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Summary

This ***Fiscal Research Brief (FRB)*** provides an overview of nonmedical switching and the practice of drug product selection (substitution). This ***FRB*** includes information regarding who may initiate and who may block a nonmedical switch; the roles of several actors such as patients, pharmacies, pharmacists, pharmacy benefits managers, prescribing practitioners, and the United States Food and Drug Administration (FDA); and a comparison of the substitution laws in Iowa and Iowa's surrounding states.

Affected Agencies

Iowa Board of Pharmacy
Iowa Department of Health and Human Services
Iowa Insurance Division, Department of Commerce

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Nonmedical Switching

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Introduction

Nonmedical switching refers to a change in a patient's medication for a nonmedical reason. Common examples of reasons for a nonmedical switch include a change in the patient's insurance plan or the availability of a less expensive, but therapeutically, equivalent, drug. Across the U.S., the laws surrounding the topic have been the focus of some legislatures, and the criteria for nonmedical switching varies. This ***FRB*** is intended to provide an overview of nonmedical switching, the laws around nonmedical switching, and how Iowa's neighboring states have handled nonmedical switching. There is an appendix at the end of this ***FRB*** with the definitions of several of the terms used throughout the ***FRB***.

Overview

One actor that may call for a nonmedical switch is a pharmacy benefits manager (PBM). PBMs are companies that represent health insurers, self-insured employers, union health plans, and government purchasers in the selection, purchase, and distribution of pharmaceuticals. PBMs influence which drug products are used most frequently and set terms for how much pharmacies are paid for their part in the process. As participants in the administration of drug benefits for over 266,000,000 Americans with health insurance, PBMs use their volume-buying leverage to negotiate discounts from manufacturers, typically in the form of rebates. PBMs are paid for their services using a mixture of fees, retained rebates, and other means.

PBMs are regulated in Iowa Code chapter 510B. Iowa Code section 510B.6 handles the selection of a substitute prescription drug for a prescribed drug, allowing a PBM to request the dispensing of a substitute prescription drug for a prescribed drug under either of the following conditions:

- If the substitution is for a lower-priced generic and therapeutically equivalent drug to replace a higher-priced prescribed drug, the PBM may request the substitution.
- If the substitute drug's net cost to the covered individual or covered entity is greater than the cost of the prescribed drug, the substitution shall only be made for medical reasons that benefit the covered individual.

Iowa Code section 510B.6 additionally states the following:

- A PBM is required to obtain the approval of the prescribing practitioner prior to requesting any substitution in accordance with this section.
- A PBM is not allowed to substitute an equivalent prescription drug if the existing prescription drug order prohibits a substitution.

A prescribing practitioner can write a variety of messages on the prescription to prevent substitutions from taking place. Messages that state that the brand-name drug is "medically necessary," or that state "no substitution should be made," "do not interchange," or "dispense as written/D.A.W.," would all prevent a substitution. According to the National Conference of State Legislatures (NCSL), these messages would prevent a substitution in all 50 states.

A vital part of nonmedical switching revolves around the idea that the substitution is "therapeutically equivalent." The United States Food and Drug Administration (FDA) classifies drug products as therapeutically equivalent only if they meet the following criteria:

- They are pharmaceutical equivalents (contain the same active ingredient(s), dosage form and route of administration, and strength).
- They are assigned by the FDA the same therapeutic equivalence codes starting with the letter "A."

- The drug product designates a brand-name drug or generic drug to be the reference drug product.
- The drug product has therapeutic equivalence codes assigned to it based on data that a drug sponsor submits in an abbreviated new drug application number to demonstrate that its product is bioequivalent (i.e., performs in the same manner as the reference drug product).

In simple terms, a drug is deemed therapeutically equivalent if the substituted drug has the same clinical effect and safety profile as the reference drug product. This also requires the strength of the drug, method of uptake, and other factors to be the same as the reference drug product. Once a drug has passed the FDA's requirements for therapeutic equivalence, the drug is placed into the publication "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Some states, including Iowa, use the Orange Book to help determine which medicines can be safely substituted by pharmacists for one of equal standing. This is called a positive formulary, whereby the drugs on the list are approved as equal to the brand-name drug. Some other states use what is known as a negative formulary, which creates a list of drugs that are not equivalent to a brand-name drug. It is important to keep in mind that therapeutic equivalence does not refer to two different ingredients that are used to treat the same condition (e.g., ibuprofen and naproxen).

