Pharmacy Purchasing Outlook

Our **Only** Issue Is Pharmacy Purchasing

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Facts & Myths About Generics

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Today, 7 in 10 prescriptions filled in the U.S. are for generic drugs. This fact sheet, released by the FDA on October 13, 2009, explains how generic drugs are made and approved, and debunks some common myths about these products.

FACT: The FDA requires generic drugs to have the same quality and performance as brand name drugs.

When a generic drug product is approved, it has met rigorous standards established by the FDA with respect to identity, strength, quality, purity and potency. Some variability can and does occur during manufacturing, for both brand name and generic drugs. When a drug, generic or brand name, is mass produced, very small variations in purity, size, strength and other parameters are permitted. The FDA puts limits on how much variability in composition or performance of a drug is acceptable.

Generic drugs are required to have the same active ingredient, strength, dosage form, and route of administration as the brand name (or reference) product. Generic drugs do not need to contain the same inactive ingredients as the brand product.

Through review of bioequivalence data, the FDA assures that the generic product will perform the same as its respective brand name (or reference) product. This standard applies to all generic drugs, whether immediate or controlled release.

A generic drug must be shown to be bioequivalent to the reference drug; that is, it must be shown to give blood levels that are very similar to those of the reference product. If blood levels are the same, the therapeutic effect will be the same. In that case, there is no need to carry out a clinical effectiveness study and they are not required.

All generic manufacturing, packaging, and testing sites must pass the same quality standards as those of brand name drugs and the generic products must meet the same exacting specifications as any innovator brand name product. In fact, many generic drugs are made in the same plants as innovator brand name drug products.

If an innovator of a brand name drug switches drug production to an alternative manufacturing site, or they change formulation of their brand name drug, these companies are held to the same rigorous manufacturing requirements as those that apply to generic drug companies.

FACT: Research shows that generics work just as well as brand name drugs.

A recent study evaluated the results of 38 published clinical trials that compared cardiovascular generic drugs to their brand-name counterparts. There was no evidence that brand-name heart drugs worked any better than generic heart drugs. [Kesselheim et al., "Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a

systematic review and meta-analysis," *Journal Of the American Medical Association*, Vol. 300 No. 21, December 3, 2008].

FACT: When it comes to price, there is a big difference between generic and brand name drugs. On average, the cost of a generic drug is 80-85% lower than the brand name product.

An IMS National Prescription Audit shows that a typical formulary now charges $6 for generic medications, $29 for preferred branded drugs, and $40 or more for non-preferred branded drugs. [Aitken et al., "Prescription drug spending trends in the U.S.-looking beyond the turning point," *Health Affairs*, 2009, 28(1):w151-60].

Independent research has shown that total prescription drug expenditures in the U.S. only increased by 4.0% from 2006 to 2007, with total spending rising from $276 billion to $287 billion. This is a sharp decrease from the 8.9% growth rate observed in prescription drug expenditures in 2006. One factor cited as a reason for the slowdown is an increase in availability and use of generic drugs [Hoffman et al., "Projecting future drug expenditures-2009," *American Journal of Health System Pharmacy*, January 2009, Volume 66, Issue 1].

Recently, misinformation in the media has raised concerns over generic drugs. Below are some common myths in circulation.

MYTH: The FDA lets generic drugs differ from the brand name counterpart by up to 45%.

FACT: This claim is false. Anyone who repeats this myth does not understand how FDA reviews and approves generic drugs.

The FDA recently evaluated 2,070 human studies conducted between 1996 and 2007. These studies compared the absorption of brand name and generic drugs into a person's body. These studies were submitted to FDA to support approval of generics. The average difference in absorption into the body between the generic and the brand name was only 2.3%. Some generics were absorbed slightly more, some slightly less. This amount of difference would be expected and acceptable, whether for one batch of brand name drug tested against another batch of the same brand, or for a generic tested against a brand name. In fact, there have been studies in which branded drugs were compared with themselves as well as with a generic. As a rule, the difference for the generic-to-brand comparison was about the same as the brand-to-brand comparison.

Any generic drug modeled after a single, brand name drug (the reference) must perform approximately the same in the body as the brand name drug. There will always be a slight, but not medically important, level of natural variability, just as there is for one batch of brand name drug to the next.

MYTH: People who are switched to a generic drug are risking treatment failure.

FACT: There is no evidence for this claim. Treatment failures can and do occur when taking generic or brand name drugs. If someone is switched to a generic drug around the time they are relapsing, they may attribute the problem to the switch.

Many people who have recovered from major depression have a relapse despite continued treatment. These relapses have been shown in trials of long-term therapy. [Byrne and Rothschild, "Loss of antidepressant efficacy during maintenance therapy-possible mechanisms and treatments," *Journal of Clinical Psychiatry*, June 1998, vol. 59].

