

Authorized generics

INTRODUCTION

A generic drug is one that has been determined to be bioequivalent to a brand-name drug and has the same dosage, safety, strength, route of administration, quality, performance characteristics and intended use. Approximately 63% of all prescriptions in the United States are filled with generic drugs; the estimate of generic drug sales amounts to \$35 billion dollars annually.¹ Generic drugs are chemically identical to the branded drug, but they are generally sold at substantial discounts from the brand-drug price. According to the Congressional Budget Office, generic drugs save consumers an estimated \$8 billion to \$10 billion a year at retail pharmacies.² Even more billions are saved when hospitals use generics.

Authorized generics are a type of generic drug. They are manufactured and distributed by a subsidiary of the brand-name drug company or by a generic company approved by the brand-name company. Even though authorized generics may be manufactured by a subsidiary of the brand-name drug manufacturer they, like generic drugs, are less expensive than the brand-name drug.

This lesson will review the origin of generic drugs, the development of authorized generics and their benefits/advantages, and customer questions that may arise

about brand-name, generic and authorized generic drugs.

GENESIS OF GENERIC PHARMACEUTICALS

The generic drug industry developed following the passage of the Drug Price Competition and Patent Term Restoration Act, generally known as the Hatch-Waxman Act. Enacted in 1984, the law created the framework for generic drugs to compete with brand-name drugs. In that year, only 18.6% of U.S. prescriptions were written for generic products.¹ The goal of the Hatch-Waxman Act was to encourage greater price competition in the prescription-drug market without jeopardizing the intellectual property rights of the brand-name drug manufacturers, which had spent many years and considerable money researching and developing the drugs. (A brand-name drug company's investment is protected by a patent, which gives the company the exclusive right to sell the drug while the patent remains in effect).^{2,3}

There are three significant ways in which the new law changed the rules of competition. First, prior to enactment of the Hatch-Waxman Act, generic-drug manufacturers were required by the FDA to perform the same safety and efficacy trials as had the brand-name manufacturers. Faced with these expensive and extensive requirements, many potential

generic-drug manufacturers determined that it was not economical to develop a generic formulation. The Hatch-Waxman Act shortened the approval process for generic-drug manufacturers. Through an abbreviated new drug application, generic-drug companies are required only to establish that their product is the bioequivalent of the original drug and that their manufacturing processes meet the Food and Drug Administration standards. The institution of ANDAs meant that generic-drug manufacturers no longer have to replicate the clinical trials that had been conducted by the brand-name manufacturers.¹

Second, generic-drug manufacturers can conduct bioequivalence tests of a drug and apply for FDA approval before the applicable patents expire without incurring risk of patent-infringement lawsuits.¹

Lastly, the Hatch-Waxman Act provided mechanisms to resolve patent disputes between brand-name manufacturers and generic-drug firms. The need to resolve legal conflicts has been a critical — and necessary — element of the Hatch-Waxman Act. A generic-drug manufacturer realizes significant gains if it is the first company to successfully come to market; its ANDA is granted a 180-day period of exclusivity. Generic-drug manufacturers that want to compete with a brand product must assert that their product will not infringe current

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This program is accredited for 1.0 (one) hour of continuing education credit of which 1.0 (one) hour is considered pharmacology credit.

Program Goal: To increase retail clinicians' understanding of the characteristics of authorized generics and the role they play in optimizing patient care.

Learning Objectives:

Upon completion of this program, the clinician should be able to:

1. Relate the reasons for increased interest in and usage of generic drug products
2. Define authorized generics
3. Identify advantages/benefits of authorized generics
4. Counsel patients regarding authorized generics
5. Collaborate with other healthcare professionals on the use of authorized generics

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patents. If a brand-name manufacturer institutes a patent-infringement action within 45 days of the generic firm's non-infringement claim, the FDA cannot approve a generic product for 30 months or until the litigation is resolved.

AUTHORIZED GENERICS

Authorized generics result from the decision of the original, brand-name manufacturer to contract with another company to market a generic version of its drug. Authorized generics provide cost savings and give patients the confidence that they are getting the same products. Although it does not carry the brand name, an authorized generic drug contains all the same ingredients, even the inactive ones. Customers who have become accustomed to a branded product can be assured that they are taking the same product.

