U.S. FOOD & DRUG ADMINISTRATION

FDA Drug Topics:
Counseling Patients on Generic Drugs

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Learning Objectives

At the end of this presentation, the participant will be able to:

- Describe the requirements for a generic drug to be considered equivalent to the brand-name drug.
- Explain why generic medicines cost less than brand-name medicines.
- Review the methods used by FDA to monitor the safety and effectiveness of generic drugs.
- Identify the source for locating therapeutically equivalent generic drugs for patients.

Generic Drug Approval Pathway

Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments)

- Created the basic scheme under which generic drugs are approved today
- Allows FDA to approve generic applications for duplicates of brand-name drugs
- May conduct non-clinical and/or clinical studies for generics to support a demonstration of bioequivalence

Access to Generics

- Generic medications saved Americans $313 billion in 2019
- **90%** of the of the prescriptions filled in the United States during 2019 were dispensed as generics
- Generic medications accounted for only **20%** of all drug spending in 2019
- **92%** of generic prescriptions were filled at ≤ $20
  - the average generic copay in 2019 was **$6.97** compared to the average brand-name copay of **$56.32**

*AAM Report: 2020 Generic Drug & Biosimilars Access & Savings in the U.S. (https://accessiblemeds.org)

The Value Proposition of Generic Drugs

Generic drugs:

- are substitutable for brand-name drugs
- are held to the same rigorous FDA quality standards as brand-name drugs
- increase patient access to needed treatment
- typically cost less than brand-name drugs

Counseling Patients about Generic Drugs

- Effective communication can
  - help patients make informed decisions
  - enhance trust in generic drugs
  - improve compliance with taking medications as prescribed
- More affordable medication increases accessibility

Patients May Have Questions About Generic Drugs

- Do generic medicines work the same as brand-name medicines?
- Why do brand-name medicines look different from the generic?
- Why do generic medicines cost less than brand-name medicines?
- Are generic medicines as safe as brand-name medicines?

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Do generic medicines work the same as brand-name medicines?

Do generic medicines work the same as brand-name medicines?

- A generic medicine is the same as an existing approved brand-name medicine in:
  - active ingredient(s)
  - dosage form
  - safety
  - strength
  - route of administration
  - quality and effectiveness
  - performance characteristics

Do generic medicines work the same as brand-name medicines?

Yes, because of how FDA approves generic drugs

- A brand-name drug, which is also referred to as the reference listed drug (RLD), and its generics have the same standards for quality
- Bioequivalence (BE)
- Therapeutic Equivalence (TE)
- Pharmaceutical Equivalence (PE)

Bioequivalence and Therapeutic Equivalence

- Bioequivalence (BE)
  - The absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.
- Therapeutic Equivalence (TE)
  - Approved drug products that are pharmaceutical equivalents for which BE has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.
  - TE → clinical substitutability

Pharmaceutical Equivalence (PE)

- Identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug ingredient
- Delivers identical amounts of the active drug ingredient over the identical dosing period
- Do not necessarily contain the same inactive ingredients
- Meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates
- May differ in characteristics such as shape, scoring configuration, release mechanisms, packaging, excipients (including colors, flavors, preservatives), expiration date/time, and, within certain exceptions, labeling

Source: The Orange Book Preface

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Why do brand-name medicines look different from the generic?

Why do brand-name medicines look different from the generic?

Generic products can sometimes differ in:

- Shape
- Release mechanisms
- Packaging
- Excipients
- Expiration time
- Labeling
- Device component

Brand - Advair Diskus (Glaxo SmithKline) NDA approved in 2003

Generic - Wixela Inhub (Mylan) approved in January 2019

Guidance for Industry: Determining Whether to Submit an ANDA or a 505(b)(2) Application (May 2019)
NDA – New Drug Application; ANDA – Abbreviated New Drug Application

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Why do generic medicines cost less than brand-name medicines?

Why do generic medicines cost less than brand-name medicines?