The world of pharmaceuticals includes many classifications. One relevant classification is narrow therapeutic index drugs (NTIs). According to the FDA, NTIs are drugs for which small differences in dose or blood concentration may lead to serious therapeutic failures and/or adverse drug reactions that are life-threatening or result in persistent or significant disability or incapacity. There are concerns that switching from a reference drug product, which is an approved drug product, to a generic version, even if it has been cleared as therapeutically equivalent, may trigger an adverse reaction. Due to this, there are restrictions in some states for substitution for entire therapeutic categories. For example, in Connecticut, Hawaii, Illinois, Tennessee, and Utah, generic substitution for antiepileptic drugs is prohibited due to concerns of potential adverse reactions due to their narrow therapeutic index. As of the publication date of this ***FRB***, Iowa does not have restrictions on drug classifications in this manner.

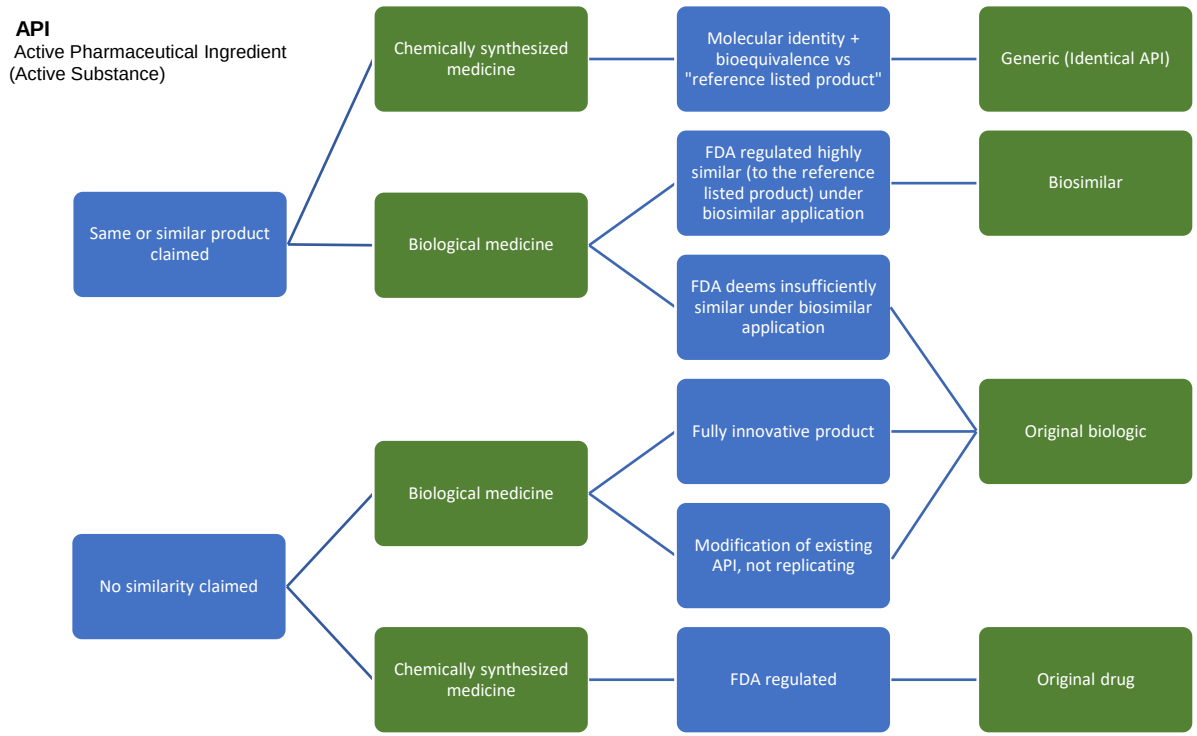
The FDA notes that broad implementation of tighter standards for NTI drugs is challenging, as most potential NTI drugs lack an NTI classification. The FDA explains that the lack of the classification is, in part, due to the difficulty in characterizing the therapeutic index. Within the FDA, there is an Office of Generic Drugs (OGD), which is tasked with ensuring that high-quality, affordable generic drugs are available to the American public. The OGD's responsibilities include reviewing applications for the approval of generic drugs and interacting with external stakeholders, such as physicians, pharmacists, patients, and patient advocacy groups, to investigate reports of adverse events or therapeutic inequivalence of generic drugs. Numerous methods have been tried for analyzing drug approval data and safety/efficacy usage data to ensure interchangeability between reference listed drugs and generic NTI drugs. The OGD states that it focuses on methods for identifying NTI drugs and ensuring risk-based bioequivalence and product quality standards. Additionally, the OGD states that the movement from "one-size-fits-all" to product-specific standards is a sign of the maturation of the generic drug program.[1]

