Focus On INTERCHANGEABLE BIOSIMILARS

This resource offers pharmacists a concise overview of recent developments in interchangeable biosimilar medications across various medical conditions. It equips pharmacists with fundamental information to educate patients and address inquiries regarding biosimilars as well as identify the availability of interchangeable biosimilar medications.

INTRODUCTION

In March 2010, the U.S. Congress enacted the Biologics Price Competition and Innovation Act (BPCIA), thereby establishing an approval pathway for biosimilar medications. BPCIA created a regulatory pathway for the review and approval of biosimilars and interchangeable biosimilars, which are lower-priced versions of reference biologics.[1] This legislation mirrors the Hatch-Waxman Amendments of 1984 that introduced the Abbreviated New Drug Application pathway for conventional small-molecule and generic drugs.[2] Both laws share patient-centric objectives, aiming to reduce health care costs through expanded patient access to lower-cost medications.

BIOLOGICS AND BIOSIMILARS

The global market for biologics has experienced significant growth. According to market research data from Precedence Research, the global market size was $367.17 billion in 2023 and is projected to reach $620.31 billion by 2032. North America currently holds the largest market share in this industry.[3]

According to a 2023 report from IQVIA, the U.S. biologics market has experienced an annual growth rate of 12.5% over the past 5 years, based on invoice prices, and now represents 46% of total pharmaceutical spending but only 2% of total prescriptions.[4] Biologics encompass a wide array of products, including vaccines, gene therapies, monoclonal antibodies, insulins, and more. Biosimilars are a subset of biologics that are highly similar to the reference biologic without any clinically meaningful difference. Table 1 provides a comparative overview of key aspects concerning their origin, clinical trial phases, regulatory approval pathways, postmarketing considerations, patentability, exclusivity, immunogenicity, route of administration, manufacturing process, development time, and development cost.

INTERCHANGEABLE BIOSIMILARS

Interchangeable biosimilars are a subset of biosimilars. A distinction is that interchangeable biosimilars can be substituted at pharmacies without consulting the prescriber. This practice, known as pharmacy-level substitution, is subject to state pharmacy laws and is applicable to both new and existing patients.[6] FDA may determine that an additional study, known as a switching study, may need to be completed for interchangeable biosimilars. However, FDA has emphasized that the interchangeable designation does not indicate interchangeable biosimilars are safer or more effective than biosimilars that are not approved as interchangeable.[7]

Health care teams and patients can anticipate that the interchangeable product is highly similar to the reference biologic with no clinically meaningful differences.

Table 1. Overview of reference biologics and biosimilars

	Reference biologics	Biosimilars
Origin	Living organism	
Clinical trial phases	Phase I–III	Phase III
Regulatory approval pathways	351 (a): Clinical Safety and Efficacy Study for Each Indication; Clinical Pharmacology; Animal; Analytical	351 (k): Comparative Clinical Studies, Clinical Pharmacology; Animal (optional); Analytical
Postmarketing	Phase IV, Pharmacovigilance	
Patentability	Patentable	Non-patentable
Exclusivity	12 years	None
Immunogenicity	Yes	
Route of administration	Intravenous or subcutaneous	
Manufacturing process	Complex, process-dependent	
Development time	8–10 years	7–8 years
Development cost	$800 million–$1 billion	$100–$250 million

Source: References 3–5.

Table 2. Comparison of biosimilars and interchangeable biosimilars

	Biosimilars	Interchangeable biosimilars
Indications	Generally, the same as the reference product	
Regulatory pathway	351 (k)	351 (k) + sBLA
Pharmacy-level substitution	No	Yes Exceptions: Alabama, Indiana, Puerto Rico, South Carolina, Washington

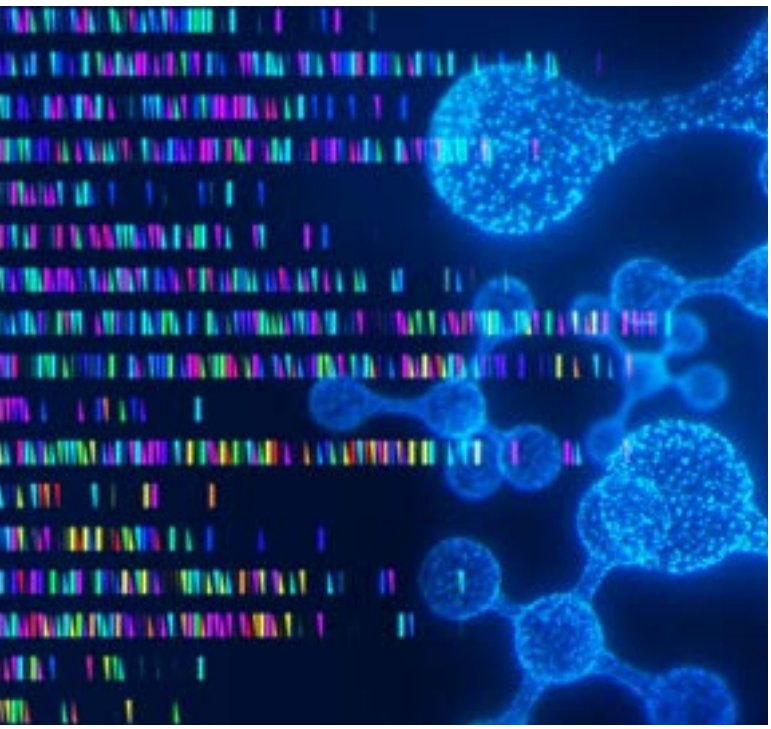
sBLA, supplemental Biologics License Application.
Source: References 8–10.

