Biosimilar FAQs and Terminology

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BIOSIMILAR FAQs

QUESTION	ANSWER
What is a biosimilar?	The term biosimilar means different things in different parts of the world. In the United States, the term is defined by the regulatory process used for biosimilars. The FDA states that a biosimilar is a biological product that is **highly similar** to the reference product notwithstanding **minor differences in clinically inactive components**. There are **no clinically meaningful differences** between the biological product and the reference biologic product in terms of safety, efficacy, purity, and potency of the product.
How are biosimilars approved?	Biologic agents are approved by a different pathway than non-biologic medications (often called small molecules). Biologics are approved under the Public Health Service Act (PSHA). Originator biologics, often called reference products when discussing biosimilars, are approved with a Biologic License Application, or 351(a), pathway. During this process, the safety and the efficacy of the biologic must be demonstrated. Biosimilars use an abbreviated FDA process known as the 351(k) pathway. Biosimilar manufacturers must prove that the biologic product is highly similar to the originator or reference biologic. It must be demonstrated that there are no clinically meaningful differences in purity, safety, and potency when compared to the reference product. The comparability exercise used to demonstrate that a biosimilar is "highly similar" to a reference biologic is scientific, robust, and regulated. Based on the totality of evidence, biosimilars can be approved to treat indications, even without clinical trials in that indication. This is called extrapolation. For a biosimilar product to be designated as an interchangeable biosimilar, additional clinical data must be provided. If a biosimilar is designated as interchangeable, the drug could be substituted for, at the pharmacy, without a prescriber's approval.

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QUESTION	ANSWER
What is the importance of immunogenicity when talking about a biosimilar?	Biologics confer a risk of being recognized by the immune system as a "foreign protein" and result in an immune response such as development of an antibody to the biologic (or antidrug antibody). The immunogenicity of an antibody is important to establish during the evaluation process for a number of reasons. This will be evaluated during the development process and must not result in clinically meaningful differences for the biosimilar. Potential clinical consequences of antidrug antibodies include the following: • Loss of efficacy • Toxicities related to general immune effects (e.g., allergy, serum sickness, and anaphylaxis) • Cross-neutralization of endogenous protein and biologic drug

How are biologics named?	The United States Department of Health and Human Services has established a process for naming of biosimilars that also includes a change to the way that originator biologics are named. Nonproprietary Naming of Biological Products gave recommendations for all reference biologic and biosimilar suffixes.
	• The name must include a nonproprietary name of the reference product and a four-letter suffix.
	• The suffix must be:
	  ○ Unique
	  ○ Devoid of meaning
	  ○ Four lowercase letters, of which at least three are distinct
	  ○ Nonproprietary
	  ○ Attached to the core name with a hyphen
	  ○ Free of legal barriers that would restrict its usage

What is the FDA Biosimilars Action Plan?	The FDA created four goals to accelerate biosimilar competition: • Improve efficiency of the biosimilar and interchangeable product development and approval process • Maximize scientific and regulatory clarity for the biosimilar product development community • Develop effective communications to improve understanding of biosimilars among patients, providers, and payers • Support market competition by reducing attempts to unfairly delay market competition of follow-on products