There is also a more requirement-laden type of drug product, which are therapeutic biological products ("biological drug products" or "biologics"). The FDA defines these as "a protein derived from living material (such as cells or tissues) used to treat or cure disease." These products are newer and more difficult to replicate than traditional chemically synthesized drugs. The chemical composition of traditional drugs can be tested to help determine equivalence. Biological drugs, due

[1] Source: FDA, FY 2015 Regulatory Science Research Report: Narrow Therapeutic Index Drugs

to their use of living material, can vary even within the same process by a single manufacturer. Due to this potential for variation, biological drugs do not have generic equivalents in the same sense that chemically synthesized drugs do. Instead, there are biosimilar drugs that are produced. The FDA has a listing of approved biological products, alongside biosimilar and interchangeable biological products, in a database known as the Purple Book. This database allows an individual to see which biological products have been approved by the FDA, as well as which biological products have been deemed biosimilar due to similarity to the original reference drug product. **Figure 1** displays the FDA approval process applied to generic drugs, biological drugs, and biosimilar drugs.

Figure 1 — Chemically Synthesized vs. Biological Drugs and the Path to FDA Approval



Sources: FDA, Approval Process for Generic Drugs, Approval Process for Biosimilar Products
British Journal of Clinical Pharmacology, Biosimilar: What It Is Not

As published in the NCSL's Prescription Drug Resource Center column, according to the IQVIA Institute for Human Data Science, generic drugs make up approximately 90.00% of all prescriptions but comprise only a fraction of overall drug spending. Brand-name drugs make up the remaining approximately 10.00% of prescriptions but account for approximately 79.00% of all drug spending. Much of the debate around nonmedical switching comes down to the cost-saving potential of generic and biosimilar drugs versus the uncertain effects of the switch. Factors that have an impact on the cost profile of a medication include drug price, rebates, health care resource utilization, administrative costs, and more.

Current Iowa Law

As mentioned earlier, Iowa Code section 510B.6 regulates the scenarios in which PBMs are allowed to request a change in a patient's medication. Iowa Code section 510C.2 requires each PBM to provide an annual report to the Iowa Insurance Division's (IID) Commissioner. The report must include the following:

- The aggregate dollar amount of all rebates received by the PBM.

- The aggregate dollar amount of all administrative fees received by the PBM.
- The aggregate dollar amount of all health carrier administrative service fees received by the PBM.

Additionally, the report must also include both the aggregate dollar amount of all rebates received by the PBM that were not passed through to the third-party payor (see appendix) and the aggregate amount of all administrative fees received by the PBM that were not passed through to the third-party payor. The report must also include the aggregate retained rebate percentage as calculated in the formula shown in **Figure 2** below.

Figure 2 — Calculation of the Percentage of the Aggregate Rebate Retained by the PBMs

Source: Iowa Code section 510C.2

Finally, the annual report that the PBM is required to submit to the IID Commissioner must include the highest and lowest aggregate retained rebate percentages across all third-party payors with which the PBM was contracted. The 2022 summary indicates, for PBMs claiming an aggregate rebate of $1,000,000 or more, that the aggregate retained rebate percentage varies between 0.00% and 24.01%. The average aggregate retained rebate percentage of the PBMs claiming an aggregate rebate of $1,000,000 or more is approximately 18.04%. This equates to approximately $34,557,300 of $191,562,449 in aggregate rebates for PBMs claiming an aggregate rebate of $1,000,000 or more. **Figure 3** below summarizes the reports for PBMs claiming an aggregate rebate of $1,000,000 or more.

