Biosimilar Substitution Laws

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In 2010, the Patient Protection and Affordable Care Act was enacted into law in the United States. A section of this law amended the Public Health Service Act resulting in the creation of an abbreviated licensure pathway for biological products found to be biosimilar to, or interchangeable with, an existing Food and Drug Administration (FDA)–approved biologic product.[1,2] Per the FDA, a biosimilar is defined as "a biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, known as a reference product, and has no clinically meaningful differences in terms of safety and effectiveness from the reference product."[1]

Generally, biosimilars are only allowed to have minor differences in clinically inactive ingredients. Interchangeable biologic products are biosimilar to a reference product as well; however, these products are required to meet additional standards to demonstrate interchangeability with the reference biologic.[3] Basically, an interchangeable product "is expected to produce the same clinical results as the reference product in any given patient." In addition, for those products that may be administered more than once, clinical data need to show that switching a patient back and forth between the reference and interchangeable products presents no greater risk to a patient in terms of efficacy and safety when compared with continuously treating the patient with the reference product.

In March 2015, the FDA approved the first biosimilar product in the United States—filgrastim (Zarxio). Since this initial approval, 4 more biosimilars have become available including 2 biosimilars for infliximab (Inflectra; Renflexis) and 1 biosimilar each for etanercept (Erelzi) and adalimumab (Amjevita).[4] With the approval of these biosimilars, there has been an increase in the number of state laws surrounding appropriate substitution of these agents for an original biologic product. Many states have a concern that traditional statutes regulating generic medications may be misapplied to newly approved biosimilars that are not necessarily identical to a reference product.[5] Accordingly, in the past 5 years, at least 45 states have evaluated legislation establishing standards for substitution of a biosimilar product for a reference biologic. As of July 1, 2017, 35 states and the unincorporated US territory of Puerto Rico have passed laws regarding biosimilar substitution requirements. The provisions of these state laws vary, but there are several features and requirements that are often included such as the following[5]:

- Any biological product under consideration as a substitution for a reference product must first be approved as "interchangeable" by the FDA.
- Prescribers must be able to prevent substitution by writing "dispense as written" or "brand medically necessary" on the prescription.
- Legislative language requiring that the prescriber "must be notified" of any allowable substitution made at a pharmacy or that the prescriber be "communicated with" regarding the substitution in some manner such as a notation in an electronic medical record.
- Requiring that the individual patient be notified of the biosimilar substitution or switch; at least 12 states include this provision in their biosimilar substitution laws. In addition, some state laws require that the affected patient must give consent before such a substitution is made.
- Requiring that both the pharmacist and the prescriber retain records of the substituted biologic medication.
- Providing immunity for pharmacists who make a biosimilar substitution in compliance with state law.
- Requiring the state to maintain a public or web-based list of permissible interchangeable products.
- Ensuring that the pharmacist has to explain the cost of the biologic and the interchangeable biosimilar to the patient or prescriber; some states such as Colorado, Georgia, Illinois, North Carolina, and Texas require that any substituted product must be associated with the lowest cost to the patient.

Currently, all 5 approved biosimilars in the United States are not designated as interchangeable per the FDA; therefore, none of the state biosimilar substitution laws are applicable to dispensing decisions.[5] A summary of biosimilar substitution laws by state may be found at http://www.ncsl.org/research/health/state-laws-and-legislation-related-to-biologic-medications-and-substitution-of-biosimilars.aspx.

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In summary, as the FDA evaluates and approves more biosimilars, state legislatures have become increasingly concerned regarding the appropriate method for substituting a biologic reference product with a biosimilar. Over the past few years, many state legislatures have enacted laws calling for a variety of requirements necessary for a legal biosimilar substitution. Currently, none of the approved biosimilars in the United States are designated as interchangeable by the FDA; however, once this occurs, these laws will begin to take effect across the nation and pharmacists should be aware of how these will impact their pharmacy practice.

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