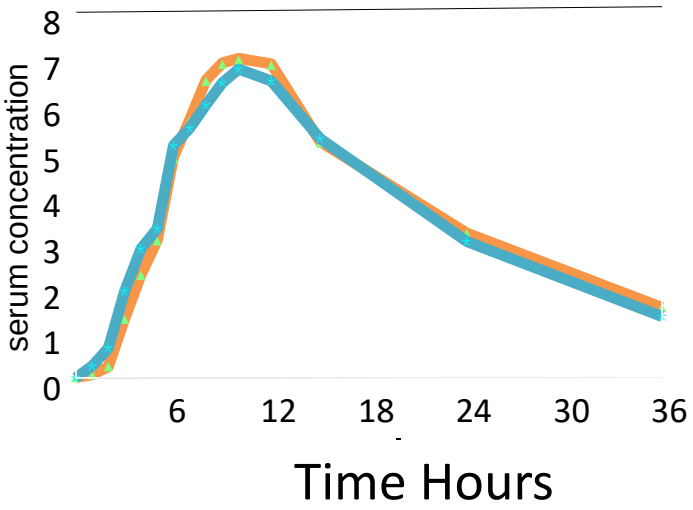
- Effectiveness is established during brand-name drug approval process
  - Generic drugs do not have to repeat costly animal and clinical (human) studies that were required to demonstrate safety and effectiveness
- Greater competition among generic drug makers is associated with lower generic drug prices

U.S. FDA Drug Approval Requirements

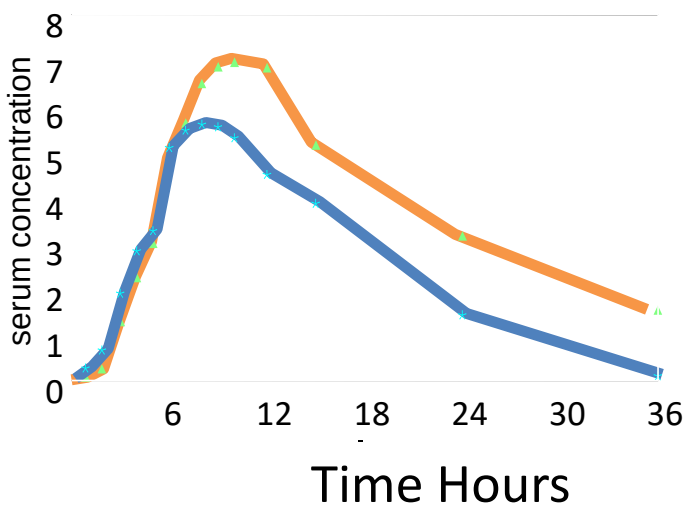
Brand-Name Drug	Generic Drug
Drug Substance	Drug Substance
Drug Product	Drug Product
Manufacturing Process	Manufacturing Process
Manufacturing Facilities	Manufacturing Facilities
Microbiology	Microbiology
Biopharmaceutics	Biopharmaceutics
Labeling	Labeling
Animal Studies	Bioequivalence
Clinical Studies	

Bioequivalence

Bioequivalent



Inequivalent



Test/Generic

Reference/RLD

Dispelling the 80-125% Myth

- **Myth:** Misconception that a generic can contain between 80% and 125% of the active ingredient that is present in the brand-name. This is false!
- **Fact:** The “80% to 125%” criteria is part of a statistical tool when measuring drug concentration in the blood and drug exposure over time. It does not pertain to a range of allowable active ingredient in the generic.
- Bioequivalence is determined by pharmacokinetic (PK) parameters
  - Ideal PK ratio of the generic drug to the reference drug is 1:1, or 1.00 (indicating perfect bioequivalence)
  - Every time a human takes a drug product (either the brand or generic) the PK measurement varies a little bit
  - FDA uses a statistical tool to account for this variability (the 90% confidence interval of the PK ratio should lie between 0.80 and 1.25)

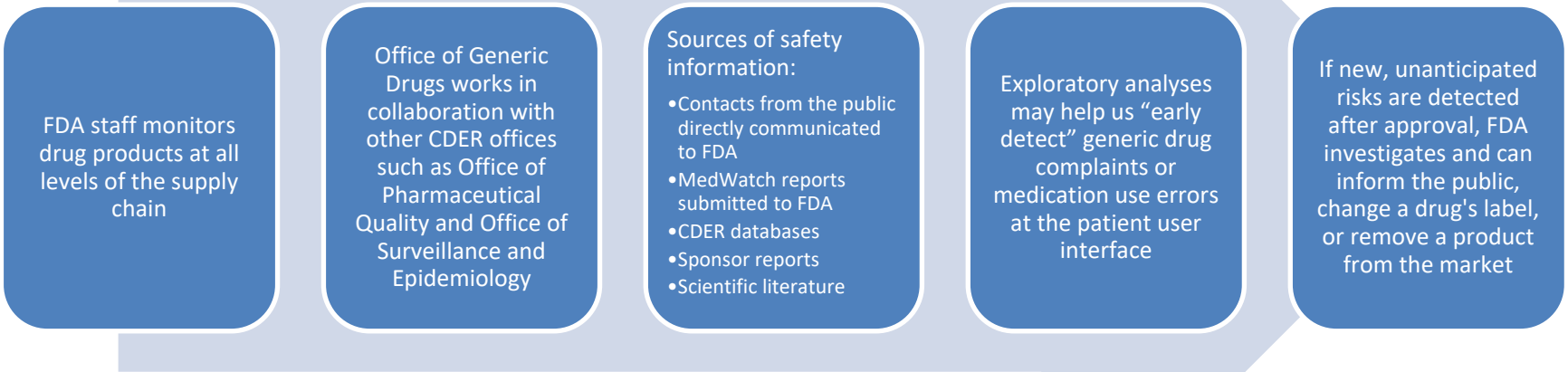
Are generic medicines as safe as brand-name medicines?

