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ALLOW DISPENSING OF INTERCHANGEABLE BIOLOGICAL DRUGS; REQUIRE NOTIFICATION TO PRESCRIBER AFTER DISPENSING

House Bill 4812 (H-2) as reported from committee
Sponsor: Rep. John Bizon, MD
Committee: Health Policy
Complete to 11-10-15

BRIEF SUMMARY: The bill would allow pharmacists to dispense FDA-designated interchangeable biological drug products; and require that a pharmacist notify the prescriber, within five business days after dispensing a biological product, of the product name and manufacturer.

FISCAL IMPACT: House Bill 4812 could generate a minimal, but likely negligible, amount of short-term fiscal savings on state and local units of government, and could generate moderate long-term fiscal savings through the Medicaid program in particular. Cost savings estimates vary from 15% to 30% for a biosimilar when compared to its interchangeable biological product, meaning for every $10.0 million in gross Medicaid expenditures on a biologic product, a biosimilar could save between $500,000 and $1.0 million GF/GP (based on the state's FY 2016 Medicaid match rate of 65.60%). The first biosimilar was approved by the U.S. Food and Drug Administration in March 2015.

The bill would have no fiscal impact on the Department of Licensing and Regulatory Affairs.

THE APPARENT PROBLEM:

Most of the drugs that pharmaceutical companies manufacture are constituted by chemicals combined in specific ways for particular effects. They are formulaic, their ingredients are stable, and batch after batch are identical. When cheaper synthetic versions of these chemical combinations become available, we call them generic drugs, and we know they, too, are identical to their original counterparts.

Biologic drugs are different. Pharmaceutical companies manufacture biological drugs in a living system—within the actual cells of plants or the cells of animals. Consequently, batches of drugs are not identical one to the other. Their cell-sources differ, their biologic interactions vary, and consequently, it is possible that the drugs' effectiveness will vary. Because it is impossible to create an exact replica, we call the different batches of these drugs 'bio-similar' biologics. See ***Background Information*** below.

While biologic drugs have been around for more than 100 years—for example, as vaccines, and insulin—only now with the mapping of the human genome to reveal countless genetic clues are biologic drugs preparing to explode onto the market, as 21st century cures. These

new and complex drugs are designed to treat very serious illnesses—diabetes, cancers, and autoimmune diseases.

States across the country are adopting statutes to regulate biologics and bio-similar pharmaceuticals. In Michigan, legislation has been introduced to do the same. Chief among the concerns during legislative deliberations has been patient protection. Because bio-similar biologics can have different effects on patients when they are substituted by pharmacists, the original prescriber needs to be notified of the substitution, to understand possible adverse reactions when and if they occur.

THE CONTENT OF THE BILL:

House Bill 4812 (H-2) would amend the Michigan Public Health Code to allow pharmacists to dispense FDA-designated interchangeable biological drug products. The bill would also require that a pharmacist notify the prescriber, within five business days after dispensing a biological product, of the product name and manufacturer.

The bill would go into effect 90 days after being enacted into law. A detailed description of the bill follows.

Now under the law, a pharmacist who receives a prescription for a brand-name drug product *may* unilaterally substitute a lower cost generically equivalent drug, and if a purchaser requests a lower cost drug, the pharmacist *must* dispense the lower cost product (if it's available in the pharmacy).

Substitution. House Bill 4812 (H-2) would modify this provision described in the paragraph above, to *extend it to biological drug products and to interchangeable biological drug products*. Specifically, under the bill, when a pharmacist received a prescription for a brand name drug or a biological drug product, the pharmacist could dispense a lower cost (but not higher cost) generically equivalent drug product or an interchangeable biological drug product. If a purchaser requested a lower cost generically equivalent drug or an interchangeable biological drug product, the pharmacist would be required to dispense it.

Notification & labeling of biological drug product. Further, under the bill, the pharmacist would be required to notify the purchaser if a drug or biological drug product was dispensed that was not the prescribed brand. If the dispensed biological drug product did not have a brand name, then the prescription label would have to indicate the generic name of the drug or the biological drug product dispensed.

Pass along cost savings. Under the bill, if a pharmacist dispensed a generically equivalent drug or an interchangeable biological drug product, the pharmacist would be required to pass on the cost savings to the purchaser.

Prohibition if 'dispensed as written'. Under the current law, a pharmacist is prohibited from dispensing a generically equivalent drug product if the prescriber writes "dispense as written" or "d.a.w." on the prescription; or, (in the case of an unwritten prescription), the

prescriber expressly indicates the prescription is to be dispensed as communicated. House Bill 4812 would retain these prohibitions, and extend them so they also apply to *an interchangeable biological drug product.*

Total charge capped. Now under the law, a pharmacist may not dispense a drug product with a total charge that exceeds the total charge of the drug originally prescribed, unless agreed to by the purchaser. House Bill 4812 (H-2) would retain this provision.