Currently, authorized generics accounts for 9% of prescriptions written in the United States, according to data from IMS Health reported in 2007.⁵ However, this is a growing industry, and it is likely that consumers and clinicians will see an increasing number of products available as an authorized generic.

BRAND-NAME V. GENERIC DRUGS — WHAT ARE THE DIFFERENCES?

The FDA has requirements for bioequivalence and manufacturing standards. To obtain FDA approval, a generic drug must:

- Contain the same active ingredients as the brand-name drug (inactive ingredients may vary)
- Be identical in strength, dosage form and route of administration
- Have the same use indications
- Be bioequivalent (Bioequivalence studies must demonstrate only that the generic version produces virtually the same levels of drug in the blood over time and require only a small number [24 to 36] of healthy volunteers.)

- Meet the same batch requirements for identity, strength, purity and quality
- Be manufactured under the same strict standards of FDA's manufacturing practice regulations required for innovator (i.e., brand-name) products

Although traditional generic products are similar to branded products in many ways, there are some differences. U.S. trademark laws do not allow generic drugs to look exactly like the brand-name drug. As a result, color and shapes, as well as the flavor, of generic drugs may be different from their brand-name counterparts.²

Inactive ingredients are generally harmless substances that have no adverse effects, but some may cause unusual and possibly severe allergic reactions in a few people. Consequently, one version, or brand, of a drug may be preferable to another in specific patients. For example, chemicals called bisulfites (such as sodium metabisulfite), which are used as preservatives in many products, may cause asthmatic allergic reactions. Drug products that contain bisulfites have prominent labels indicating this ingredient.³

There may be other reasons, particular to an individual patient, why substitution with traditional generic products may not be appropriate or desired. For example, some patients might be confused by differences in the shape or color of generic substitutes, while others may be allergic to the coating of the generic drug but not to that of the brand-name product (the reverse may also be true). These minor risks are increased when a pharmacy dispenses multiple manufacturers' versions of a generic drug.⁶ And some patients may not want a generic product, due to a perception that generic products are less effective or of lower quality.

Not all brand-name drugs have generic versions. A drug may be too difficult to

duplicate, or adequate tests are unavailable or cannot prove that the generic drug is the bioequivalent of the brand-name drug. It is possible that the market for a drug is so small that producing another version is not economically viable.³

The FDA publishes "Approved Drug Products with Therapeutic Equivalence Evaluations" (also known as the "Orange Book" because of its bright orange cover) annually, and it is available both in print and online (www.fda.gov/cder/ob/). Each new drug application in the "Orange Book" must list data about all the patents held by the manufacturer of each drug.

There is a steady increase in the number of brand-name drugs that are becoming available in generic form. In fact, according to the Generic Pharmaceuticals Association of the almost 12,000 branded products listed in the FDA's "Orange Book," almost 9,000 have a generic counterpart. The introduction of authorized generics has been more recent, with 100 to 150 authorized generic products currently available. However, this number is growing. Each year, additional authorized generic products are becoming available.

COST OF GENERIC DRUGS

The price of a generic drug tends to fall when the number of manufacturers of that generic drug increases. Most, but not all, generic forms of a branded drug, have an AB rating. Drugs with an AB rating can be substituted. The availability of multiple AB-rated generic forms of a specific drug creates price competition. When a generic drug first comes on the market, the generic manufacturer's suggested retail price may be 70% of the branded version. As competition among generic manufacturers becomes more intense, that price generally falls to 20% to 50% of the brand-name equivalent. Of course, the actual amount an individual pays will depend on whether they are enrolled in a program, such as employer health insurance or Medicaid Part D, that provides coverage for drug costs.