Are generic medicines as safe as brand-name medicines?

The safety and effectiveness of the drug product was demonstrated to support the approval of the RLD

Generic drugs are carefully reviewed to ensure same safety profile

Proactive Generic Drug Safety Surveillance



MedWatch

FDA's medical product safety reporting program for health professionals, patients, and consumers to report:

- Unexpected side effects or adverse events
- Product quality problems
- Product use/medication errors that can be prevented
- Therapeutic failures

MedWatch Web Page

← Home / Safety / MedWatch: The FDA Safety Information and Adverse Event Reporting Program

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Medical Product Safety Educational Resources

Medical Product Safety Information

Reporting Serious Problems to FDA

MedWatch, the FDA's medical product safety reporting program for health professionals, patients and consumers.

Report a Problem | Safety Information | Stay Informed

MedWatch receives reports from the public and when appropriate, publishes safety alerts for FDA-regulated products such as:

- **Prescription and over-the-counter medicines**
- **Biologics** such as blood components, blood/plasma derivatives and gene therapies.
- **Medical devices** such as hearing aids breast pumps, and pacemakers.
- **Combination products** such as pre-filled drug syringe, metered-dose inhalers and nasal spray.

Content current as of:
02/10/2022

Regulated Product(s)
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Cosmetics
Dietary Supplements
Drugs
Medical Devices
Radiation-Emitting Products
Medical Food/Beverage

Topic(s)
Recalls
Postmarket

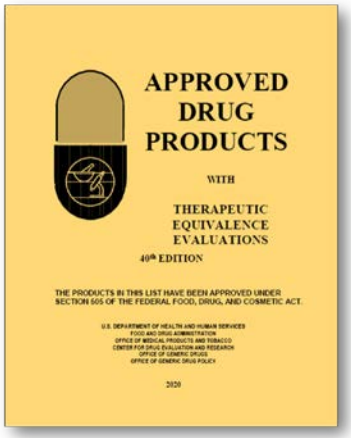
FDA Adverse Event Reporting System

- FDA Adverse Event Reporting System (FAERS) is a database that contains:
  - Adverse event reports
  - Medication error reports
  - Product quality complaints
- Reports are from healthcare professionals, patients, and manufacturers
  - Manufacturers are required to send reports from patient and healthcare professionals to FDA
- FAERS Public Dashboard
  - User-friendly
  - Several limitations to raw data

