The Basic Facts About Biosimilars

October 2018

What Are Biosimilars?

Biosimilars Are Confirmed by the FDA to Be Safe and Effective Medicines

Biosimilars belong to the broader category of biologic drugs, also referred to as biologics. Biologics are produced in a living system, such as a microorganism, animal, or plant cell. Biologics are used to treat a growing range of diseases, including cancer, rheumatoid arthritis, diabetes, and anemia, among others. The United States (US) Food and Drug Administration (FDA) defines a biosimilar as "a biologic product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product."[1] Biosimilar manufacturers must establish that the product performance is clinically equivalent to their reference product in a rigorous evaluation process defined by the FDA.

Safety, Efficacy, and Quality

The FDA holds biosimilars to the same product and manufacturing quality standards as any biologic medicine. All biologics, including biosimilars, have slight batch-to-batch differences because they are made in complex living systems, but such differences are kept within an acceptable range as a condition of approval by the FDA. The FDA requires biosimilar manufacturers to establish that there are no clinically meaningful differences in the safety, purity, or potency of the product.[1] Like all drug products in the US, biosimilars are subject to the FDA's highly rigorous post-approval pharmacovigilance system that is designed to detect, understand, and prevent adverse effects or any other drug-related problem.[2] Pharmacovigilance and the monitoring and tracking of drug safety are important activities supporting the safety and efficacy of all drugs, including biosimilars.

Definitions

Biologic Product

Biologics can be "composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources: human, animal, or microorganism"[5]

Biosimilar Product

A biologic product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product[1]

Reference Product

An FDA-approved biologic product against which a biosimilar's safety, purity, and potency characteristics are compared[6]

Interchangeable Product

A biosimilar that has satisfied additional requirements, allowing it to be substituted at the pharmacy for a reference product without the involvement of the prescribing clinician.[7] Most biologics are typically dispensed by doctors in their offices

Transitioning

In addition to the use of biosimilars to treat new patients, transitioning from a reference biologic to a biosimilar product may become a common practice. Recent studies have suggested that there is no significant difference in safety or efficacy when transitioning from a reference product to its biosimilar or biosimilars.[3,4]

The Promise of Biosimilars[8,9]

- Expands treatment options and can potentially improve patient outcomes by increasing or providing earlier access to therapies
- Increases market competition, incentivizing manufacturers to lower prices, and results in increased cost savings to patients[8]
- Supports medication adherence by providing a clinically equivalent option at a potentially lower cost[9]
- Increases the number of suppliers of biologic medicines, helping ensure reliable patient access to these therapies while lessening the potential for drug shortages
- Provides system-wide cost savings

Interchangeability

"Interchangeability" is a regulatory designation that is meant to facilitate pharmacist substitution of a biosimilar without the involvement of the prescribing clinician. It is not a quality designation. In order to demonstrate that a product is interchangeable, a sponsor must submit to the FDA additional information evaluating the safety and efficacy of switching back and forth between the interchangeable product and its reference biologic.[7] In January 2017, the FDA issued draft guidance on the requirements for demonstrating interchangeability including study design recommendations.[10] As of October 2018, the FDA has not approved an interchangeable product.[7] At present, 45 states and Puerto Rico have passed legislation allowing for substitution at the pharmacy level if the biosimilar has been designated by the FDA as interchangeable.[11]

Misconceptions: Dispelling Myths About Biosimilars

MYTH	FACT
Myth #1: Biosimilars are very different from their reference biologics.	Biosimilars are highly similar versions of their reference biologics. They can only be approved by the FDA if it is demonstrated that there are no clinically meaningful differences from their reference biologics.
Myth #2: Biosimilars are not as safe as their reference biologics.	Biosimilars undergo rigorous testing. The FDA's approval process ensures that they are just as safe and effective as their reference biologics.
Myth #3: Biosimilars must be less effective than their reference biologics if they cost less.	Some estimate that biosimilars could cost 15% to 35% less than their reference biologics, but their lower cost does not reduce their safety or effectiveness. They cost less because of lower development cost, allowing the savings to be passed on to the healthcare system and improving patient access to these much-needed medications.
Myth #4: There isn't enough real-world evidence to really know that biosimilars are safe and effective.	Biosimilars are already commonly used throughout the world. In Europe alone, there have been more than 700 million patient-days of biosimilar use since 2006, with no pattern of negative health outcomes that was not already observed with reference biologics. US data on biosimilar use are currently being collected on an ongoing basis and, as in Europe, no adverse events have been reported to date related to biosimilars marketed in the US that were not already reported with their reference biologic.[4]

References

1. US Food and Drug Administration. What is a biosimilar? https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM585738.pdf. Accessed August 20, 2018. **2.** World Health Organization. Essential medicines and health products: pharmacovigilance. http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/. Accessed August 20, 2018. **3.** Moots R, Azevedo V, Coindreau JL, et al. Switching between reference biologics and biosimilars for the treatment of rheumatology, gastroenterology, and dermatology inflammatory conditions: considerations for the clinician. *Curr Rheumatol Rep*. 2017;19(6):37. **4.** Cohen HP, Blauvelt A, Rifkin R, et al. Switching reference medicines to biosimilars: a systemic literature review of clinical outcomes. *Drugs*. 2018;78:463-478 **5.** US Food and Drug Administration. What are biologics questions and answers. https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber/ucm133077.htm. Accessed August 20, 2018. **6.** US Food and Drug Administration. Biological product definitions. https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedHowDrugsare/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM581282.ppd. Accessed August 20, 2018. **7.** US Food and Drug Administration. Biosimilar and interchangeable products. https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ Biosimilars/ucm580419.htm. Accessed August 20, 2018. **8.** Puckrein G, Xu L, Ryan A, et al. Potential Medicare beneficiary out-of-pocket reductions through using biosimilar filgrastim-sndz over reference filgrastim: a simulation analysis. Poster Presented at: National Minority Quality Forum; Washington, D.C. **9.** AW Mulcahy, Predmore Z, Mattke S. The cost savings potential of biosimilar drugs in the United States. RAND Corporation. https://www.rand.org/pubs/perspectives/PE127.html. Accessed September 10, 2018. **10.** US Food and Drug Administration. Considerations in demonstrating interchangeability with a reference product. Draft guidance. January 2017. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537135.pdf. Accessed August 23, 2018. **11.** National Conference of State Legislatures. State laws and legislation related to biologic medications and substitution of biosimilars. December 1, 2017. http://www. ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-andsubstitution-of-biosimilars.aspx. Accessed August 20, 2018.

Endorsed by the Biosimilars FORUM