Table 2 provides a comparison between biosimilars and interchangeable biosimilars regarding their indications, regulatory pathways, and the availability of pharmacy-level substitution, should state legislation allow for it.

Pharmacy laws and practices vary across states, including a range of state-specific guidelines and laws for interchangeable biosimilars. To ensure compliance, health care professionals should refer to regulatory resources, such as *State Laws for Biosimilar Interchangeability*, for detailed information on state-by-state regulations.[10]

FORMULARY CONSIDERATIONS FOR PHARMACISTS AND PATIENTS

Insurance coverage and reimbursement for biologics and biosimilars are influenced by various factors, including health plan coverage and formulary and utilization management practices. Similar to other medications with formulary restrictions, the most effective method to confirm coverage or to address a product-specific utilization management issue, such as a prior authorization request, is to contact the insurance provider directly to obtain details regarding the specific plan. For patients covered by Medicare and Medicaid, consultation with the plan or the contracted claims



processor is recommended. For patients exploring other coverage options, such as "off-benefit" manufacturer copay cards and patient assistance programs, information related to product discounts and patient cost sharing is often available via the program websites and call center representatives.

CURRENTLY AVAILABLE INTERCHANGEABLE BIOSIMILARS IN THE UNITED STATES

As of March 1, 2024, FDA has approved 8 interchangeable biosimilars. Table 3 provides details about currently available interchangeable biosimilars, including the applicant, date approved, reference medication, reference medication sponsor, and indications.

Table 3. Interchangeable biosimilars in the United States as of March 1, 2024

Interchangeable biosimilar	Applicant	Date approved	Reference medication	Reference medication sponsor	Indications
Abrilada (adalimumab-afzb)	Pfizer	11/15/2019	Humira	AbbVie	RA, JIA, PA, AS, HS, CD, UC, PP, UV
Cyltezo (adalimumab-adbm)	Boehringer Ingelheim	8/25/2017	Humira	AbbVie	
Simlandi (adalimumab-ryvk)	Alvotech/ Teva	2/23/2024	Humira	AbbVie	
Byooviz (ranibizumab-nuna)	Biogen	9/17/2021	Lucentis	Genentech	Neovascular (wet) AMD, ME, DR, mCNV
Cimerli (ranibizumab-eqrn)	Coherus Biosciences	8/2/2022	Lucentis	Genentech	
Rezvoglar (insulin glargine-aglr)	Eli Lilly	12/17/2021	Lantus	Sanofi	DM, DK
Semglee (insulin glargine-yfgn)	Mylan	7/28/2021	Lantus	Sanofi	
Wezlana (ustekinumab-auub)	Amgen	10/31/2023	Stelara	Janssen Biotech	PP, CD, UC, PA

AMD, age-related macular degeneration; AS, ankylosing spondylitis; CD, Crohn's disease; DK, diabetic ketoacidosis; DM, diabetes mellitus; DR, diabetic retinopathy; HS, hidradenitis suppurativa; JIA, juvenile idiopathic arthritis; mCNV, myopic choroidal neovascularization; ME, macular edema; PA, psoriatic arthritis; PP, plaque psoriasis; RA, rheumatoid arthritis; UC, ulcerative colitis; UV, uveitis.

Source: References 11 and 23.

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CONVERSATION STARTERS FOR YOUR PATIENTS

Pharmacists play a pivotal role in educating patients about biosimilars. Here are some talking points to consider when discussing biosimilars with your patients.

1. **When were biosimilars first available in the United States?**
   BPCIA was signed into law by Congress in March 2010. This legislation established a regulatory pathway for the review and approval of biosimilars and interchangeable biosimilars, both of which are lower-priced versions of reference biologics.[1]

2. **What is the difference between biologics and biosimilars?**
   Biosimilars are highly similar to the reference biologics with no clinically meaningful differences. Health care teams and patients can expect biosimilars to have the same safety, effectiveness, and quality as that of their reference biologic.[1]

3. **What is the difference between biosimilars and interchangeable biosimilars?**
   Interchangeable biosimilars are biosimilars that pharmacists, subject to state law, may substitute without consulting the prescribing physician. There are no safety, efficacy, or quality differences between biosimilars and interchangeable biosimilars. Like biosimilars, interchangeable biosimilars have the same scientific characteristics, but pharmaceutical companies may choose to voluntarily submit additional data to permit pharmacy substitution without a physician intervention, similar to how a generic medication is handled. Following approval, these interchangeable biosimilars may be substituted at the pharmacy level, contingent upon the laws of the respective state.[8]

4. **Are interchangeable biosimilars better than biosimilars?**
   Interchangeable biosimilars do not indicate superiority to biosimilars with regard to safety, efficacy, or quality. The distinction between them is related to pharmacy practices rather than product quality.

5. **How can biosimilars benefit me?**
   Biosimilars offer patients enhanced access to essential medications, potentially alleviating financial burden. Moreover, they reduce administrative burdens for both health care teams and patients in managing medications.[12]

6. **Are biosimilars less expensive than biologics?**
   Yes, biosimilars are typically less expensive than their reference biologics. This cost difference is one of the key advantages of biosimilars, making them more accessible to patients and potentially reducing overall health care costs. However, the extent of cost savings can vary depending on factors such as market competition and individual insurance coverage.[12]

7. **Where can I find additional resources?**
   Additional resources on biologics and biosimilars can be found through FDA's *Center for Biologics Evaluation and Research*,[13] including its database known as the *Purple Book*.[11] Pharmaceutical companies specializing in biologics and biosimilars, as well as pharmacy associations such as the *American Pharmacists Association*,[14] offer numerous resources on their respective websites. These resources can provide valuable information on regulatory updates, safety considerations, and other relevant topics pertaining to biologics and biosimilars.

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