In these programs, the cost for generic drugs is usually relatively low. Persons without insurance must, of course, pay the full cost.⁸

The cost savings associated with generics can be significant. Using average national retail price data from IMS Health's National Prescription Audit *Plus*®, patients whose needs can be fully satisfied with generics could enjoy reductions of 52% in the daily costs of their medications. This analysis is based on the average national retail price of drugs in retail pharmacies (i.e., chain, independent and food-store pharmacies, excluding Internet, mail-order and long-term care pharmacies), a measure that averages pharmacies' revenues from uninsured customers, insured customers and Medicaid beneficiaries. The savings are total cost savings — including to Medicaid and insurance companies — and not necessarily out-of-pocket savings to patients.⁹

In 2004, the average price of a generic prescription drug was \$28.74, while the average price of a brand-name prescription drug was \$96.01, according to the National Association of Chain Drug Stores.¹⁰ This is an average; costs for specific drugs may be more or less, as seen in the following examples. NDC Health, which collects data on the pharmaceutical industry, lists the following estimates of average community retail prices in 2004:

- Brand-name angiotensin-converting enzyme inhibitors were \$55.84, compared with \$27.75 for generic products.
- Brand-name beta blockers were \$41.39, compared with \$18.84 for generics.
- Brand-name calcium channel blockers were \$66.06, compared with \$47.40 for generics.
- Brand-name potassium-sparing diuretics were \$34.27, compared with \$16.25 for generics.

The comparisons of these blood pressure medications included similar

dosing, numbers of pills and strength of prescription.

Authorized generics also provide cost savings. A study by Berndt and colleagues reinforces findings that authorized generics increase competition and lower prices for pharmacy customers. Indeed, customers will most likely benefit from authorized generics due to lower generic prices during the 180-day exclusivity period.¹¹

According to another analyst, policies that prohibit authorized generics would most likely increase federal spending because authorized generics reduce drug cost for consumers in the short run, without adversely affecting generic manufacturers' incentives to develop new generic drugs.¹² In other words, "restricting entry of authorized generics would delay the onset of full generic competition, raising costs for all payers without providing offsetting long-run benefits."¹²

Clearly an opportunity exists for healthcare providers to talk with patients about the cost of the medication they are prescribing or have prescribed. It is important to consider cost issues, especially when new medications are prescribed. Pharmacists, who live with medication costs as part of their jobs, can be a good resource for the provider regarding appropriate medication selection as well as for brand-name and generic-price comparisons.¹³ Healthcare providers also should take into consideration the possibility of changes in patients' circumstances. If a local factory or large business has recently shut down or undergone layoffs, patients who previously could afford their medications may no longer have the income or health insurance that makes this possible. As a result, there may be changes in a patient's adherence with his or her medication regimen. Clinicians should be sensitive to cost as a possible reason for lack of adherence and should be prepared to discuss options that may be available to the patient to help him or her manage medication costs.

ATTITUDES TOWARD GENERIC DRUGS

While many persons are familiar with and use generic drugs and authorized generic drugs, there are others who would benefit from a talk with their clinician or pharmacist about the lower costs and equivalent safety and efficacy of generics.

This is especially important because, although patients may assume that their clinician is up-to-date on drug costs, a survey by Steinman and colleagues indicated otherwise. The investigators studied data from the 2003 "National Ambulatory Medical Care Survey," a nationally representative survey of 25,288 community-based outpatient visits in the United States. The study authors, who published their results in 2007, found that providers referred to most drugs by their brand names, even for those drugs that were available in generic form. Findings included:

- For 20 commonly used drugs, the median frequency of brand-name use was 98%.
- For 12 medications with no generic formulation when the survey was conducted, the median frequency of brand-name use was 100%.
- Among eight medications with generic competition, the median frequency of brand-name usage was 79%.

