Understanding Reference Biologics & Biosimilars

What is a biologic?

A biologic is a prescription medicine – administered through subcutaneous self-injection or intravenous infusion – produced from living material, usually cells, to be used for the prevention or treatment of disease.[1] Biologics are made up of large, complex molecules with many different ingredients such as sugars, proteins, cells and tissues.[1] Their elaborate structures and precise formulation make them difficult to characterize (identify and define all of their components) and impossible to copy versus small molecule drugs (i.e., aspirin), which are made from chemical compounds and can be duplicated exactly.[2] Because biologic manufacturing involves living organisms, the process is extremely intricate and sensitive to any changes.[3]

What is a biosimilar?

Due to their intricate manufacturing and purification process and the complexity of the living cells from which they are made, biologics cannot be copied exactly. Biological products known as biosimilars have started coming to market in the U.S. Biosimilars, although highly similar to biologic treatments,[4] are not exact or synthetic copies of original biologics (called reference biologics)—even when using the most sophisticated scientific techniques.[2]

A biosimilar product can only be approved by the U.S. Food & Drug Administration (FDA) through the biosimilar approval process if it has the same mechanism(s) of action (specific biological process of how the medication works to reduce symptoms), route(s) of administration, dosage form(s) and strength(s) as the reference product.[4] Further, it can only be approved for the indication(s) and condition(s) of use that have been approved for the reference product.[5] Health authorities may allow the manufacturer of a biosimilar studied in one indication (disease area) to receive approvals for additional indication(s) consistent with the reference biologic product.[6]

Can a biosimilar be substituted for a reference biologic product?

A biosimilar should only be treated as interchangeable if FDA has approved it as interchangeable.

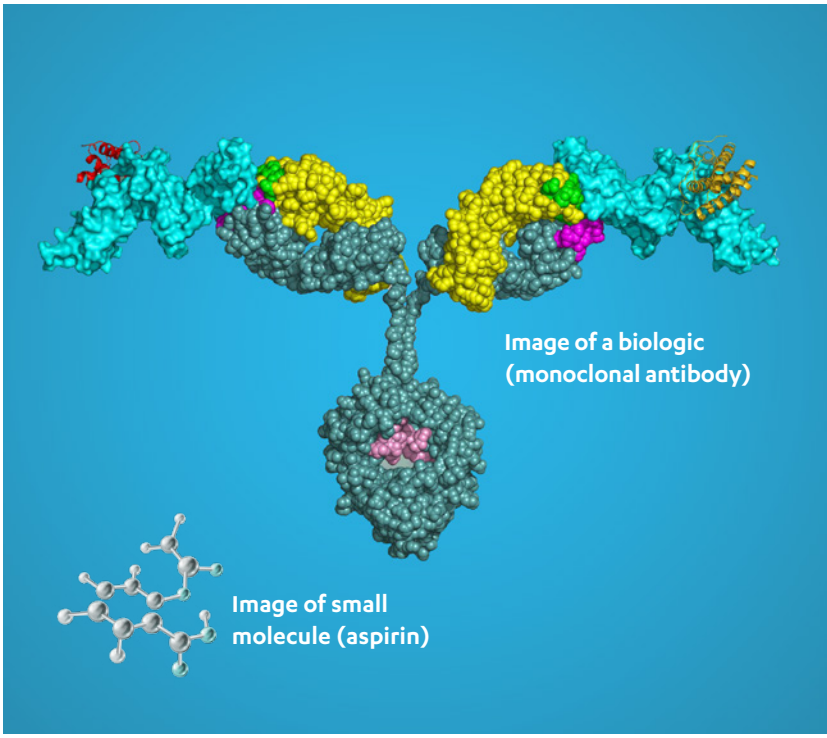
An interchangeable biosimilar must demonstrate the same clinical results as a biologic reference product in any given patient.[5] To be interchangeable, the FDA also requires that alternating or switching back and forth between the biosimilar and the reference product should produce similar safety and efficacy results as using the reference product without alternating or switching.[5]

What does this all mean for people prescribed biologics?

If a biologic therapy is prescribed for a chronic condition and a biosimilar becomes available, it is important for a discussion of treatment options to occur between the patient and the healthcare team.

Some key topic areas/questions to consider regarding biosimilars.

- **What is the scientific evidence that supports the use in the approved disease states?**
- **Is a biosimilar being prescribed by a healthcare provider? Or, can it be substituted by a pharmacist without a healthcare provider's or patient's consent?**
- **If a patient is doing well on a biologic therapy and is thinking about switching to a biosimilar, are there any considerations that need to be understood?**
- **Once patients switch to a biosimilar, can they switch back to the reference biologic?**



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About Janssen

For more than 30 years, Janssen has been dedicated to discovering and developing new medicines to treat today's most serious, life-changing illnesses. Fueled by an unwavering focus on meeting the needs of patients and healthcare professionals, Janssen has introduced 14 novel therapies and received 35 new indications for existing medicines since 2009. Janssen discoveries not only lead to new treatments, but also new ways to empower people using these products and expand their access to quality care—because Janssen believes that changing people's lives for the better takes more than medicine.

Information is an important element of patient empowerment. We offer this guide on the changing options in biologic care not to replace a conversation with your healthcare provider, but as a tool to inspire your discussion.

Glossary of Additional Terms:

As you learn more about biologics and biosimilars, you may come across certain words or phrases you are not familiar with. Outlined below are several terms commonly used when discussing biosimilars.

Extrapolation: In some cases, health authorities may allow the manufacturer of a biosimilar studied in one indication (disease area) to receive approvals for additional indication(s) consistent with the reference biologic product.[6] This is termed extrapolation.

High similarity: A biosimilar must be shown to have high similarity to its reference product through rigorous side-by-side analytical testing. Afterwards, comparative clinical testing is required. This clinical testing must show no clinically meaningful differences in safety, purity, and potency.[7]

Immunogenicity: Therapeutic proteins, such as those used in biologic products, are inherently immunogenic, meaning they may trigger the body's "attack response."[8] Very small differences between biologic and biosimilar therapies—even those too small to be detected—can cause unpredictable and varying immune responses among patients, from adverse reactions (side effects) to a loss of efficacy of the drug (the drug doesn't work as well).[9] One product can cause an immunogenic response while another highly similar drug does not.[10]

Interchangeability: In order for a biosimilar product that is to be administered more than once to an individual to be designated interchangeable, that product must be both highly similar to its reference product with no clinically meaningful differences in safety or efficacy.[5] Further, to be designated interchangeable, the risk of switching between the biosimilar and the reference product should be no greater than the risk of using the reference product without switching.[5]

Reference product: A reference product refers to the original biologic drug on which a biosimilar is based. The reference product has undergone full clinical development programs including pre-clinical and robust clinical trials in each of its indicated uses in order to achieve approval by the FDA.[11]

Naming: Whether a biosimilar's nonproprietary name should be the same as that of its reference product or be distinct remains the subject of global debate. The naming of biosimilars could have important patient safety implications, including: pharmacovigilance (see definition below), product switching and extrapolation of indications. A distinct nonproprietary name that is similar to, but not the same as, that of a reference product or of other biosimilars allows for product-specific tracking and monitoring for safety purposes.[12]

Non-proprietary name: Refers to the active ingredient in the medicine that is decided by an expert committee and is understood internationally. For a small molecule drug example, "acetaminophen" is the non-proprietary name for Tylenol®

Pharmacovigilance: Defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse reactions (side effects) or any other drug-related problem, according to the World Health Organization. In other words, pharmacovigilance refers to actions taken to enhance patient safety and care in relation to a drug or medication.[13]

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