Case Study

Level 1: Foundational Concepts

Introduction

Biological products(biologics) have been used as therapies in the United States for several decades. They also represent a growing proportion of treatment options and costs in the U.S. health care market. Biologics treat a number of chronic illnesses like cancer, rheumatoid arthritis, and diabetes. In this case study, you will learn about the transition of insulins to the biologics regulatory framework, the impact of biosimilar and interchangeable insulin products on providers and patients, prescribing considerations, and other resources available to you as you learn about biosimilars.

Topics

- Variation in biological products
- Terms related to biological products
- Approval pathways
- Comparative studies to assess safety and efficacy
- Purple Book and naming
- Biosimilar labeling
- Addressing patient questions

As You Read...

- Are biologics and biosimilars exclusive to specialty health care?
- Are there differences in the ways that providers prescribe biosimilar products?
- Do pharmacies inform the provider or patient when there is a pharmacy-level substitution?
- What is the Purple Book?
- What resources are available to address patient questions?

Biosimilar and Interchangeable Biosimilar Insulin Products

A physician-in-training learns biosimilar insulin products are available in primary care and other everyday clinical settings

What Is a Biosimilar?

Richard is a physician in training completing his residency program in a rural community family practice. He asks his attending physician, Dr. Thompson, about the biosimilar products that patients in the practice use to manage their diabetes. "I have noticed that many of our patients take biosimilars. I talked to a patient this morning taking nilusni-bhrq."*

Dr. Thompson, recognizing a key teaching moment, decides to expand on biosimilar insulins and their importance in primary care. "You're right. Biologics and their corresponding biosimilar or interchangeable biosimilar products are used in several specialty practice areas, but as you've noticed, they are growing in availability in other areas. We prescribe biosimilar insulins for many of our patients, and sometimes patients in our practice receive interchangeable biosimilar insulins from their pharmacists, like they would generic medications. As more become available, we expect biosimilars and interchangeable biosimilars to be prescribed more routinely in primary care and dispensed at retail pharmacies."

Biosimilar and Interchangeable Insulins: Entering Mainstream Practices

"Recognizing that there have been changes to the regulation of insulin products, Dr. Thompson shares more of her knowledge on the topic of insulin biosimilars. "For historical reasons, insulin had been regulated under the chemical or small molecule drug approval pathway even though it is made from living cells like most biologics. Now insulin and other proteins are regulated under the biologics pathway because they meet the definition of a biological product."

Dr. Thompson continues, "This transition of insulins from being regulated under the drug framework to the biologics framework also created the opportunity for manufacturers to submit applications for biosimilar and interchangeable biosimilar insulin products such as nilusni-bhrq. These products are based on an existing or 'reference' insulin product. The very first interchangeable insulin biosimilar was approved in the summer of 2021. Since then, additional biosimilar and interchangeable insulin products have been approved and introduced to the market. The growing numbers of available products and the volume of patients seen in primary health settings who use these products is why it is an important topic for primary care practitioners to know about."

Richard considers this new information and asks, "What are the benefits to the

Biologics Price Competition and Innovation Act		
New Legislation Enacted 2010	Deemed to be a License Provision 2020	Interchangeability 2021
Established the abbreviated approval pathway for biosimilar biological products under the Public Health Service Act and the transition of insulin (and other proteins that had been regulated as drug products) to the biological product regulatory framework	Insulins (and other proteins that had been regulated as drug products) transitioned to the biological product regulatory framework	FDA approved the first interchangeable biosimilar insulin product

Figure 1: Descriptions of Reference Product, Biosimilar Product, and Interchangeable Product

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patient? Why should we consider prescribing a biosimilar or interchangeable biosimilar product such as nilusni-bhrq?"

"That's a great question," Dr. Thompson remarked. "If a reference product (or the brand name originator product that the biosimilar or interchangeable biosimilar insulin is compared to) does not work for a patient, there is no need to switch them to a biosimilar or interchangeable. This is because biosimilars have no clinically meaningful differences from the reference product. This means you can expect the same safety and effectiveness from the biosimilar over the course of treatment as you would the reference product. We may consider prescribing a biosimilar to a patient because of a change to the formulary, or we see a patient who is taking one product but whose insurance plan covers a different product."

