Biosimilar and Interchangeable Biologics: What Is What?

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By Loan Pham and Vien Lai

For decades, everybody has become familiar with many brand-name and generic chemically synthesized drugs that are small molecule drug products, such as amoxicillin, Lipitor, and Crestor. Biological products, on the other hand, are practically and conceptually different as a class of therapeutic medicinal products. Biological products may be broadly considered inclusive of vaccines, blood components, or proteins (unless chemically synthesized polypeptides), as well as other defined products. Currently in the United States, a number of biological products have been approved for prevention of diseases (e.g., vaccines), for treatment of autoimmune diseases (e.g., arthritis, psoriasis), and for treatment of cancer (e.g., non-Hodgkin lymphoma, some types of colorectal cancer).

As the proliferation of biologic products continues, so will the proliferation of biosimilar products with respect to innovator products, also known as the reference biologic product (RBP) to which a biosimilar is compared. Consequent to the expanded development and approval of biosimilars will be determining whether a biosimilar product is interchangeable with, and can be used in lieu of, an RBP.

Interchangeability, by definition [section 351(k)(4)(A) of the Public Health Service Act (PHS Act)], requires that a proposed interchangeable product be biosimilar to the RBP. In addition, it is considered fundamental to interchangeability as a paradigm that the presumptive interchangeable biosimilar product will produce the same efficacy and safety profiles in all patients, and will demonstrate comparable risks as that observed in a therapy without a switch from the RBP to an interchangeable biologic. It is possible that a newly licensed biosimilar product may have peremptorily achieved such demonstrations of “sameness” with respect to effectiveness and overall product safety; however, there are many other factors that determine interchangeability. Just because a new therapy is approved as biosimilar to an RBP does not imply interchangeability.

The key prerequisite for a generic chemically synthesized drug product is analytical sameness relative to a specific reference product. A biosimilar product, on the other hand, is "similar" but not "identical" to the RBP, and therein lies the difference and distinction between generic and biosimilar product types as regards product interchange. It is a common practice at drug stores for patients to ask for a generic instead of a brand-name small molecule chemically synthesized drug, but substitution is more complex for biologics. The United States regulatory authority allows *interchangeable* biological products to be freely exchanged with the reference brand-name biologic without seeking permission from the prescriber. Compared to a *biosimilar* biological product, being an interchangeable biologic offers flexibility of use and potentially warrants a greater market share.

The evolving importance of biosimilarity and prospective interchangeability is highlighted by the release of the final guidance for biosimilar products and the recent (January 12, 2017) release of a draft guidance for industry from the Food and Drug Administration (FDA) entitled *Considerations in Demonstrating Interchangeability With a Reference Product*. Not unexpectedly, the interchangeability guidance document provides more explicit clarifications regarding product requirements and data necessary to support interchange, including, but not necessarily limited to the conduct of a clinical switching study (or studies) to demonstrate interchangeability between the test and reference biologic products. Such studies apply to any product for which more than a single use is intended.

Do you feel safer taking medicines knowing that they are not just "similar" but also "interchangeable?"

How can a biological product be determined as interchangeable? *Join us for a deeper dive into the interchangeability guidance in tomorrow's blog post!*

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