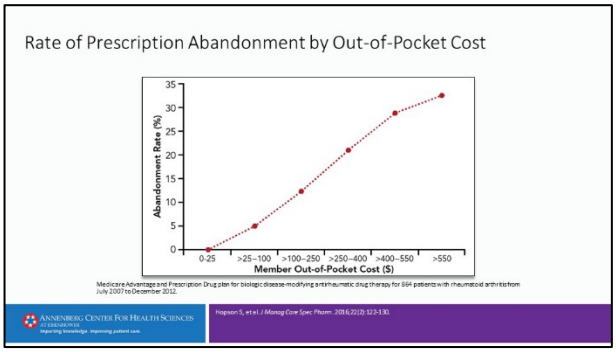
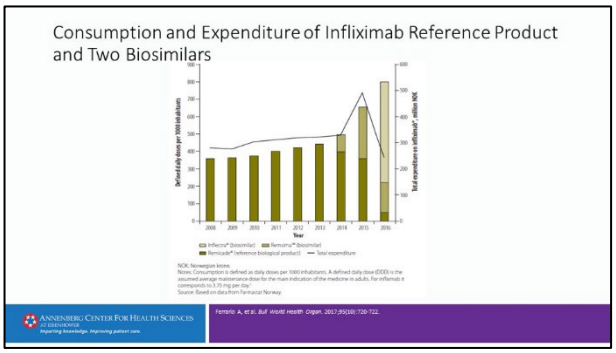
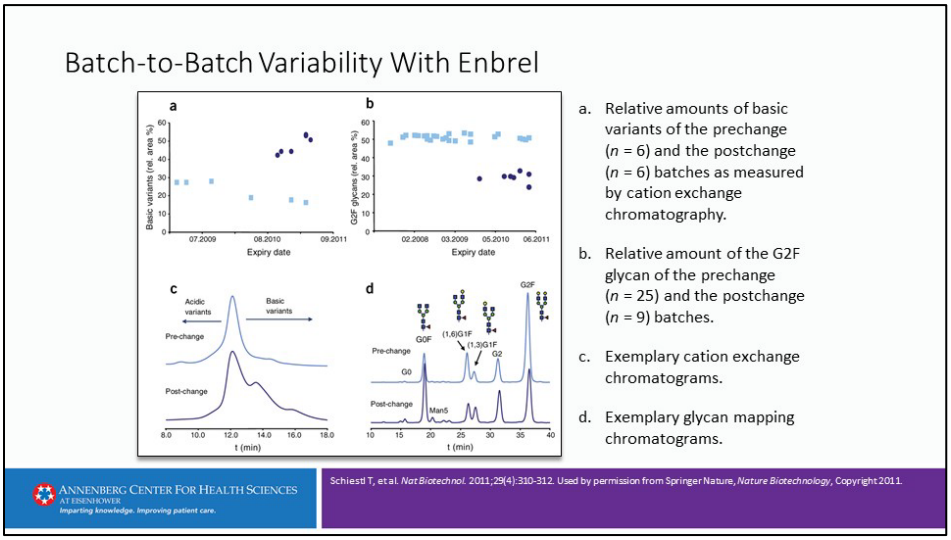
# Study Companion: Answers to Clinicians' Questions About Biosimilar Use in Inflammatory Conditions


***Introduction of a biosimilar can increase patient access to expensive biologics.*** The rate of abandonment of biologic therapy is directly related to out-of-pocket costs. A key goal of biosimilar development is to reduce patient cost and increase patient access to biologic therapy. The achievement of these goals was demonstrated in a Norwegian study of infliximab prescribing patterns, showing that adopting a biosimilar increased the number of infliximab prescriptions even as total spending on infliximab decreased.




***Biologic drift is the variation in a biologic's quality attributes that arise over its lifecycle.*** The complexity of biologic macromolecules, their production in living systems, and the purification processes for them introduce variability in the end product. Additional changes arise postapproval when changes are made to the manufacturing process. As a result, no 2 batches of a biologic are identical—they may differ in a number of quality attributes, which are molecular or product characteristics (eg, posttranslational modifications) that contribute to their identity, potency, or stability. In a study of batches of brand name etanercept (Enbrel®) produced between 2007 and 2010, variations were found in several quality attributes, including the charge and glycosylation profiles.[1,2]