The authors concluded that such drug recommendations may result in higher drug costs by encouraging the use of brand-name drugs when generic formulations were available.¹⁴

Surveys indicate a general, although not complete, acceptance among consumers of generic drugs. According to a 2001 National Consumer League report, more than 80% of consumers ages 65 and older think that generic drugs are as effective as their brand-name counterparts, and more than 90% would be very likely or somewhat likely to try a generic drug if their clinician or pharmacist rec-

ommended it as a safe, effective and less costly alternative to brand-name drugs. In a 2002 AARP survey, there was slightly less acceptance of generic drugs among persons ages 45 and over. While 95% of respondents reported hearing about generic drugs, 22% thought that generic drugs may be less effective or of poorer quality than brand-name drugs. However, despite the fact that, in general, survey respondents had a positive opinion of generics, only 37% of respondents in the AARP survey reported that they always or often ask their clinician or pharmacist for generic prescription drugs when they are available.⁶

As noted previously, some organizations that represent patients with specific diseases or medical conditions support efforts to require the express permission of the prescribing clinician before a pharmacist can substitute a generic drug. Of course, patients should always contact their prescriber if they are concerned about a drug's effectiveness, or if they feel their reaction to a drug is different from what they had experienced with a previous prescription.⁶

NARROW THERAPEUTIC RATIO DRUGS

Whether generic versions of narrow therapeutic ratio drugs should be substituted for their brand-name counterparts remains a topic of discussion. NTR drugs have less than a twofold difference in the median lethal dose and the median effective dose values; in other words, less than a twofold difference in the minimum toxic concentrations and minimum effective concentrations in the blood. NTR drugs (e.g., warfarin, quinidine, procainamide, theophylline, lithium, phenytoin, carbamazepine and valproic acid) are used in clinical situations in which small variations in tissue levels may cause subtherapeutic or toxic clinical outcomes. NTR drugs need frequent adjustments and careful patient monitoring, regardless of whether a brand-name or generic product is used.

The FDA maintains that its bioequivalency criteria are appropriate for all

drugs and has resisted calls to establish different standards for NTR drugs. Moreover, it maintains that there has been no confirmation of adverse health outcomes having occurred as a result of alleged differences in bioequivalence between generic and brand-name NTR drugs.⁶

The American Academy of Neurology, in a 2006 position statement, opposed generic substitution of anticonvulsant drugs for the treatment of epilepsy without the attending provider's approval, saying that variation between generic and name-brand anticonvulsants can be "highly problematic" for patients with epilepsy.¹⁵

Antiarrhythmic and anticoagulation drugs present a concern for some cardiovascular providers.¹⁶ According to Dr. Peter Kowey, "For antiarrhythmic drugs with an [NTR], bioequivalence in formulation substitution may not necessarily mean clinical equivalence. Certainly this will not be true for most patients, but there is enough documented evidence that such consequences may occur so that erring on the side of caution is advised."

There also has been concern about levothyroxine medications. The American Thyroid Association, in a joint statement with the Endocrine Society and the American Association of Clinical Endocrinologists, stated concern about the FDA's standards for bioequivalence of levothyroxine products and recommended that providers maintain patients on the same brand and that patients request their provider and pharmacy to maintain them on the same brand. Patients should not change from one brand of thyroid medication to another, from the brand of thyroid medication to a generic product or from one generic product to another generic without the approval of the patient's provider.¹⁷

The concerns expressed regarding the use of generic products for NTR drugs relate to generics that have not been authorized by the brand manufacturer. The concern is that, although the active ingredient is the same, the small variations in inactive ingredients or manufacturing process may lead to enough of

a difference at the active site to have a medical impact. These concerns would not apply to authorized generics because there is no variation in inactive ingredients, manufacturing process or any aspect (other than the cost) between the brand product and its authorized generic. With this in mind, an authorized generic product may be a good choice for a patient seeking a generic form of one of the NTR drugs.

HOW TO MAKE PATIENTS MORE COMFORTABLE WITH — AND KNOWLEDGEABLE — ABOUT GENERICS

As noted previously, many consumers are familiar and comfortable with generics. However, others are not. It also should be kept in mind that patients may be willing to accept generics due to the cost benefit, without having a full understanding of what a generic product is. For these reasons, healthcare providers should be prepared to increase patients' understanding of generics. Specific examples of how healthcare providers may help patients include the following:

- Patients who have been taking a branded medication for a long time have likely become accustomed to the appearance of that product. If switched to a generic, the patient may become confused as to which medication is which, or have a feeling that the generic — because it doesn't look like the "real" medication — is not as effective or important to take. For this person, the use of an authorized generic can provide cost savings and the comfort level of a medication that looks the way they have come to expect.
- Many generic products look somewhat similar. Patients who are taking several medications that are generics may, at times, have difficulty telling them apart, and this could result in difficulty adhering to their regimen. Authorized generics, because they have the

same appearance as the branded products, are more likely to have a visually distinct appearance and, as such, be easier to identify.

