.\textsuperscript{1}

**The development of biosimilars involves substantial investment of time and resources\textsuperscript{21}\n
A biosimilar may take up to 9 years and cost up to $135 million to develop, whereas development of a small molecule generic may take 2 years and cost $1-$4 million.\textsuperscript{22-24}\n
Although the FDA has indicated that interchangeability is possible, it has not provided detailed guidance on approval requirements.\textsuperscript{1}\n
**Interchangeability of a Biosimilar and a Reference Biologic\n
Biosimilarity must be established before designation of interchangeability. The risk, in terms of safety profile or diminished efficacy, of alternating or switching between the biosimilar and the reference biologic must not be greater than the risk of using the reference biologic without such alternation or switch.\textsuperscript{20}\n
Extrapolated Indications Are Not Automatic

Data collected for approval of a biosimilar in 1 indication may be extrapolated to 1 or more indications originally approved for the reference biologic.\(^1,2,5\)

- An extrapolated indication has not been directly studied in a comparative clinical trial with a reference biologic\(^6\).
- Comparative clinical data from the studied indication may help support extrapolation to other indications\(^1\).

![Biosimilars Pathway](image)

Image adapted from Sherman RE. Biosimilar biological products [biosimilar guidance webinar]. February 15, 2012.\(^{26}\)

Key aspects that may be considered for extrapolation\(^1\):

- Mechanism of action in each condition
- Pharmacokinetics and biodistribution
- Expected toxicities
- Other factors such as patient comorbidities and concomitant medications

Substitution of a Biosimilar for a Reference Biologic

Several states have enacted legislation on biologics and biosimilar substitution that may typically include the following\(^2,7,8\):

- Substitution is permitted only if the biosimilar has been designated as interchangeable
- Substitution may be prohibited if the prescriber has indicated a preference for the reference biologic
- The prescriber must be notified of any substitution made by the pharmacy