PATIENT FAQs

PATIENT QUESTION	NURSE RESPONSE
What is a biologic?	A biologic is a type of drug that is made from proteins. Biologics refer to several types of drugs used for treatment of diseases including cancer. They include vaccines, gene therapy, and therapeutic proteins like monoclonal antibodies. Some of the immunotherapies that you hear about are actually proteins that are given to patients to help turn on their immune systems. Biologic agents are made from natural and living sources and have a large, complex structure. In other words, "biologic" refers to genetically engineered proteins produced by living cells.
What is a biosimilar?	The FDA states that a biosimilar is a type of biologic drug that is developed to work like a biologic drug that is currently on the market. Because of the complexity of biologic drugs, it is virtually impossible to make an exact copy of the drug, so a process was developed to compare new agents (biosimilars) to the original biologic to assure they are highly similar. It is important that these biosimilar agents work in the body like the biologic agent, and that any differences don't result in a change in how they act in a patient. A biosimilar must be proven to show no clinically meaningful differences from an originator medicine. They are carefully monitored to ensure consistent quality.
What does "clinically meaningful differences" actually mean to me?	This means that the biosimilar drug and the original biologic drug have the same effect in terms of efficacy and side effects when used to treat a patient. A biosimilar drug is not better than the originator molecule, nor is it less effective.
Is a biosimilar drug the same as a generic drug?	It is easy to make an analogy between the two types of drugs, but the term biosimilar is used when talking about biologic drugs. Biologic drugs tend to be complex agents and biosimilar drugs are made to be "highly similar." Generic drug is a term used for drugs that are not biologic agents but are chemicals that can be copied.
Will a biosimilar work as well as the reference product?	Biosimilars were developed to produce the same effects as the biologic reference drug. The differences should not affect the efficacy or side effects of the drug.

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PATIENT QUESTION	NURSE RESPONSE
What is the benefit to receiving a biosimilar?	Biosimilars are being developed worldwide to help decrease the overall cost of drug therapy in healthcare. Biologics tend to be expensive. The hope is that the introduction of competition into the healthcare marketplace, without decreasing efficacy, will help decrease the cost of these agents. We are seeing this decrease in cost as more biosimilar agents are developed and approved. The intended result is that more patients will have access to these important biologic therapies with the biosimilars. More patients may have access to biologics which can improve outcomes. It also allows for greater development of other drugs. The benefit for a specific individual may be based on a lower cost to them and/or their insurer. The efficacy and the biologic effect should be the same.
What type of biosimilars could I receive for my cancer?	There are many biosimilars approved in the United States including biologics that treat diseases such as cancer. There are also biosimilars available to help prevent or manage side effects of cancer and cancer treatment. You may receive supportive care or therapeutic biosimilars. Supportive care may include growth factors to help you tolerate the side effects from treatment. Therapeutic biosimilars include the anticancer drugs you may receive to fight your cancer.

GLOSSARY

TERM	DEFINITION
Biologic	U.S. Federal Code of Regulation defines biologic as any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment, or cure of disease or injuries of man. Biologics tend to be large and generally complex molecules that are produced from living organisms.
Biosimilar	A biosimilar is a biological product that is **highly similar** to the reference product notwithstanding **minor differences in clinically inactive components**.
Generic drug	A low molecular weight medication that is reproducible with the same dose, safety, strength, route, and efficacy. This is unlike the highly complex biologic, which is unable to be identically reproduced.
Indication Extrapolation	Indication extrapolation is when a biosimilar is approved for use in an indication held by the reference product in which the biosimilar has not been evaluated. If a proposed biosimilar product meets all the requirements for approval as a biosimilar, the applicant may seek approval of the proposed product for additional indications for which the reference biologic is currently licensed. Therefore, the product is not directly studied against the reference product in all indications. This helps to streamline the process of approval and reduce unnecessary studies which can also help save money. It is important to note that some biosimilars are not marketed with all the indications of the reference product.
Interchangeability	Biosimilar products may be designated by the FDA as interchangeable with the reference product. Interchangeable products have an FDA designation beyond "biosimilar" that requires additional data. None of the currently approved biosimilars are designated as interchangeable at this time. Biosimilars that are designated as interchangeable may be substituted for the reference product without the authorization of the prescribing healthcare provider and must demonstrate that it can be expected to produce the same clinical result as the reference biologic in any given patient. State substitution laws exist in many states that regulate interchangeability of biosimilars that are designated by the FDA as interchangeable.
Reference drug (also called originator product)	Reference drug (or originator product) refers to the original biologic drug that is used for comparison to the biosimilar product. It is important to note that biosimilars are not compared to other biosimilars during the development and approval process.