

WHY DOCTORS NEED TO KNOW WHEN PHARMACISTS SUBSTITUTE BIOLOGICAL MEDICINES

By David Charles, MD and Mary Ann Chapman, PhD

Lawmakers in many states are currently considering legislation that would allow pharmacists to substitute biological medications—those made by living cells or organisms—with other medications deemed “therapeutically interchangeable.” A major policy issue with this legislation is whether or not physicians should be notified when such a substitution is made. Due to the exceptionally complex and unique nature of biological medications and the many ways they differ from conventional drugs like aspirin and ibuprofen, there are important reasons for pharmacists to notify physicians when they make substitutions.

BIOLOGICAL MEDICATIONS (“BIOLOGICS”) DIFFER FROM CONVENTIONAL DRUGS

Although pharmacists can legally substitute generic conventional drugs for one another without physician notification, therapeutically-interchangeable biologics are not generics. Generic drugs have been chemically verified to contain exactly the same active ingredient as the name-brand drug. However, generics are not possible for biologics because they have large, complex chemical structures that are extremely difficult to characterize.¹ Additionally, unlike conventional drugs, biologics are highly sensitive to their manufacturing methods. Even seemingly minor changes in the manufacturing process can lead to significant chemical alterations in biological medications.² Because of the substantial differences between biologics and conventional drugs, the two classes of products are regulated differently by the Food and Drug Administration (FDA).

PHYSICIAN NOTICE PROMOTES PATIENT SAFETY

Physicians are committed to providing the safest and most effective treatments for their patients. When prescribing treatments, doctors carefully weigh the expected benefits and risks, and take responsibility for treating side effects.



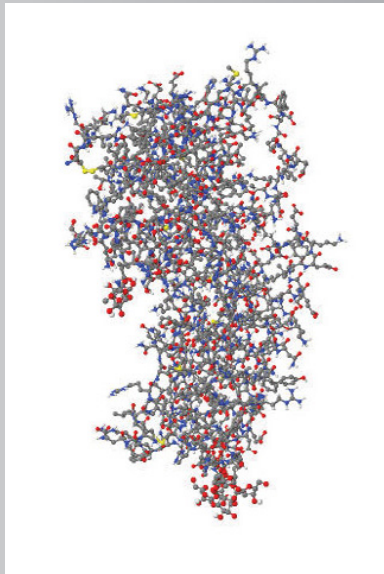

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For patients with serious conditions such as multiple sclerosis, cancer, rheumatoid arthritis, and certain movement disorders, biological medications often produce substantial, life-changing improvements that are not seen with conventional drugs. Like all treatments, biologics may be associated with side effects in some patients. If patients do experience side effects, physician notice of a pharmacist's substitution allows the doctor to identify which product caused the adverse reaction so that the patient can be switched to a different biologic if needed.

Moreover, physicians must be able to track the exact biological medication associated with major or unexpected side effects so that they can be reported to the manufacturer and the FDA. Although rare, real-world instances have been documented in which a change in the manufacturing method of a biologic led to a change in the protein structure³ or

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SOME DIFFERENCES BETWEEN BIOLOGICAL PRODUCTS AND CONVENTIONAL DRUGS¹

Characteristics	Biological Protein Product	Conventional Drug
Source	Made by living cells or organisms	Made in a laboratory using chemical reactions
Size	Large	Small
Structure	Complex	Simple
Example of Structure	 <p>Protein structure from RCSB Protein Data Bank, Identifier #1AU1</p>	 <p>Ibuprofen</p>
Generics possible?	No	Yes

caused a detrimental immune reaction.⁴ In both of these cases, the exact biological medications could be identified and the problems could be solved. If patients begin experiencing major side effects that can't be traced to a specific product, manufacturing of all the biological medications in that class may need to be shut down until the problem can be identified. For patients with progressive conditions like multiple sclerosis and cancer, lack of access to their biological medication could lead to permanent disability and even death.

Thus, to promote patient safety and well-being, physicians should receive prompt notification when pharmacists switch a prescribed biological medication.

PHYSICIAN NOTICE OPTIMIZES PATIENT OUTCOMES

Another important reason for physician notification of biologic substitution is the optimization of patient outcomes. Although two biological medications may not show any differences in the outcomes measured in clinical studies, they may still have significant differences that could influence how

the medications act in individual patients. As a result, even though two biologics may be therapeutically interchangeable, their biochemical or manufacturing differences may mean that some patients fare better on one biological medication better than another.

For example, patients with certain genetic variations or multiple health problems may have more intense immune reactions or metabolize one or the other biologic differently, leading to a higher likelihood of side effects. In such cases, it is critical that the physician know exactly which biological medication the patient received. If a patient complains that he or she doesn't feel well after filling a new prescription, the physician can only change him or her back to the originally prescribed biological medication if given prompt notice as to which biologic was dispensed by the pharmacy.

PHYSICIAN NOTICE FURTHERS HEALTHCARE TRANSPARENCY

Today's healthcare climate is witnessing a trend toward increased transparency, such that patients, physicians, and, when appropriate, insurers all have access to health-related

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information that may benefit patients. This permits a better understanding of which therapies are working for which patients. Additionally, pharmacies are offered financial incentives to switch medications, and they may or may not pass the savings on to patients and insurers. Notifying physicians when a therapeutically interchangeable biologic is substituted provides a necessary measure of transparency.

REBUTTING THE ARGUMENTS AGAINST NOTIFYING PHYSICIANS OF A BIOLOGIC SUBSTITUTION

Despite the strong reasons for notifying physicians when a therapeutically interchangeable biologic is substituted, some believe that this notification is not necessary or even detrimental. Opponents of notification contend that identifying which product was given to patients could lead to patient and prescriber confusion, causing medication errors. However, the opponents of physician notification cite no evidence that notifying a patient's physician that a substitution has taken place will lead to confusion or medical error. Furthermore, patients uniquely trust their physicians to be responsible for prescribing their therapy.

Another contention of those opposed to physician notification is that requiring notice would interfere with state laws on generic substitution of conventional drugs. As previously noted, biological medications are fundamentally different from conventional drugs and, because of these differences, there can be no generic biologics—a point that has already been accepted by the FDA and regulatory agencies in many other countries worldwide. Thus, biologics are already regulated differently than conventional drugs, and requiring physician notice when a biologic has been switched would be in keeping with this distinction.

WHAT DOES IT MEAN TO SAY THAT BIOLOGICAL MEDICATIONS ARE THERAPEUTICALLY INTERCHANGEABLE?

Due to differences in manufacturing processes and the exceptionally complex structure of some biologics, creating a generic copy is not possible. However, clinical comparison studies may show that two biologics used at the same doses are similarly safe and effective. If enough evidence is available, the FDA may consider such medications “therapeutically interchangeable.”

CONCLUSIONS

Biological medications differ substantially from conventional drugs and are classified differently by the FDA; as a result, laws and regulations developed for conventional drugs cannot be applied to biologics. Under current state laws, pharmacists may substitute conventional generic drugs for name-brands without notifying the physician. However, with therapeutically interchangeable biologics, underlying differences in the medications or their manufacturing methods may cause adverse events in some patients or may lead individual patients to respond better to one biologic than another. Physicians must be able to determine exactly which biological medication was given so that they can optimize treatment for each patient. Moreover, in a transparent healthcare system, patients and physicians have a right to know exactly which medication patients receive. In short, physicians must be notified when pharmacists substitute biologics so that they can direct the best course of treatment for their patients, whose well-being is in the balance.

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