Figure 3 — Summary of the Annual Report Data for PBMs Claiming an Aggregate Rebate of $1,000,000 or More

Name	Aggregate Rebate	Aggregate Retained Rebate	Aggregate Retained Rebate Percentage
PBM 1	$ 102,364,949	$ 19,827,183	19.37%
PBM 2	1,374,966	200,288	14.57%
PBM 3	6,589,221	20,028	0.30%
PBM 4	59,389,215	14,258,440	24.01%
PBM 5	6,057,098	0	0.00%
PBM 6	15,787,000	251,361	1.59%
Composite	**$ 191,562,449**	**$ 34,557,300**	**18.04%**

Source: IID, Pharmacy Benefits Manager 2022 Annual Report for Calendar Year 2021

Iowa Code chapter 155A (Iowa Pharmacy Practice Act) states that the purpose of the chapter is to "promote, preserve, and protect the public health, safety, and welfare through the effective regulation

of the practice of pharmacy and the licensing of pharmacies, pharmacists, and others engaged in the sale, delivery, or distribution of prescription drugs and devices." Under Iowa Code section 155A.32, pharmacists are allowed to substitute a drug product with the same generic name (see Appendix on p. 11) and demonstrated bioavailability as the prescribed drug product. Similarly, pharmacists are allowed to substitute a biological product that is an interchangeable biological product for the prescribed biological product. If any portion of the drug product or biological product is paid for by public funds authorized under Iowa Code chapter 249A, the pharmacist is required to select a substitution or an interchangeable biological product, respectively. The drug product selection must be consistent with the Preferred Drug List Program as established under Iowa Code section 249A.20. The pharmacist may not substitute the prescribed drug if either of the following conditions exist:

- The prescriber indicates that no substitution shall be made.
- The person presenting the prescription objects to the substitution (unless any portion of the prescription is paid for by public funds).

If a substitution occurs, the pharmacist must notify the patient. When a biological product is dispensed, the name and manufacturer of the biological product must be communicated to the prescriber, unless there is no FDA-approved interchangeable biological product for the product prescribed or the refill prescription is not changed from the previous filling of the prescription.

Other States

The six states that border Iowa (Illinois, Nebraska, Minnesota, Missouri, South Dakota, and Wisconsin) have their own laws regarding the conditions under which drug product selection, the practice of substituting either a therapeutically equivalent or an interchangeable biological product for a prescription drug order, may occur. See **Figure 4** at the end of this section for a summary comparison of all seven states.

All six bordering states require the FDA to determine that the substituted drug product is either therapeutically equivalent to or, in the case of biological products, interchangeable with the prescribed drug product. Each state's statute refers to the FDA's Orange Book, while some also refer to the FDA's Purple Book.

Whether the substituted product is required to be less expensive than the prescribed product varies by state, the funding source for the prescription, and whether the drug is a biological product. States also vary in the requirements to inform patients of substitution that has taken, or may take, place. The requirements include factors such as relative drug cost, prescription coverage, and type of drug (biological vs. nonbiological).

Each state allows the prescribing practitioner to block substitution. The blocking of substitution can be done via a "dispense as written," or a similarly worded, message on the prescription order. Some states prohibit the prescriber from maintaining this wording as a default on all prescriptions. In Missouri, certain portions of the state, which is determined by the prescriber's location, allow substitution without the prescriber's approval. The patient's ability to block substitution also varies by state and, for Iowa, prescription funding source.

Some states have a requirement to inform patients of any substitution for biological drugs. Iowa, and all six surrounding states, requires a notification to the prescribing practitioner when a biological drug product is dispensed, unless there are no FDA-approved interchangeable biological products for the product prescribed or a refill prescription is not changed from the prior filling of the prescription. Nebraska requires this notification to be within three business days; each other state requires this notification to be within five business days.

Protections for pharmacists and prescribing practitioners facing negligence accusations vary by state and drug type (legend vs. nonlegend). Legend drugs are drugs that require a prescription to be dispensed; nonlegend drugs do not require a prescription. In the state summaries in **Figure 4**, if the drug type is not indicated, both biological and nonbiological drugs are included in the protections.

Some states have additional substitution restrictions dependent upon what the drug is meant to treat. Substitution of antiepileptic drugs is additionally restricted in Illinois, while Minnesota has a trigger to add restrictions on the substitution of antiepileptic drugs if the FDA finds that the substitution of these drugs poses a health risk to patients.

Of the six states analyzed, Minnesota and Wisconsin require signage indicating that substitution may occur and detailing what input the patient has regarding the substitution.

Finally, there are many laws addressing substitution for hospitals, persons under a managed health care plan that maintains a closed drug formulary, and non-brand-name refills.

Illinois — The Illinois Pharmacy Practice Act provides that pharmacists may substitute prescription drug orders in accordance with the following requirements:

- Nonbiological drug products require the substituted drug product to have a unit price less than the prescribed drug product.
- For all drug products, the pharmacist must inform the patient if the drug costs less without prescription drug coverage.

