
EXPERT perspectives

Dear Colleague:

Patients with various inflammatory diseases, such as rheumatoid arthritis, psoriasis, and Crohn's disease, have achieved remarkable benefits when treated with biologics. However, the limited patient access to these medications, due to high costs, led to the creation of a regulatory pathway for the development of biosimilars. Several biosimilars have been approved for use in the United States. This CME-certified activity, *Navigating Biosimilars: Translating Evidence Into Clinical Practice* is intended to help health care providers navigate their way through the evolving world of biosimilars so that they can make informed choices about the use of these biologics in clinical practice.

**Patients may not take a biologic as prescribed**

- The rate of prescription abandonment increases as the out-of-pocket expenditure increases
- Out-of-pocket expenditures for biologics continue to increase

**The production of a biologic is complicated and leads to batch-to-batch variation**

- Biologics are large, complex molecules of variable structure, whereas small-molecule drugs have a simple, well-defined, relatively stable structure
- The manufacturing of a biologic results in a mixture of molecular structures with slight differences
- Manufacturers of biologics are required to demonstrate comparability of a new batch with previous batches

**A biosimilar is not a generic version of its reference product**

- Similarly, a biosimilar is not a biobetter of its reference product

**A biosimilar must be shown to be highly similar to its reference product in terms of safety, purity, and potency**

- The regulatory pathway for biosimilar development is a stepwise, scientifically rigorous process
- A totality-of-evidence approach is utilized to demonstrate biosimilarity
- No differences in safety or efficacy are expected between a biosimilar and its reference product

**Biosimilars are reverse engineered**

- Development begins with the utilization of information about the reference product that is in the public domain
- Extensive analytical and preclinical studies are utilized, more so than clinical studies
- A phase 3 clinical study is utilized to resolve any remaining uncertainty about the biosimilar being highly similar to its reference product

**A biosimilar may be approved for multiple indications by extrapolation**

- Biosimilar must be shown to be physicochemically, immunochemically, pharmacokinetically, and pharmacodynamically similar to the reference product
- Biosimilar must be shown to be efficacious and safe in one of the diseases for which the reference product is approved

# NAVIGATING BIOSIMILARS: TRANSLATING EVIDENCE INTO CLINICAL PRACTICE

**A biosimilar may be approved as interchangeable with its reference product**

- Interchangeability requires that the biosimilar meet a higher set of standards than those required for demonstrating biosimilarity
- Product approved as interchangeable may be substituted for the reference product by a pharmacist according to state law
- As of December 2017, no biosimilars have been approved as interchangeable

**Following the availability of biosimilars, early evidence indicates greater use of biologics**

- Lower cost of a biosimilar often leads to lower cost of its reference product
- Overall expenditures for biologics for which a biosimilar has been approved appear to be declining

**Pharmacovigilance plays an important role in biosimilar development**

- Pharmacovigilance plays a key role in determining the safety and efficacy of a biosimilar in the real world
- Registries, real-time data, accurate tracking, and health care provider communication and reporting, potentially play important roles in pharmacovigilance

**There are several suggestions providers may wish to keep in mind regarding biosimilars**

- Be aware of which biosimilar product is being prescribed, dispensed, and used
- Prescribe using the proper name or trade name with suffix
- Contribute to local pharmacovigilance efforts
- Monitor long-term safety

**Patients are in need of education about biosimilars**

- A survey of persons in the United States and Europe showed low awareness about biosimilars
- Persons who are aware of biosimilars are generally more comfortable regarding the safety and efficacy of biosimilars than persons who are not aware of biosimilars
- Affordability and access to treatment are major concerns of patients

This program has reviewed the stepwise, scientifically rigorous, totality-of-evidence process required for the development of biosimilars to demonstrate that there are no clinically meaningful differences in safety, purity, or potency between the biosimilar and its reference product. Other issues discussed include extrapolation, naming, and interchangeability, as well as suggestions for integrating biosimilars into clinical practice, including educating patients. With this greater understanding, we anticipate you are better able to navigate biosimilars and translate the evidence into your clinical practice.

Sincerely,

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