

The Dangers of Drug Importation

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INTRODUCTION

The U.S. spends more on health care than any other industrialized country.¹ Readily available access to health information on the Internet²⁻⁴ and the increasing cost of health care, particularly the rising cost of brand-name prescription medications, have led American patients to seek new ways to cut their health-related expenses. The news of prescription drug products being sold at considerably lower prices in other nations and easy access to online pharmacies have prompted a number of American patients to import some prescription drugs into the U.S. In 2003, approximately 12 million prescription drug products entered the U.S. from Canada. An equivalent number of prescription drugs are thought to be imported from other countries as well.⁵

WHY DRUG IMPORTATION IS PROHIBITED

After 1938, the U.S. Federal Food, Drug, and Cosmetic Act ("the Act") prohibited interstate shipment of unapproved new drugs.⁶ As a consequence, the importation of drugs that have not been approved by the U.S. Food and Drug Administration (FDA) is considered illegal. Under the Act, drugs made in the U.S. that are exported can be brought back into the country only by their manufacturers.

In the U.S., medications must comply with labeling regulations.⁷ Companies must also be compliant with good manufacturing practices (GMPs) to ensure that the identity and strength of the medications are correct and that they meet quality and purity standards.⁸

The FDA recognizes that some American patients have medical conditions for which no prescription drugs are available in the U.S.⁹ To accommodate these situations, the FDA developed a personal importation policy that identifies circumstances under which the agency may allow the entry of foreign drug products. This guidance provides the FDA's field offices the opportunity to exercise its discretion in regard to allowing the entry of drugs when certain criteria are met (Table 1).¹⁰ However, this guidance does not create legally enforceable rights for the public, and it does not intend to allow importation of foreign varieties of American drugs that are already approved in the U.S.

Further information about the FDA's Import Program is provided on the Office of Regulatory Affairs (ORA) Web site (www.fda.gov/ora/import/ora_import_program.html).

SAFETY ISSUES

Foreign-made medications have the potential to put patients in the U.S. at risk. The FDA is concerned about the safety of

foreign unapproved drugs purchased by American patients while they are visiting overseas or surfing the Internet. These medications:

- might not be manufactured under quality assurance procedures.
- might be counterfeit.
- might contain non-FDA-approved ingredients.
- might require careful dosing or monitoring.
- might have labeling that is difficult to read and that might contain unapproved claims.

There are also safety concerns when storefront businesses offer to order drug products for patients from a foreign source.¹¹ Therefore, at this time, there is insufficient information to ensure the safety and efficacy of foreign drug products compared with those available for purchase at state-licensed pharmacies in the U.S.

Lack of Quality Assurance

A main concern of the FDA is that quality assurance procedures, which are designed to produce safe and effective medications, might not have been used in the manufacture of drugs that are not FDA-approved for marketing in the U.S.¹¹ The FDA regulates pharmaceutical manufacturing to ensure the quality of all drugs manufactured in the U.S.¹² However, the FDA does not have authority to regulate foreign drugs for quality assurance procedures.

The FDA recently analyzed samples of three commonly

Table 1 FDA-Approved Reasons for Personal Importation of Medications

- The drug is unapproved and intended for use for a serious medical condition, for which effective treatment might not be available domestically, either through commercial or clinical means.
- There is no known commercialization or promotion of the drug to persons residing in the U.S. by those involved in the distribution of the product.
- The product is not considered to represent an unreasonable risk.
- The individual seeking to import the product affirms in writing that it is for the patient's own use (generally not more than a three-month supply) and provides the name and address of the doctor licensed in the U.S. responsible for his or her treatment with the product, or provides evidence that the product is for the continuation of treatment begun in a foreign country.

Data from the FDA. Available at: www.fda.gov/ora/compliance_ref/rpm_new2/ch9pers.html.¹⁰

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Dangers of Drug Importation

prescribed drugs purchased from a Canadian Web site. The products purchased were so-called generic versions of sildenafil citrate (Viagra®, Pfizer) lovastatin (Mevacor®, Merck), and zolpidem tartrate (Ambien®, Sanofi-Synthelabo). Currently, none of the three products has a U.S.-approved generic equivalent; therefore, all three of the purchased “generic” versions are unapproved for use in the U.S.