In general, the patient is not allowed to block substitution. However, Illinois prohibits the substitution of antiepileptic drugs without patient and prescriber consent when the prescriber has originally indicated "dispense as written." This does not apply to in-patient care in a licensed hospital.

Illinois also requires that the patient be informed when substitution occurs for biological drug products. A pharmacy must also notify the prescribing official when a biological drug product is dispensed, unless there are no FDA-approved interchangeable biological products for the product prescribed or a refill prescription is not changed from the prior filling of the prescription. This notification must occur within five business days of the biological drug product being dispensed. Illinois provides protection against negligence accusations for pharmacists and prescribing practitioners for nonlegend drugs. All pharmacies must post a notice informing customers that customers may request the price of any prescription drug.

Nebraska — The Nebraska Pharmacy Practice Act provides that pharmacists may substitute prescription drug orders in accordance with the following requirements:

- The substitution of biological drug products requires the patient to be informed of the substitution.
- The substitution of nonbiological drug products requires the patient to consent to the substitution.

A pharmacy must notify the prescribing official when a biological drug product is dispensed, unless there are no FDA-approved interchangeable biological products for the product prescribed or a refill prescription is not changed from the prior filling of the prescription. This notification must occur within three business days of the biological drug product being dispensed. The notification timeline is two business days shorter than the notification timeline for Iowa and the other states that border Iowa.

Nebraska provides protection against negligence accusations for pharmacists and prescribing practitioners who are substituting within reason. Additionally, Nebraska law dictates that when "dispense as written" is indicated by the prescriber, the party that has contracted to reimburse the patient is required to make reimbursements on the amount for the brand-name drug, unless the contract specifically requires generic reimbursement.

Minnesota — Minnesota Statutes chapter 151 (Pharmacy Practice and Wholesale Distribution Act) provides pharmacists may substitute prescription drug orders in accordance with the following requirements:

- A substituted drug product must cost less than the prescribed drug product and, when a pharmacist is dispensing a substituted drug product, the pharmacist is required to dispense the least expensive alternative.
- A pharmacist must disclose any substitutions to the patient and, unless the patient objects, dispense the substituted drug product.
- Substitution is not allowed for persons under a managed health care plan that maintains a mandatory or closed drug formulary.

A prescribing practitioner may not maintain "dispense as written" as a default on all prescriptions. Minnesota requires pharmacies to post a sign indicating that substitution may occur and detailing what input the patient has regarding the substitution. Finally, Minnesota has formed a Drug Formulary Committee, which established, and annually updates, a list of drug products that are excluded from substitution. Minnesota has a trigger for antiepileptic drugs to become restricted from substitution if the FDA finds that the substitution of these drugs poses a health risk to patients.

Missouri — Missouri Revised Statutes chapter 338 (Pharmacists and Pharmacies) provides that pharmacists may substitute prescription drug orders in accordance with the following requirements:

- Drug product substitution requires the substituted drug product to cost less than the prescribed product.
- Certain areas of Missouri allow for drug product substitution without the prescribing practitioner's approval, dependent on the laws in the portion of the state the prescriber is located.
- The substitution of biological drug products requires the patient to be informed of the substitution.

Patients are allowed to block substitution for both biological and nonbiological drugs. Missouri provides protection against negligence accusations for pharmacists substituting generic or interchangeable biological drug products.

South Dakota — South Dakota Codified Law chapter 36-11 (Pharmacies and Pharmacists) provides that pharmacists may substitute prescription drug orders in accordance with the following requirements:

- The prescriber may not maintain "dispense as written" as a default on all prescriptions.
- The patient receiving a substituted drug product must be informed of the substitution and of the patient's right to refuse the substitution.
- Upon the request of the prescribing practitioner, the pharmacist is required to provide information regarding the substitution of equivalent drug products.
- The pharmacist may not substitute a drug product unless there are therapeutic equivalency ratings available for that drug product.

Protections are granted to pharmacists and prescribers with regard to substitutions under the above conditions, exposing them to no greater liability than had the substitution not taken place. South Dakota does not require the substituted drug product to be less expensive than the prescribed drug product.

Wisconsin — Wisconsin Statutes chapter 450 (Pharmacy Examining Board) provides that pharmacists may substitute prescription drug orders in accordance with the following requirements:

- A substituted drug product must cost less than the prescribed drug product, and a pharmacist must disclose any substitution options to the patient.
- The prescribing practitioner is not permitted to preprint a statement regarding substitution.
- The patient is allowed to block substitution.

