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Genetic Engineering & Biotechnology News

GEN Exclusives: January 12, 2015

Substitution Allowed? State Biosimilar Laws Are Evolving

Only eight states have enacted laws but legislation is pending in many more.

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Biosimilar products have not yet reached the U.S. market, but debates on the laws and regulations that will govern them have been raging for some time. It isn't just federal law at issue. State law may have a profound impact as well. State law governs the ability of a pharmacist to make substitutions for a prescribed branded drug. Thus, at the end of the day, these laws impact the sales ratio of branded to generic drugs.

State laws governing the substitution of generic versions of small molecule (chemical) drugs primarily divide into two categories: permissive and mandatory. Under permissive regulations, a pharmacist may substitute the generic version, whereas under mandatory laws, the pharmacist must make the substitution if a generic version is available. Both types of laws allow the prescriber to prohibit generic substitution with a "do not substitute" or similar indication on the prescription.

Currently, only eight states have enacted biosimilar substitution laws (Delaware, Florida, Indiana, Massachusetts, North Dakota, Oregon, Utah, and Virginia). All these laws are of the permissive type—even where the same state requires mandatory generic substitution for small-molecule drugs, as in Florida. The current laws are limited to substitution of biosimilars designated "interchangeable" by the FDA. These interchangeable products must meet higher standards, including that the product is expected to produce the same clinical result in any given patient as the original branded version and that there is no greater risk in switching to the biosimilar as compared to continuing use with the original product.

Many newly enacted laws also include provisions that further restrict the substitution or place additional requirements on the pharmacist. For example, Indiana only allows a biosimilar substitution if the prescriber writes "may substitute" on the prescription. Utah, North Dakota, and Oregon all require the pharmacist to notify the prescriber of the substitution within one to three days (although, ironically, Utah's notification provision expires in May 2015, likely before the first biosimilar enters the U.S. market). Notification provisions have attracted considerable attention. Some organizations claim these provisions will result in fewer substitutions, a hypothesis based on the effect predispensation notification requirements had on the substitution of epilepsy drugs in some states.

An additional 13 states have considered or currently have legislation pending to govern biosimilar substitution, including Georgia, New Jersey, Pennsylvania, Washington, and Vermont, which have newly introduced legislation or bills under active consideration. While many state efforts have faced an uphill battle, surprisingly, Washington state's efforts have garnered support from both the branded biologic and biosimilar manufacturers. The proposed legislation would require a written prescription form to show two choices—"dispense as written" and "substitution permitted"—with the prescriber indicating by signature the intended choice. The pharmacist would then have 10 days post-

dispensation to notify the prescriber of the substitution. This notification can use an interoperable health records system shared with the prescriber if the system is available.

In addition to the ongoing debates on substitution legislation, another related debate continues to brew—the naming of biosimilars. With current small-molecule drugs, pharmacists are generally permitted to make substitutions for a generic with the same active ingredient, such as those listed as a pharmaceutical equivalent in the FDA's Orange Book and which carry the same United States Adopted Names (USAN) or International Nonproprietary Name (INN).

Biosimilars may not easily conform to this system because it is still undetermined if they will carry the same USAN/INN as their branded counterparts. Unlike small-molecule generic drugs, biosimilar drugs need only be "highly similar" rather than identical to the branded version. Biosimilars may differ, for example, in post-translational modifications to the protein that is the drug's active ingredient (i.e., modifications to chemical groups that are attached to the protein when it is produced by living cells). Accordingly, differently modified proteins may receive different USAN/INN designations.

The naming convention is likely to impact the rate at which biosimilars are substituted by pharmacists. For example, the American Medical Association recommends that prescriptions of current generic drugs contain the USAN assigned name for the drug. Under this recommendation, a biosimilar with a different USAN designation would not be listed on the prescription, making it less likely to be substituted. The Federal Trade Commission held a roundtable workshop on naming regulations in February 2014. While these hearings fleshed out the debate, no consensus has yet emerged.

Currently, there are at least three biosimilar products under review by the FDA. The most advanced in the process, Sandoz's biosimilar of Amgen's Neupogen® (filgrastim), recently gained a recommendation for approval from the Oncologic Drugs Advisory Committee (ODAC) at the FDA. Notably, this approval appears to be directed to the product only as a biosimilar and not as "interchangeable." Thus, the state substitution laws as they are currently written, will not direct pharmacists to make the substitution. Whether the biosimilar will share the same USAN/INN as the branded version also is not yet known. In a Citizen Petition to the FDA, Sandoz has urged the agency to give biosimilars the same USAN/INN as the branded counterpart. As this and other biosimilars enter the market, it should bring more clarity as to how these laws and regulations will affect the balance of original branded and biosimilar versions.