Laboratory analyses on an average of 20 tablets for each product were performed. Two of the three drugs failed FDA chromatographic purity testing and were considered potentially unsafe because of their elevated levels of impurities.¹³

Counterfeit Products

The growing incidence of counterfeit medications is another concern.¹¹ In some cases, the counterfeit drug bears the name or logo of the U.S.-approved product and is visually indistinguishable from the U.S.-manufactured version. Counterfeit drugs sometimes contain subpotent or superpotent concentrations of active ingredients, have unknown inactive ingredients, or have been manufactured using methods that render the product impure. As a result, counterfeit medications may be therapeutically ineffective at best, or worse, unsafe, causing potentially serious or fatal consequences for consumers.

In July 2004, the FDA warned the public about counterfeit versions of simvastatin (Zocor®, Merck) and carisoprodol

(Soma®, Wallace), which were recently imported from Mexico by patients in the U.S. Tests indicated that the counterfeit simvastatin did not contain any active ingredients and the counterfeit carisoprodol differed in potency when compared with the authentic product.¹⁴

As another example, in March 2003, the FDA identified counterfeit lots of epoetin alfa (Procrit®, Ortho Biotech). The counterfeit product contained a clear liquid, with no active ingredient. The lots were found to be contaminated with *Acinetobacter* and *Pseudomonas* species. The product vial and packaging were alarmingly similar to authentic Procrit® (Figures 1 and 2).¹⁵

Untested Ingredients

Imported drug products may contain ingredients that have not been evaluated by the FDA for safety and efficacy.¹¹ The presence of these untested substances may be dangerous to patients, especially if the products have addictive potential or pose a risk of a serious adverse drug effect (ADE), such as hospitalization or death.

In July and August 2003, the FDA, in conjunction with the U.S. Customs and Border Protection agency, Department of Homeland Security, performed a series of spot examinations of mail shipments of foreign drugs to U.S. consumers. These spot examinations were conducted in the Miami, New York (JFK), San Francisco, and Carson, California, mail facilities.

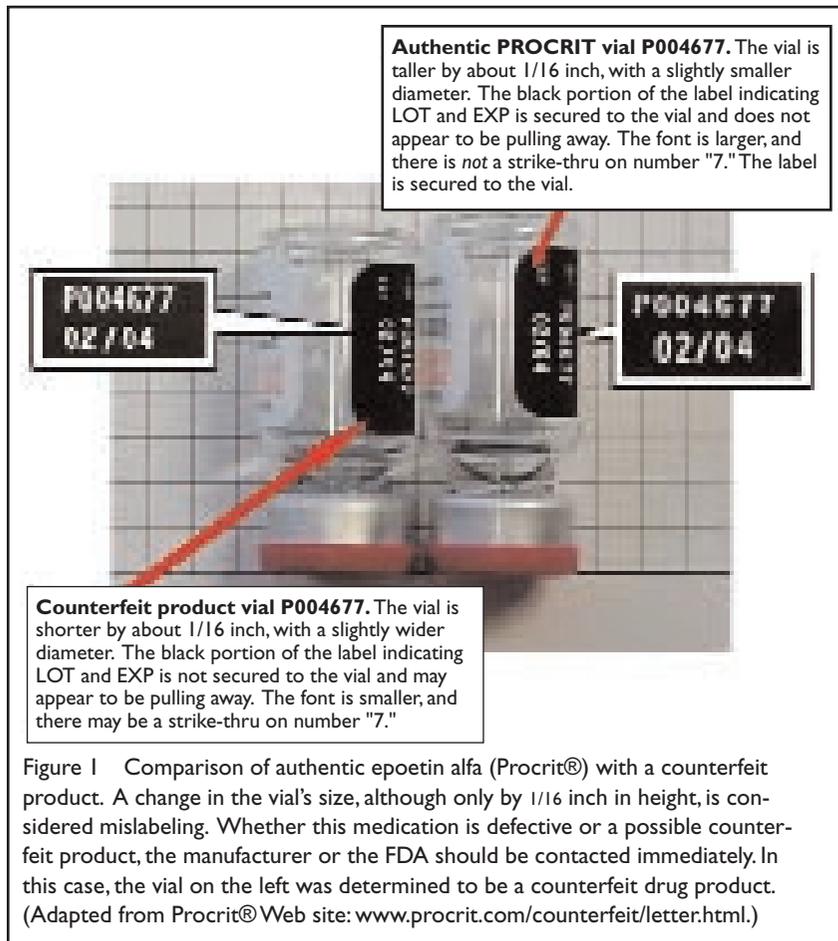
In each location, packages shipped by international mail through U.S. Postal Service facilities were examined over a three-day time span. The FDA and the Customs and Border Protection team identified approximately 100 packages per facility per day that were likely to contain drug products.