Additionally, non-brand-name drug refills may be substituted for different non-brand-name equivalent drugs, but only if the patient is informed of the change. Protections are granted to pharmacists with regard to substitutions under the above conditions, exposing them to no greater liability than had the substitution not taken place. The dispensing of drug product equivalents in hospitals may ignore the above requirements and follow the written guidelines or procedures previously established by a pharmacy and therapeutics committee of the hospital and approved by the hospital's medical staff if the use of the drug product equivalent has been approved for a patient during the period of the patient's stay within the hospital by the patient's individual physician, the patient's advanced practice nurse prescriber who has a written agreement to collaborate with a physician, or the patient's physician assistant.

Figure 4 below summarizes the laws for Iowa and the six surrounding states.

Figure 4 — Summary Comparison of Substitution Laws for Iowa and the Surrounding States

	Iowa	Illinois	Nebraska	Minnesota	Missouri	South Dakota	Wisconsin
Substitution Allowed	Yes[1]	Yes	Yes[2]	Yes	Yes[3]	Yes	Yes
Less Expensive Required	No[4]	Yes[5]	No	Yes	Yes	No	Yes
Additional Requirements	[1]Patient must be informed of substitution [4]Required if any portion of the prescription is funded with public Medicaid funds	[5]For nonbiologics, and the pharmacist must inform customer if the drug costs less without Rx drug coverage	[2]Patient must be informed for biologic and consent for nonbiologic substitution	Patient disclosure and consent required	[3]Patient must be informed for biologic substitution	Prescriber may require pharmacist to provide substitution information	Pharmacist must inform patient of substitution option(s)
Prescribing Practitioner Allowed to Block	Yes	Yes	Yes	Yes	Yes[6]	Yes	Yes
Conditions	No	No	No	Prescribers may not maintain "D.A.W." as a default on all prescriptions	[6]Prescriber's location may allow substitution w/o prescriber's approval	Prescribers may not maintain "D.A.W." as a default on all prescriptions	No preprinted statement regarding substitution permitted

[1] The patient must be informed of the substitution. [2] The patient must be informed for biologic and consent for nonbiologic substitution. [3] The patient must be informed for biologic substitution. [4] Required if any portion of the prescription is funded with public Medicaid funds. [5] For biologics, and the pharmacist must inform the customer if the drug costs less without prescription drug coverage. [6] The prescriber's location may allow substitution without the prescriber's approval.

Figure 4 Continued — Summary Comparison of Substitution Laws for Iowa and the Surrounding States

	Iowa	Illinois	Nebraska	Minnesota	Missouri	South Dakota	Wisconsin
Patient Allowed to Block	Yes[7]	No	Yes	Yes	Yes	Yes	Yes
Conditions	[7]Unless any part of the prescription is paid for with public Medicaid funds	N/A	No	No	No	Must inform patient of, and allow patient to refuse the substitution	No
Substitution Signage Required	No	No	No	Yes	No	No	Yes
Additional Requirements for Biological Drugs	No	Patient informed of substitution	Patient informed of substitution	No	Patient informed of substitution	No	No
Biological Drug Notification to Prescriber Requirements	Yes, 5 business days	Yes, 5 business days	Yes, 3 business days	Yes, 5 business days	Yes, 5 business days	Yes, 5 business days	Yes, 5 business days
Orange Book Mentioned in Statute	Yes	Yes	Yes, and Purple Book	Yes, and Purple Book	Yes	Yes	Yes
Protection Against Negligence Accusations	No	Yes, for nonlegend drugs	Yes	No	Yes, for pharmacists	Yes	Yes, for pharmacists
Other Restrictions	No	Antiepileptic drugs may not be substituted without patient and prescriber's consent. Does not apply to in-patient care in a hospital	No	Substitution not allowed for persons under a managed health care plan that maintains a mandatory or closed drug formulary	No	No	Drug product equivalent dispensation in hospitals follows the guidelines of hospital medical staff and requires approval of the patient's physician
Other	No	Pharmacy must post notice informing customers they may request the price of any prescription drug	When "D.A.W." indicated, reimbursement amount must be based on brand-name drug, unless contract requires generic reimbursement	The drug formulary committee shall establish a list of excluded drug products	None	Therapeutic equivalency ratings required, hospitals must follow prescriber order	Non-brand-name refills may be substituted for different non-brand-name equivalent drugs only if the patient is informed of the change

[7] Unless any part of the prescription is paid for with public Medicaid funds.