Biological drug product notification. Finally, the bill requires that a pharmacist must notify a prescriber within five business days after dispensing a biological drug product.

Under the bill, a pharmacist who dispensed the biological drug product, a pharmacy technician, or a pharmacist intern would be required to communicate to the prescriber the specific biological drug product dispensed, including, but not limited to, the name and manufacturer of the biological drug product.

The pharmacist's communication could be made (a) by making an entry in an inter-operable electronic medical records system, through the use of electronic prescribing technology, or through the use of a pharmacy benefits management system, or through the use of a pharmacy record that is electronically accessible by the prescriber; or (b) by facsimile, telephone, electronic transmission, or other prevailing means. The information received by a prescriber would have to be included in the patient's medical record.

House Bill 4812 (H-2) specifies that the notification requirement described above would not apply if either of the following occurred: (a) there was no interchangeable biological drug product for the drug product prescribed; or (b) the prescription was refilled with the same drug product that was dispensed on the prior filling of the prescription.

Definitions. The bill defines three new terms—*biological drug product*, *biosimilar*, and *interchangeable biological drug product*.

First, the term *biological drug product* means a biological product as defined in the federal law at 42 USC 262. There, (1) the term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

Second, the term *biosimilar* means that term as defined in 42 USC 262. There, the term "biosimilar" or "biosimilarity", in reference to a biological product that is the subject of an application under subsection (k), means—

(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

(B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

Third, the bill defines *interchangeable biological drug product* to mean either of the following: (a) a biological drug product that is licensed by the FDA and determined to be interchangeable with the prescribed drug product pursuant to 42 USC 262(k)(4); or (b) a biological drug product that is approved by the FDA pursuant to an application filed under 21 USC 355(b)(2) and that the FDA has determined to be therapeutically equivalent to the prescribed drug product.

MCL 333.17702, 333.17704, and 333.17755

BACKGROUND INFORMATION:

The Biotechnology Industry Organization offers the following primer that briefly explains how drugs and biologics differ. Visit their website at https://www.bio.org/articles/how-do-drugs-and-biologics-differ

Drugs versus Biologics

- A biologic is manufactured in a living system such as a microorganism, or plant or animal cells. Most biologics are very large, complex molecules or mixtures of molecules. Many biologics are produced using recombinant DNA technology.
- A drug is typically manufactured through chemical synthesis, which means that it is made by combining specific chemical ingredients in an ordered process.
- Drugs generally have well-defined chemical structures, and a finished drug can usually be analyzed to determine all its various components. By contrast it is difficult, and sometimes impossible, to characterize a complex biologic by testing methods available in the laboratory, and some of the components of a finished biologic may be unknown.
- Therefore, for biologics, "the product is the process." Because the finished product cannot be fully characterized in the laboratory, manufacturers must ensure product consistency, quality, and purity by ensuring that the manufacturing process remains substantially the same over time. By contrast, a drug manufacturer can change the manufacturing process extensively and analyze the finished product to establish that it is the same as before the manufacturing change.
- The living systems used to produce biologics can be sensitive to very minor changes in the manufacturing process. Small process differences can significantly affect the nature of the finished biologic and, most importantly, the way it functions in the body. To ensure that a manufacturing process remains the same over time, biologics manufacturers must tightly control the source and nature of starting materials, and consistently employ hundreds of process controls that assure predictable manufacturing outcomes.
- Process controls for biologics are established separately for each unique manufacturing process/product, and are not applicable to a manufacturing process/product created by another manufacturer. These process controls may also be confidential to the original manufacturer. Therefore, it would be difficult or impossible for a second manufacturer to make the "same" biologic without intimate knowledge of and experience with the innovator's process.

Generics Drugs versus Follow-On Biologics

- To be approved as a generic, a drug must have the same active ingredient, strength, dosage form, and route of administration as the reference drug, and it must also be "bioequivalent." This means that generic drugs are the same chemically as their innovator counterparts and that they act the same way in the body. The bioequivalence of the generic drug is demonstrated through relatively simple analyses such as blood level testing, without the need for human clinical trials. In approving a generic drug under 505(j) of the FDCA, FDA determines that the generic is "therapeutically equivalent" to the innovator drug, and is interchangeable with it.
- Historically, FDA has permitted interchangeability only when two products are "therapeutic equivalents." However, when the follow-on manufacturer establishes a new manufacturing process, beginning with new starting materials, it will produce a product that is different from and not therapeutically equivalent with that of the innovator. Because of the complexity of biologics, the only way to establish whether there are differences that affect the safety and effectiveness of the follow-on product is to conduct clinical trials.

