COURSE TRANSCRIPT

**Module title: Developments in Biosimilars**

Overview

Welcome to the Developments in Biosimilars course.
After completing this course, you will be able to:

- Define biosimilars and how they differ from other types of drugs
- Explain how biosimilars are approved and come to market
- Describe current developments for biosimilars

What are Biosimilars?

Many people have heard of biosimilars, but may have limited knowledge and experience with one of these drugs. Biosimilars are drugs that are "highly similar" to already approved biological products. However, they are not generic drugs and must meet certain criteria to be approved for use in the United States.[1] Biosimilars have steadily been making their way into use in recent years.
This course will focus on this emerging type of drug therapy and how biosimilars are entering the market.

Before we further explore **biosimilars**, it is important to fully understand **biologics**, which are the product type on which biosimilars are based.
Biologics are large, complex molecules that may be produced through biotechnology in a living system, such as a microorganism, a plant cell, or an animal cell.[2]
Biologic therapies are used to treat a number of diseases and conditions, including some that are serious and life threatening, such as cancers and rheumatoid arthritis. Vaccines may also be biologics.[3]

A biosimilar product, in turn, is demonstrated to be highly similar to a single biologic, or **reference product**.
Biosimilars have no significant clinical differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.[4]

It is also important to note the difference between a **biosimilar** and a **generic drug**.

While both are versions of brand-name drugs, a generic's active ingredients are the same as those of brand-name drugs, and it must be "bioequivalent" to, or considered biologically the same as the brand-name drug. A biosimilar has a comparable but not identical structure, and may have minor differences in chemically inactive components.[5]

In approving biosimilars, the agency does not require the manufacturer to independently establish the safety and effectiveness of the proposed product, but *rather* to demonstrate the biosimilarity between the proposed product and the reference product. Generally, this means that biosimilar manufacturers do not need to conduct as many clinical trials.[7]

History and Regulations

Though biosimilars existed prior to the passage of the **Affordable Care Act (ACA),** the law provided an abbreviated pathway for the products to come to market.
The biosimilar legislation is the Biologics Price Competition and Innovation (BPCI) Act.
Its goals are to enhance competition, provide better patient access to therapies, and lower the cost to consumers for biologics. [8]

One type of biosimilar is an **interchangeable** biosimilar.
An interchangeable product has to meet additional requirements from the BPCI.
For instance, it must show the same clinical results as the reference product in any given patient. It also may be substituted for the reference product *without* the involvement of a prescriber.
Manufacturers of interchangeable products have to provide additional information to the U.S. Food and Drug Administration (FDA) to show they have the same clinical result as the reference product.[9]Like other therapies in the U.S., biosimilars are approved by the FDA.

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Biosimilars in Use: Approvals

As we have mentioned, biosimilars are still very new to the market.

The first biosimilar approved in the U.S. was Zarxio in March 2015.
Zarxio (filgrastim-sndz) was approved as a biosimilar to the brand-name product "Neupogen," which helps patients make white blood cells after white blood cell counts are lowered as a result of a cancer treatment.[10]

From 2015-2017, the FDA approved eight additional biosimilars, mostly for the treatment of cancers and rheumatoid arthritis.[11] While nine products were approved in the three-year span, fewer than half of them were active in the market in 2018.

Biosimilars have a more difficult path getting to market than other therapies, owing to several factors cited by U.S. payers.
Some factors include:

- Biosimilar manufacturers have found it difficult to price their products at launch appropriately against the reference products.[12]The pricing decisions have been complicated by the way all drugs come to market with consideration for **rebates**, **net price**, and other contracting terms.
- Manufacturers of innovator products, on which the biosimilars are based, have waged legal battles to delay launch of biosimilars.
- Patients and providers have been hesitant to switch to biosimilars. Many current biosimilars treat chronic conditions, which means there may be less switching to new therapies. [13]

<u>Biosimilars in Use: Coming to Market</u>

Research has concluded that most payers expect to limit biosimilars on their **formulary** in order to keep their formulary simple and to maintain rebates on current competitor agents.
Surveyed U.S. payers believe that the cost required for a biosimilar to receive reimbursement is expected to be 20%-25% less than that of the reference brand, on average.[14]Market access strategies are largely still developing in regard to biosimilars, but quick accessibility has been achieved by some products.

As an example, just over a year after launching, Zarxio was covered on more than a third of commercial formulary plans, with the same coverage as Neupogen. One in five commercial formularies offered more favorable coverage for Zarxio over Neupogen. [15]

<u>Current Developments: Substitution</u>

While the FDA has been busy implementing guidance on biosimilars, states have also been doing so. Multiple states have passed laws that allow retail pharmacist substitution of

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interchangeable biosimilars. States have modeled substitution laws on generic drug substitution, although biosimilars are less likely to be dispensed at a retail pharmacy. Instead, the first biosimilars have primarily been physician-administered. [16]

In addition to regulating the substitution of interchangeable biosimilars, state laws also:

- Allow prescribers to prevent substitution by writing "dispense as written" on the prescription
- Require notification of any substitution to prescribers and patients
- Require pharmacists and physicians to retain records of substituted biosimilars

The state bills have been supported by manufacturers of reference products who argue they help ensure patient safety.

Biosimilar manufacturers, however, say the laws could limit cost savings for consumers.[17] Among large states that have passed substitution laws are California, Florida, Illinois, Pennsylvania, and Texas.[18]

Conclusions

Dozens of biosimilars are in development globally. More than half of them are in a pre-clinical phase of development, and nearly a quarter are in late-stage **clinical trials**. The classes of biologics most frequently targeted by biosimilar developers are monoclonal antibodies and TNF-α inhibitors, which are used in autoimmune applications.[19]Though biosimilars are approved and entering the market, many payers, physicians, and patients are taking a "wait and see" approach before there is wider adoption.

Some formularies may prefer biosimilars but allow patients to stay on their existing therapies rather than switch. In the longer term, however, it's possible payers may force substitution of biologics for biosimilars as they build formularies. [20]

Cutting the price of biosimilars versus the reference product beyond the current 15%-20% may occur when there are two or three competitors for a single type of biosimilar-related molecule. Experts believe the price difference between a biosimilar and its reference biologic product will never be as large as that of a generic and its brand-name copy. It took several years for patients, prescribers, and payers to become accustomed to generics when they were introduced in 1984, but now they are widely used and accepted. The same increase in use may also be possible for biosimilars. [21]

## GLOSSARY

**Affordable Care Act**
Federal statute that was signed into law on March 23, 2010. It includes numerous provisions designed to reform healthcare, including expanding Medicaid, mandating coverage for individuals, and providing incentives for businesses to provide health coverage.

**biologic**
A drug prepared from animal tissue or another living source.

**biosimilar**
A drug highly similar to a biological reference drug, with no meaningful difference in safety or efficacy from the original product.

**clinical trials**
These studies test new types of medical care to establish its safety and effectiveness; also used to compare different therapies for a certain condition to determine the optimal course of care.

**formulary**
A continually updated list of medications and related products supported by current evidence-based medicine, as well as judgment of physicians, pharmacists, and other experts, designed to encourage the use of safe, effective, and most-affordable medications.

**interchangeable**
A biologic product that in addition to being a biosimilar is expected to produce the same clinical result as the reference product in any patient[i]

**net price**
The actual amount that a manufacturer recoups from selling its product once fees to stakeholders such as wholesalers and payers are taken out.[ii]

**rebate**
A discount offered by pharmaceutical companies for bulk buying or for preferred formulary status.

**reference product**
The single biological product, already approved by the FDA, against which a proposed biosimilar is compared.[iii]

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