Sources: Iowa Code, Minnesota Statutes, Missouri Revised Statutes, Nebraska Revised Statutes, South Dakota Codified Laws, Wisconsin Statutes. (Refer to the sources listed at the end of this ***FRB*** for additional details.)

Conclusion

Nonmedical switching is the changing of a patient's medication for a nonmedical reason. It often occurs as a cost-saving measure. Iowa's laws regarding nonmedical switching require the substituted drug product to either have the same bioavailability as the reference drug product, or to have been determined by the FDA to be an interchangeable biological product with the reference drug product. Nonmedical switching may not occur if the prescriber has indicated that no substitution may occur. The dispensing pharmacist may exercise professional judgement in the economic interest of the patient by performing a substitution. Unless any portion of the prescription is funded through public funds under Iowa Code chapter 249A (Medical Assistance Act), the patient may decline the substitution. Additionally, when a biological product that has an FDA-approved interchangeable biological product is dispensed, the pharmacy must notify the prescriber within five business days, unless it is a refill prescription that was not changed from the previous filling.

It should be noted that biosimilar and generic drugs are not the same. Generic drugs refer to chemically synthesized drugs, which have a known structure and are typically easily identified or characterized. Biological products, and therefore biosimilars, are often complex mixtures that are not easily identified or characterized.

Appendix — Definitions

"**API**" stands for active pharmaceutical ingredient. These are the substances in drugs that are responsible for the beneficial health effects experienced by consumers. An example of an API is the acetaminophen in a pain relief tablet. An active pharmaceutical ingredient may also be referred to as an "active ingredient" or an "active substance."

"**Bioavailability**" refers to the proportion of a drug that enters the circulation when introduced into the body and is, therefore, able to have an active effect. Without bioavailability, the drug will not take effect.

"**Bioequivalent**." According to the FDA, two products are considered to be bioequivalent when they are equal in rate and extent to which the active pharmaceutical ingredient becomes available at the site(s) of drug action.

"**Biological product**" is a diverse category of products. These products are generally large, complex molecules. These products may be produced through biotechnology in a living system, such as a microorganism, plant cell, or animal cell, and are often more difficult to characterize than small molecule drugs. There are many types of biological products approved for use in the United States, including therapeutic proteins (such as filgrastim), monoclonal antibodies (such as adalimumab), and vaccines (such as those for influenza and tetanus).

"**Biosimilar**" means a biological product that is highly similar to, and has no clinically meaningful differences from, an existing FDA-approved reference product. No clinically meaningful difference checks against product safety, purity, and potency (safety and effectiveness). Biosimilar drugs must pass tests by the FDA to receive this label.

"**Chemically synthesized drug product**" refers to a drug product with well-defined structures that can be thoroughly characterized. Examples of chemically synthesized drug products include acetaminophen and ibuprofen.

"**D.A.W.**" stands for "dispense as written," an order a prescribing practitioner can make for a pharmaceutical product the practitioner prescribes. This order indicates to the dispensing pharmacist that drug product selection may not occur and that the prescribed drug product is the only drug product that may be dispensed with the prescription order. Additional terms with a similar

meaning that may be used include "brand name medically necessary," "medically necessary," "do not substitute," and "no generic."

"**Drug product selection**" refers to the interchange for a prescribed pharmaceutical product. This is typically done by a pharmacist and is often referred to as "substitution."

"**Generic name,**" as defined in Iowa Code section 155A.3, means the official title of a drug or drug ingredient published in the current official United States Pharmacopeia and National Formulary, official Homeopathic Pharmacopoeia, or other drug compendium published by the United States Pharmacopoeia (USP) Convention or any supplement to any of these compendia.

"**Health care resource utilization**" refers to the total use of all health care-related expenses by a patient. This is often used as a measure for total cost of health care, as it encompasses the broad spectrum of health care costs. Health care resource utilization may be abbreviated as HCRU.

"**Interchangeable biological product**" refers to a biosimilar product that meets additional FDA requirements. These additional requirements are outlined by the Biologics Price Competition and Innovation Act at the federal level. The requirements include showing that an interchangeable product is expected to produce the same clinical results as the reference product for any given patient. Additionally, for products administered to patients more than once, the risk in terms of safety and reduced efficacy of multiple switches between an interchangeable product and a reference product must be evaluated by the FDA.