Richard ponders the answer and considers the patient perspective. "Do your patients ever ask you about the biosimilar product and whether there are differences between the available biosimilar insulin products?" Dr. Thompson explains, "Yes, questions are common, especially since they may not have encountered a biosimilar or interchangeable biosimilar product before. As a clinician, we have an important role to educate patients and inform them about their options. Regarding biosimilars, we want patients to understand that nilusni-bhrq and other biosimilars have been rigorously assessed by FDA and determined to have no clinically meaningful differences from their reference products. Biosimilar and interchangeable biosimilar products are as safe and effective as their reference products. Like generic drugs, biosimilars may cost less because manufacturers rely on the FDA's finding that the reference products are safe and effective. This means that patients may have a wider number of products available to them—often with the potential for meaningful cost savings for them and our health system, more generally. The lower cost is not a reflection of the effectiveness or safety of biosimilars."

State Practicing Laws and Biological Product Substitution

"Do providers need to prescribe the biosimilar or are pharmacy-level substitutions allowed like the process with brand name and generic drugs?" Richard inquires. "The act of substitution is similar, but there are differences. Biosimilars generally have to be prescribed specifically, where interchangeable biosimilars may be substituted by the pharmacist without notifying the physician, depending on state laws," Dr. Thompson emphasizes. "In our state, for example, state law allows for pharmacists to substitute a prescription for a reference product with an interchangeable biosimilar product. That's why it is important for us to help educate patients because they may see a different name at the pharmacy than the brand reference product they're used to. If you practice in our state, this substitution can be made by the pharmacist without notifying the prescribing clinician. However, in other states, pharmacists may have to notify the provider before or afterwards, so it is important to understand the individual state practice laws related to interchangeable biosimilar products when discussing options with the patient.

"This is good information to have," Richard notes. Acknowledging that this topic will be increasingly important to his practice as a physician, Richard wants to know more about how he can stay informed about the approved biosimilars for insulin or other use cases. "Where can I find out more about biosimilars as more products are approved?"

"Another great question! The FDA's Purple Book Database of Licensed Biological Products is the source for facts on all approved insulins, including biosimilar and interchangeable biosimilars. Also, keep in mind that not all biosimilars are interchangeable because companies must specifically apply for their product to be approved as an interchangeable biosimilar. However, both biosimilars and interchangeable biosimilars meet the same high standard of biosimilarity for FDA approval and both are as safe and effective as the originator biologic, so they both can be used in place of the brand product."

"Great! I'll make sure to check out the Purple Book," Richard says. Empowered with exciting new details about therapeutic advancements, Richard can't wait to share the information he has learned about biosimilars with other members of his team.

Biosimilar Resources

FDA Pages

- Biosimilar Materials
- Provider Materials
- Patient Materials
- Purple Book
- Drugs@FDA (Drug Information)
- Search Page for FDA Guidances
- Advisory Committee Materials for Biosimilars
- Biosimilar Approval Process Information

Additional Resources

Slide Decks
- Foundational Concepts
- Regulatory and Scientific Concepts

Case Study
- What Is a Biosimilar?
- Biosimilars in Patient Care
- Interchangeable Biosimilars
- Insulins/Interchangeable
- Comparative Analytical Assessment

Info Sheets
- Biological Products, Biosimilar Products, and Interchangeable Biosimilar Products
- Generics and Biosimilars
- Manufacturing and Variation
- Biosimilar Regulatory Approval Pathway
- Variation in Biological Products
- Comparative Clinical Studies
- Prescribing Biosimilar and Interchangeable Biosimilar Products
- Purple Book
- Comparative Analytical Assessment
- Quality Attributes
- Labeling/Package Insert
- Insulins/Interchangeable

Explanatory Videos
- Biosimilars: Manufacturing and Inherent Variation
- Biosimilars: Approval Process
- Biosimilars: Critical Quality Attributes
- Biosimilars: Interchangeability
- Purple Book
- Procedural Purple Book
- Totality of the Evidence
- Comparative Analytical Assessment

Discussion Questions
- Foundational Concepts
- Regulatory and Scientific Concepts
- Exercises (Provided in the Resource Guide for Teaching Faculty)