ARGUMENTS:

For:

The more than 30 organizations whose members are proponents of the bill make two arguments. First, they note that biosimilar biologic drugs are the future of pharmacology. Already, interchangeable bio-similars are dispensed in Europe, saving a reported 30 percent in pharmacy costs. Further, more than 900 products are in development world-wide, although just one has been approved by the U. S. Food and Drug Administration. Proponents urge that, across the nation, all state regulatory frameworks adopted as statutes work to achieve policy coherence—complementing each other as well as federal guidelines and law—enabling research collaboration, and also competition. This bill meets these requirements. Specifically, the bill follows FDA guidelines that only interchangeable bio-similars should be substituted; requires the pharmacy to notify the prescriber after an interchangeable biosimilar is dispensed; and it embodies the national bio-similars coalition model bill language recently passed in other states.

Proponents of the bill also argue that House Bill 4812 provides greater patient protection than did an earlier bill (House Bill 4437). This legislation ensures that the physicians who prescribe the drugs to help their patients will be informed by any pharmacist who substitutes a biosimilar biologic drug. This notice is imperative, because even interchangeable bio-similars are not the same as their reference biologics, and consequently they can have different effects, including life-threatening allergic reactions. Under this bill, pharmacists must notify prescribers of interchangeable biosimilar substitutions, and subscribers must place that information in a patient's medical record.

Against:

Opponents of the legislation argue that the notice provisions of the legislation to require pharmacists to notify prescribers within five days after interchangeable bio-similar substitutions are made, will add unnecessary costs to an already costly medical system.

They note that adverse reactions to interchangeable biosimilar drugs will be few and far between, because the U.S. FDA does not approve interchangeable biosimilar drugs until clinical trials demonstrate equivalent therapeutic effects.

POSITIONS:

The Michigan State Medical Society supports the bill. (11-3-15)

Sanofi U.S. supports the bill. (11-3-15)

Spectrum Health supports the bill. (11-3-15)

McLaren supports the bill (11-2015)

CVS Health supports the bill. (11-3-16)

The Society of Hematology and Oncology supports the bill. (11-3-15)

Michigan Bioscience Industry Association (Mich Bio) supports the bill. (11-3-15)

Biotechnology Industry Organization supports the bill. (10-2-15)

The Michigan Osteopathic Association supports the bill. (11-3-15)

The Michigan Academy of Family Physicians supports the bill. (11-3-15)

The American Cancer Society supports the bill. (11-3-15)

The Generic Pharmaceutical Association supports the bill. (10-6-15)

The American Liver Foundation supports the bill. (10-16-15)

The Oakland County Medical Society supports the bill. (10-12-15)

Lupus and Allied Diseases Association, Inc. supports the bill. (10-10-15)

PhRMA supports the bill. (10-7-15)

The Arthritis Foundation supports the bill. (10-5-15)

Saginaw County Medical Society supports the bill. (10-7-15)

The National Patient Advocate Foundation supports the bill. (10-5-15)

National Physicians Biologics Working Group supports the bill. (10-2-15)

Alliance of Specialty Medicine supports the bill. (10-2-15)

The American College of Rheumatology supports the bill. (9-5-15)

American Autoimmune Related Diseases Association supports the bill. (10-5-15)

Coalitions of State Rheumatology Organizations supports the bill. (10-2-15)

Global Colon Cancer Association supports the bill. (10-7-15)

Global Healthy Living Foundation supports the bill. (10-5-15)

International Cancer Advocacy Network supports the bill. (10-5-15)

National Hispanic Medical Association supports the bill. (10-5-15)

Michigan Lupus Foundation supports the bill. (10-5-15)

RetireSafe supports the bill. (10-5-15)

The Michigan Association of Health Plans opposes the bill. (11-3-15)

National Association of Chain Drug Stores opposes the bill. (11-3-15)

The Michigan Pharmacists Association opposes the bill as currently written. (11-3-15)

Pharmacy Consulting Services oppose the bill. (11-3-15)

Diplomat Pharmacy opposes the bill. (11-3-15)

HealthPlus of Michigan opposes the bill. (11-3-15)

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■ This analysis was prepared by nonpartisan House Fiscal Agency staff for use by House members in their deliberations, and does not constitute an official statement of legislative intent.