Target audience: healthcare professionals, providers

Format: electronic newsletter

Content to cover: generic drug safety and efficacy, effectiveness, access and cost

Safety and efficacy

Generic drugs are important options that allow greater access to healthcare for all Americans. They are the same as brand-name drugs in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use.

All generic drugs approved by the U.S. Food and Drug Administration (FDA) through abbreviated new drug applications (ANDAs) have the same high quality, strength, purity, and stability as brand-name drugs. Also, the generic manufacturing, testing, and packaging sites must pass the same quality standards as those of brand-name drugs.

As part of the ANDA, the generic drug manufacturer must prove its drug is bioequivalent to the brand-name drug. This means that the generic drug must deliver the same amount of active ingredient(s) into a patient's bloodstream or other target action site in the same amount of time as the brand-name drug. Through review of bioequivalence data, the FDA ensures that the generic product performs the same as its reference brand-name product. This standard applies to all generic drugs, whether immediate- or modified-release.

Healthcare providers can search therapeutic equivalence codes for generic drugs in the Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book). Recently, the Orange Book 2.0 mobile app, which provides fast and easy searching of the Orange Book, became available free of charge at Apple and Android app stores. Additionally, availability (manufacturer, approval date, and strength) of generic drugs can be searched in the Drugs.com Generic Drug Database.

Effectiveness

A systematic review and meta-analysis published in 2008 evaluated the results of 38 published clinical studies that compared cardiovascular generic drugs to their brand-name counterparts. There was no evidence that brand-name cardiovascular drugs worked any better than generic cardiovascular drugs.[1] An updated systematic review and meta-analysis published in 2016 further strengthens the evidence for clinical equivalence between brand-name and generic cardiovascular drugs.[2]

However, although recent evidence has supported generic substitution for drugs with narrow therapeutic index (such as some antiepileptics,[3] immunosuppressants,[4] and psychotropic drugs[5]), it remains controversial in medical practice. Changes in patients' clinical status during a switch to a generic substitute can be related to psychological, interactional, physiological, and pharmacological factors that may or may not be related to the change to a generic drug. For example, patients have expressed concerns that the lower cost of generics is associated with reduced medication quality.[6] This perception may contribute to adherence barriers in regimens using generic alternatives.

Communication

Patients who report talking to their healthcare providers about generic substitution are more likely to fill generic medications than those who do not have a discussion with their providers.[7] Therefore, effective communication between patients and healthcare providers regarding generic drugs and generic substitution plays a critical role in optimizing patient outcomes.

Access and cost

The Office of Generic Drugs (OGD) in the U.S. FDA's Center for Drug Evaluation and Research (CDER) continues to provide access to cost-saving generic drugs. In 2016, OGD approved 630 abbreviated new drug applications (ANDAs) and tentatively approved 183—the highest number of generic drug approvals and tentative approvals in the history of the generic drug program (OGD Annual Report for 2016). FDA-approved generic drugs account for 89% of prescriptions dispensed in the United States (IMS Institute for Healthcare Informatics). On average, the cost of a generic drug is 80% to 85% lower than the brand-name product. Use of generic drugs has saved the U.S. healthcare system almost $1.7 trillion in the past 10 years, leading to cost savings for consumers.[8]

OGD has published more than 1,500 product-specific guidance documents related to developing generic drugs, which are posted on the FDA's website. These guidelines are intended to help generic drug manufacturers develop and evaluate their generic drugs in a scientifically sound way. The public can also access available educational resources regarding generic drugs such as brochures, posters, and audio/multimedia presentations on the FDA's website.

Pricing Resources for Generic and Brand-name Drugs

	Micromedex 2.0®	**Epocrates®**
Available from	Truven Health Analytics®	athenahealth
Cost	Individual subscription or Institutional subscription	Free
Access	Web Mobile app	Web Mobile app
Price location	Red Book® tab	Manufacturer/Pricing section
Searchable by	Product name Active ingredient	Product name Active ingredient
Price source	Red Book®	GoodRx.com
Price type	Average wholesale price (AWP)	Approximate retail price
Prices by	Generic or brand Strength Package- and unit-quantity Dosage form Manufacturer National Drug Identifier Code (NDC)	Generic or brand Strength Select quantities Dosage form