"**Legend drug**" refers to a drug that is available only with a prescription.

"**Nonlegend drug**" refers to a drug that is available without a prescription.

"**Nonmedical switching**" means the changing of a stable patient's medication for reasons unrelated to the patient's health. The practice may also be referred to as "formulary-driven switching," "therapeutic switching," or simply "switching."

"**NTI**" stands for "narrow therapeutic index," which refers to drugs for which small differences in dose or blood concentration may lead to serious therapeutic failures and/or adverse drug reactions, making substitution potentially unsafe. The FDA states that NTI drugs are difficult to classify; therefore, most potential NTI drugs lack NTI classification.

"**Orange Book**" refers to the FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations." The Orange Book does not include biological products; those products are found in the FDA's Purple Book.

"**PBM**" refers to pharmacy benefits managers, which are companies that represent health insurers, self-insured employers, union health plans, and government purchasers in the selection, purchase, and distribution of pharmaceuticals. PBMs influence which drug products are used most frequently and set terms for how much pharmacies are paid for their part in the process. As participants in the administration of drug benefits for over 266,000,000 Americans with health insurance, PBMs use their volume-buying leverage to negotiate discounts from manufacturers, typically in the form of rebates. PBMs are paid for their services using a mixture of fees, retained rebates, and other means.

"**Prescriber**" refers to a prescribing practitioner.

"**Purple Book**" refers to the FDA's online database that contains information about biological products, including biosimilar and interchangeable biological products, licensed (approved) by the FDA under the Public Health Service Act. The list includes the reference drug products of biosimilar and interchangeable products.

"**Reference drug product**" refers to a single drug product against which the FDA evaluates an application for a new drug product. Reference drug products are used to establish bioequivalence,

biosimilarity, interchangeable biological products, and generic drug products. This may also be referred to as a "reference listed drug product."

"**Therapeutically equivalent**" means a drug product that has been established by the FDA to be able to be substituted with the full expectation that the substituted product will produce the same clinical effect and safety as the prescribed product.

"**Third-party payor,**" as defined by House File 2384 (Pharmacy Benefits Managers), means any entity other than a covered person or a health care provider that is responsible for any amount of reimbursement for a prescription drug benefit. "Third-party payor" includes health carriers and other entities that provide a plan of health insurance or health care benefits. "Third-party payor" does not include any of the following:

- The Department of Health and Human Services (DHS).
- A managed care organization acting pursuant to a contract with the Department of Health and Human Services to administer the medical assistance program under chapter 249A or the Healthy and Well Kids in Iowa (hawki) program under chapter 514I.
- A policy or contract providing a prescription drug benefit pursuant to 42 U.S.C. ch. 7, subch. XVIII, part D.

Sources

Commonwealth Fund, Pharmacy Benefit Managers and Their Role in Drug Spending (2019), available at doi.org/10.26099/njmh-en20

Fernando de Mora, Biosimilar: What It Is Not, British Journal of Clinical Pharmacology 80(5), p. 950 (2015), available at doi.org/10.1111/bcp.12656

Homoeopathic Pharmacopoeia of the United States (HPUS)

Illinois Compiled Statutes — 225 Compiled Statutes 85 (Pharmacy Practice Act)

Iowa Code chapters 155A (Iowa Pharmacy Practice Act), 249A (Medical Assistance Act), 505 (Insurance Division), 510B (Regulation of Pharmacy Benefits Managers), and 510C (Pharmacy Benefits Manager Reporting).

Iowa Insurance Division, Department of Commerce — PBM 2022 Annual Report

Minnesota Statutes — Chapter 151 (Pharmacy Practice and Wholesale Distribution Act)

Missouri Revised Statutes — Chapter 338 (Pharmacists and Pharmacies)

National Conference of State Legislatures (NCSL)

Nebraska Revised Statutes — Chapter 38, sections 38-2801 through 38-28,116 (Nebraska Pharmacy Practice Act)

South Dakota Codified Laws — Chapter 36-11 (Pharmacies and Pharmacists)

United States Code — 42 U.S.C. §262 (Biological Products), 42 U.S.C. §1395w (Medicare Part D)

United States Food and Drug Administration (FDA)

United States Pharmacopeia and National Formulary (USP-NF)

Wisconsin Statutes — Chapter 450 (Pharmacy Examining Board)

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