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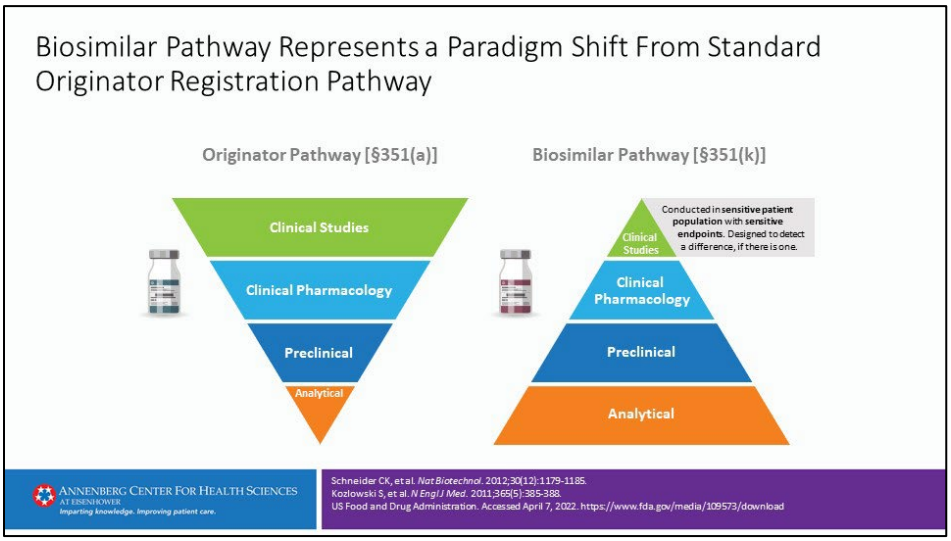
***A biosimilar is a biologic product with no clinically meaningful differences from its reference product.*** A reference product is the original biological product licensed by the FDA against which a biosimilar is evaluated.[3,4] The criteria that the FDA uses to evaluate a biosimilar are that it 1) is highly similar to the reference product, notwithstanding minor differences in clinically inactive components; and 2) has no clinically meaningful differences from the FDA-approved reference product in terms of the safety, purity, and potency.[3,5]

***Analytic studies, rather than clinical studies, are the foundation for biosimilar approval.*** Biosimilars undergo extensive analytical characterization as part of the approval process to demonstrate that any differences between the biosimilar and reference product are minor and affect only clinically inactive components.[3,6] Successive stages of the development program are designed to eliminate any uncertainty that these differences are clinically meaningful. As a result, biosimilars do not need to undergo extensive clinical testing.




***In most cases, biosimilars are approved for the same indications as the reference product.*** Biosimilars do not need to be tested in every indication for which they are approved, nor do they need to independently demonstrate clinical efficacy or safety.[3,7] In the absence of clinically meaningful differences between a biosimilar and its reference product, the totality of the evidence supports extrapolation of the biosimilar's approval to indications other than those in which it was studied during clinical development but for which the reference product has already been approved.

***Biosimilars that have been approved as "interchangeable" may be substituted for a prescribed biologic without intervention from the prescribing physician.*** Not all biosimilars are interchangeable. To demonstrate interchangeability with the reference product, the biosimilar must undergo additional clinical studies where patients switch between the reference product and biosimilar. Pharmacists can substitute an interchangeable biosimilar for the reference product according to state laws.

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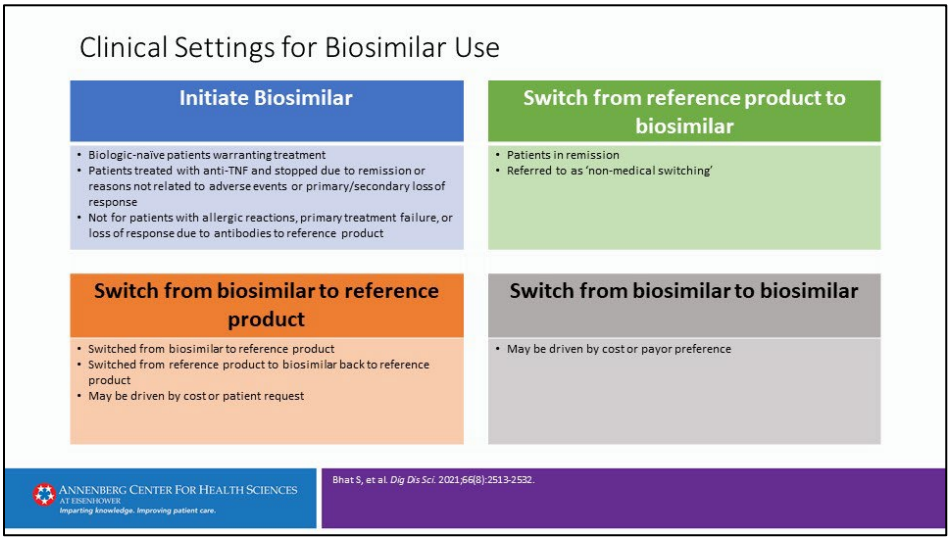
***Both patients and healthcare providers may have concerns about the efficacy and safety of biosimilars.*** These concerns are rooted in misconceptions about biosimilars (eg, that they are second- or third-line treatments, can only be used in treatment-naïve patients, or are less effective or more immunogenic than their reference products).[8] As a result, patients have reported a higher incidence of adverse events with some biosimilars than with their reference products—a phenomenon known as the "nocebo effect"—and in some biosimilar trials this has resulted in an increase in drug discontinuation in the absence of objective evidence of disease worsening. Countering the nocebo effect requires shared decision making and positive communication about biosimilars.

***Biosimilars are not appropriate for clinical scenarios where the reference product would not be used.*** Patients who have not responded, have had an allergic reaction, or developed antidrug antibodies to the reference product should not be treated with a biosimilar.[9]




**References**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