References

1. Kesselheim AS, Misono AS, Lee JL, et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. *Jama.* 2008;300(21):2514-2526.
2. Manzoli L, Flacco ME, Boccia S, et al. Generic versus brand-name drugs used in cardiovascular diseases. *European journal of epidemiology.* 2016;31(4):351-368.
3. Yamada M, Welty TE. Generic substitution of antiepileptic drugs: a systematic review of prospective and retrospective studies. *The Annals of pharmacotherapy.* 2011;45(11):1406-1415.
4. Ensor CR, Trofe-Clark J, Gabardi S, McDevitt-Potter LM, Shullo MA. Generic maintenance immunosuppression in solid organ transplant recipients. *Pharmacotherapy.* 2011;31(11):1111-1129.
5. Carbon M, Correll CU. Rational use of generic psychotropic drugs. *CNS drugs.* 2013;27(5):353-365.
6. Colgan S, Faasse K, Martin LR, Stephens MH, Grey A, Petrie KJ. Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review. *BMJ Open.* 2015;5(12):e008915.
7. Shrank WH, Cox ER, Fischer MA, Mehta J, Choudhry NK. Patients' perceptions of generic medications. *Health Aff (Millwood).* 2009;28(2):546-556.
8. Association for Accessible Medicines. Generic Drug Access and Savings in the U.S. 2017; http://accessiblemeds.org/sites/default/files/2017-06/2017-AAM-Access-Savings-Report-2017-web2.pdf.

Target audience: formulary managers, policymakers, large purchasers

Format: electronic newsletter

Content to cover: FDA generic drug approval process, bioequivalence, effectiveness, access and cost

FDA generic drug approval process

Each year, the U.S. Food and Drug Administration's (FDA) Center for Drug Evaluation and Research (CDER) approves a wide range of generic drug products submitted through abbreviated new drug applications (ANDAs). The ANDA process does not require the generic drug manufacturer to repeat costly animal and clinical research on ingredients or dosage forms already approved for safety and efficacy with brand-name products. Rather, to gain FDA approval, a generic drug must:

- Be pharmaceutically equivalent to the brand-name drug, which means it 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 as the brand-name drug
    - Have the same indications for use as the brand-name drug
- Be bioequivalent to the brand-name drug (more details below)
- Meet the same batch requirements for identity, strength, purity, and quality as the brand-name drug
- Be manufactured under the FDA's same strict Good Manufacturing Practice Regulations required for brand-name drugs

Bioequivalence

To obtain an ANDA approval, the generic drug manufacturer must prove its drug is bioequivalent to the brand-name drug. This means that the generic drug must deliver the same amount of active ingredient(s) into a patient's bloodstream or other target action site in the same amount of time as the brand-name drug. Through review of bioequivalence data, the FDA ensures that the generic product performs the same as its reference brand-name product. This standard applies to all generic drugs, whether immediate- or modified-release.

Generic and brand-name drug products are considered to be therapeutically equivalent only if they are pharmaceutically equivalent products with demonstrated bioequivalence. The coding system for therapeutic equivalence evaluations is a two-letter system. Multisource drugs are coded with a **first letter** as follows: (1) **A**: Drug products that the FDA considers to be therapeutically equivalent to other pharmaceutically equivalent products; and (2) **B**: Drug products that the FDA does not consider to be therapeutically equivalent to other pharmaceutically equivalent products at this time. The **second letter** provides additional information on the basis of the FDA's evaluations. For example, "AB" indicates a drug product for which actual or potential bioequivalence problems have been resolved with adequate in vivo and/or in vitro evidence supporting bioequivalence.

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Access	Web Mobile app	Web Mobile app
Price location	Red Book® tab	Manufacturer/Pricing section
Searchable by	Product name Active ingredient	Product name Active ingredient
Price source	Red Book®	GoodRx.com
Price type	Average wholesale price (AWP)	Approximate retail price
Prices by	Generic or brand Strength Package- and unit-quantity Dosage form Manufacturer National Drug Identifier Code (NDC)	Generic or brand Strength Select quantities Dosage form

References

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7. Association for Accessible Medicines. Generic Drug Access and Savings in the U.S. 2017; http://accessiblemeds.org/sites/default/files/2017-06/2017-AAM-Access-Savings-Report-2017-web2.pdf