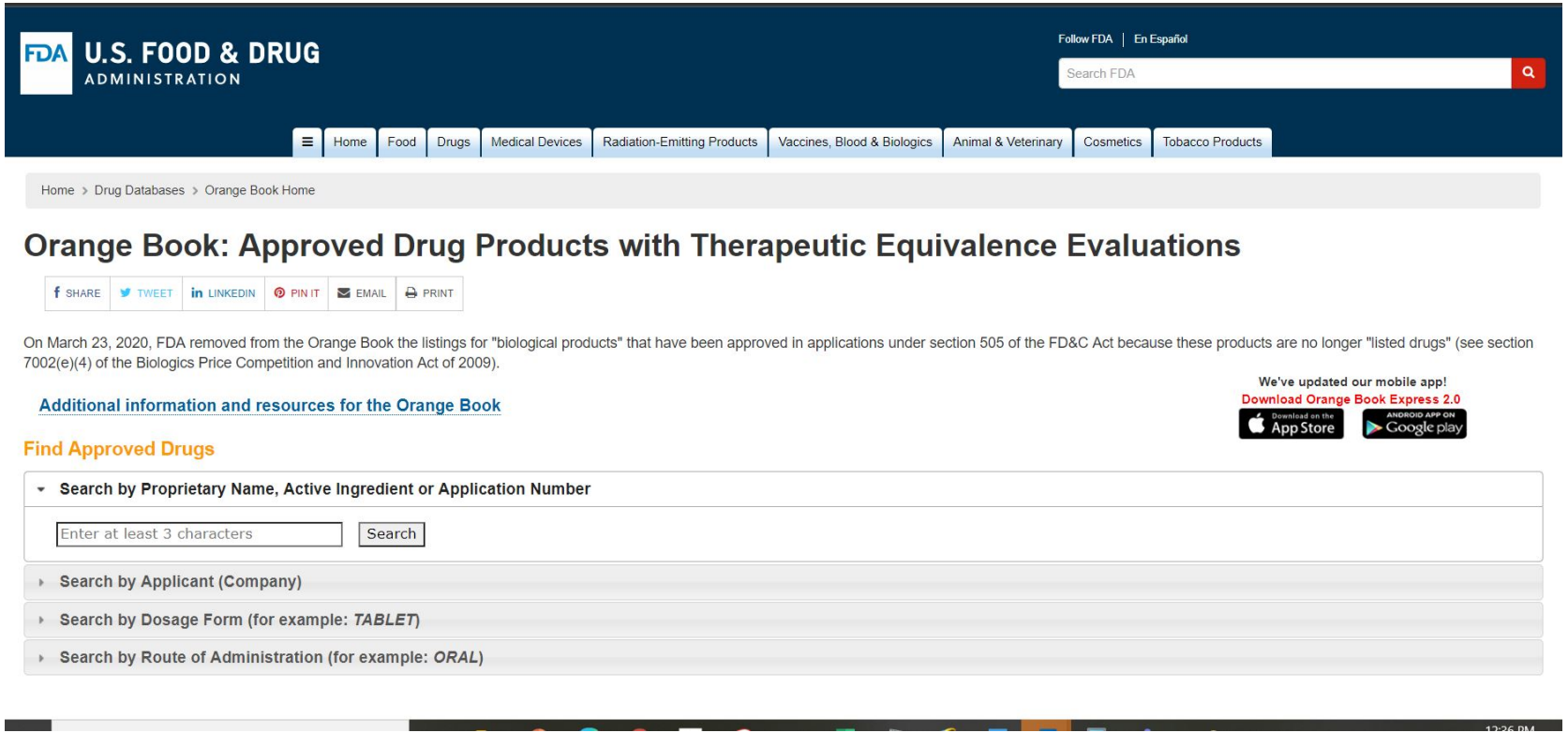
Finding Patients a Generic Drug Equivalent

"Approved Drug Products with Therapeutic Equivalence Evaluations", commonly called "The Orange Book"

- lists drug products FDA approved on the basis of safety and effectiveness
- identifies:
  - RLD and Reference Standard (RS)
  - substitutability information with respect to generic and RLD
  - patents, exclusivity, and their expiration dates
  - therapeutic equivalence codes



Orange Book Web Page



www.fda.gov

Therapeutic Equivalence Listed in Orange Book

- TE = approved drug products that are PE for which BE has been shown
  - Expected to have same clinical effect and safety profile when administered under conditions specified in the labeling

- If TE, then *A-rated* in Orange Book → *substitutable*
- **If not TE**, then *B-rated* in Orange Book (if pharmaceutical equivalents)→ ***not*** *substitutable*

References

- Patient Education https://www.fda.gov/drugs/generic-drugs/patient-education
- Your Patients Have Questions About Generics https://www.fda.gov/media/107671/download
- Generic Drug Facts https://www.fda.gov/media/107601/download
- Generic Drugs: Questions and Answers https://www.fda.gov/drugs/questions-answers/generic-drugs-questions-answers
- What is the Approval Process for Generic Drugs? https://www.fda.gov/drugs/generic-drugs/what-approval-process-generic-drugs
- Generic Competition and Drug Prices https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/generic-competition-and-drug-prices
- FDA Orange Book https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
- MedWatch https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program and Voluntary Reporting Form https://www.accessdata.fda.gov/scripts/medwatch/index.cfm
- Safety, Efficacy, and Quality Remain Top Priorities As We Continue Our Work to Expand Access to Cost-Saving Generic Drugs for the American Public https://www.fda.gov/news-events/fda-voices/safety-efficacy-and-quality-remain-top-priorities-we-continue-our-work-expand-access-cost-saving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