Many people who are on a seizure medications will re-experience a seizure despite continued treatment on a single drug. The likelihood of re-experiencing a seizure, despite staying with the same drug product, goes up with time. [Brodie et al., "Comparison of levetiracetam and controlled-release carbamazepine in newly diagnosed epilepsy," *Neurology*, Aug. 28, 2007, Vol. 69, Issue 9].

A percentage of people will re-experience gastric ulcers, despite an initial, positive response to and continued treatment with prescription strength antacids (cimetidine tablets).

MYTH: Generic drugs cost less because they are inferior to brand name drugs.

FACT: Generic manufacturers are able to sell their products for lower prices, not because the products are of lesser quality, but because generic manufacturers generally do not engage in costly advertising, marketing and promotion, or significant research and development.

When a brand name drug comes off patent and generic drugs are permitted to compete with the brand name drug, the generic products compete by offering lower prices. Unlike the manufacturers of brand name drugs, generic drug companies do not have significant expenses to recoup for advertising, marketing and promotion, or research and development activities.

MYTH: There are quality problems with generic drug manufacturing. A recent recall of generic digoxin (called Digitek), shows that generic drugs put patients at risk.

FACT: The FDA's aggressive action in this case demonstrates the high standards to which all prescription drugs, generic and brand name, are held.

In March 2008, the FDA performed a scheduled inspection of the Actavis production facility and identified products that were not manufactured to required specifications over a period of time extending back to the year 2006. Included in this list of products was one particular lot of Digitek. Actavis detected a very small number of oversized tablets in this lot (specifically, 20 double-sized tablets in a sample of approximately 4.8 million tablets).

Although Actavis attempted to remove the affected Digitek tablets through visual inspection, the FDA determined that this method of removal was inadequate to assure the product's quality and consistency in accordance with the cGMP (current good manufacturing practice) regulations.

Since the detection of the manufacturing problem, the FDA has been actively engaged with this company to ensure that ALL potentially affected lots of Digitek tablets have been recalled. In the FDA's best judgment, given the very small number of defective tablets that may have reached the market and the lack of reported adverse events before the recall, harm to patients was very unlikely.

The FDA takes action whenever we find that a drug manufacturer is not following cGMP guidelines. Over the last ten years, the FDA has taken enforcement action against many brand name and generic firms for failing to meet FDA manufacturing quality standards.

MYTH: The FDA's enforcement action against the generic drug company Ranbaxy, demonstrates quality problems with imported generic drugs.

FACT: The FDA's action demonstrates FDA's commitment to safe generic drugs.

The FDA has taken several regulatory actions against the generic drug manufacturer Ranbaxy, on the basis of problems at two of Ranbaxy's manufacturing facilities. Ranbaxy is one of many non-U.S. based generic and brand drug manufacturers.

In September 2008, the FDA issued two warning letters and instituted an Import Alert, barring the entry of all finished drug products and active pharmaceutical ingredients from 3 of Ranbaxy's facilities in India, due to violations of U.S. cGMP requirements. That action barred the commercial importation of 30 different generic drugs into the U.S.

Subsequent FDA investigations also revealed a pattern of questionable data raising significant questions regarding the reliability of certain generic drug applications from Ranbaxy.

To address the allegedly falsified data, the FDA has invoked its Application Integrity Policy (AIP) against one of Ranbaxy's facilities in question (located in Paonta Sahib, India). When the AIP is implemented, the FDA stops all substantive scientific review of any new or

pending drug approval applications that contain data generated by that facility. This AIP covers applications that rely on data generated by the Paonta Sahib facility only.

In the fiscal year 2008, the FDA performed 2,221 drug-related inspections. The FDA takes many different enforcement actions, not just against generic drug manufacturers. It is the FDA's responsibility to ensure that the drugs people use, generic or brand name, are safe and effective.

MYTH: Brand name drugs are safer than generic drugs.

FACT: The FDA receives very few reports of adverse events about specific generic drugs. Most reports of adverse events are related to side effects of the drug ingredient itself.

The monitoring of post-market adverse events for all drug products, including generic drugs, is one aspect of the overall FDA effort to evaluate the safety of drugs after approval. In most cases, reports of adverse events generally describe a known reaction to the active drug ingredient.

MYTH: The FDA does not care about concerns over generic drugs.

FACT: The FDA is actively engaged in making all regulated products, including generic drugs, safer.

The FDA is aware that there are reports noting that some people may experience an undesired effect when switching from brand name drug to a generic formulation or from one generic drug to another generic drug. Evidence indicates that if problems with interchangeability of drug formulations occur, they occur only for a very small subset of people.

The FDA is encouraging the generic industry to investigate whether, and under what circumstances, such problems occur. The Agency does not have the resources to perform independent clinical studies, and lacks the regulatory authority to require industry to conduct such studies. The FDA will continue to investigate these reports to ensure that it has all the facts about these treatment failures and will make recommendations to healthcare professionals and the public if the need arises.