- Patients may not understand why generics are less expensive. Providers can explain to them that for a drug to be brought to market, extensive testing is required. The expense of this testing is a large part of the cost of a branded product. Generic products are less expensive because they contain the same active ingredient as the brand, and thus the FDA requires less testing. Patients who remain concerned that generics may not be “the real thing” should be encouraged to use authorized generics, which are identical to the brand in every way except cost.
- Patients who are concerned that the cost structure of their health

PRACTICE POINTS

- Understand your patient’s circumstances before prescribing. The cost of a medication can have implications on patient adherence.
- Collaborate with a pharmacist to understand how to properly write prescriptions to enable generic substitution in your state.
- Extra care should be taken when prescribing drugs with a NTR.

plan is pushing them to switch a NTR drug to a generic, even though they would prefer to continue with the branded product, should be advised of available authorized generic products.

CONCLUSION

The provisions of the Hatch-Waxman Act stimulated the introduction of a large number of generic drug products to the American people, resulting in sub-

stantial savings. Recently, an increasing number of authorized generics, generic products whose production is authorized by the brand manufacturer, have become available. Authorized generics not only have the same active ingredient as the branded product; they also have the same inactive ingredients, manufacturing process and appearance. For a variety of reasons, many patients may prefer or benefit from the use of an authorized generic product.

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Learning Assessment

Successful completion of “Authorized generics” is accredited for 1.0 (one) hour of continuing education credit of which 1.0 (one) hour is considered pharmacology credit. To obtain credit, answer the following questions and complete the evaluation online at www.retailclinician.com.

1. **A generic drug and its brand-name counterpart are identical in:**
 - a. Dosage
 - b. Active ingredient
 - c. Strength
 - d. All of the above
2. **The Hatch-Waxman Act:**
 - a. Shortened the approval process for generic-drug manufacturers
 - b. Allowed generic-drug manufacturers to conduct bioequivalence tests of a drug and apply for FDA approval before the applicable patents expire
 - c. Provided processes to resolve patent disputes between brand-name manufacturers and generic-drug firms
 - d. All of the above
3. **Generic drugs and brand-name drugs may differ in the following (generally) insignificant ways:**
 - a. Shape
 - b. Color
 - c. Filler
 - d. All of the above
4. **All drugs that are available as a generic also are available as an authorized generic.**
 - a. True
 - b. False
5. **According to the Congressional Budget Office, generic drugs save consumers an estimated \$__ to \$__ billion a year at retail pharmacies.**
 - a. \$2 to \$4
 - b. \$4 to \$6
 - c. \$8 to \$10
 - d. \$16 to \$20
6. **Information reported in 2007 indicated that authorized generics account for what percent of prescriptions written in the United States?**
 - a. 9%
 - b. 19%
 - c. 29%
 - d. 39%
7. **Narrow therapeutic ratio drugs:**
 - a. Are drugs that are only used for a few, very rare, conditions
 - b. Need frequent adjustments and careful patient monitoring
 - c. Are available in only a few dosage forms
 - d. Are a concern only in the drug category of anticonvulsants
8. **Approximately __% of all prescriptions in the United States are filled with generic drugs.**
 - a. 33
 - b. 53
 - c. 63
 - d. 73
9. **Which of the following pairs of product will have the same inactive ingredients?**
 - a. Brand/generic
 - b. Brand/authorized generic
 - c. Authorized generic/generic
10. **Reasons why patients may prefer an authorized generic include:**
 - a. They have become accustomed to their medication having a particular appearance, which to them represents the “real” medication.
 - b. They are concerned about how an inactive ingredient may affect them.
 - c. They want to be able to tell their medications apart.
 - d. All of the above