A total of 1,153 imported drug products were examined; of these, 88% (1,019) contained unapproved drugs. These drugs arrived from many locations, but the majority came from four countries: 15.8% (161) entered the U.S. from Canada; 14.3% (146) from India; 13.8% (141) from Thailand; and 8.0% (82) from the Philippines.

During this spot examination, the FDA found shipments of clenbuterol (Ventipulmin® Syrup), a veterinary drug approved for the treatment of airway disease in horses but not approved for use in humans. The International Olympic Committee has banned clenbuterol as a performance-enhancing agent.¹⁶

Lack of Patient Monitoring

It is important for patients to take medications as prescribed, because an assessment from a licensed practitioner is usually needed to determine which therapy is appropriate. Also, some medications, (e.g., cardiovascular drugs, diabetic med-



Dangers of Drug Importation

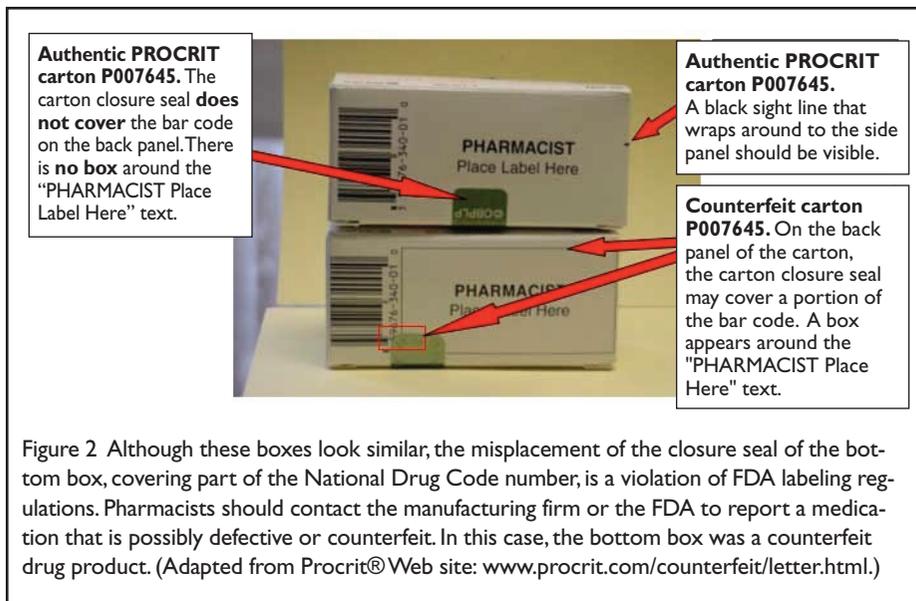


Figure 2 Although these boxes look similar, the misplacement of the closure seal of the bottom box, covering part of the National Drug Code number, is a violation of FDA labeling regulations. Pharmacists should contact the manufacturing firm or the FDA to report a medication that is possibly defective or counterfeit. In this case, the bottom box was a counterfeit drug product. (Adapted from Procrit® Web site: www.procrit.com/counterfeit/letter.html.)

ications, antipsychotic agents, and narrow-therapeutic-index drugs) need to be closely monitored by health care professionals to ensure attainment of therapeutic goals and to avoid ADEs.

In November 2003, the FDA and Customs performed another spot examination of imported parcels. They reviewed 1,982 parcels at the Buffalo, Dallas, Chicago, and Seattle mail facilities and at the Memphis and Cincinnati courier hubs. They found 1,728 unapproved drugs, including so-called "foreign versions" of FDA-approved drugs, recalled drugs, drugs requiring special storage conditions, drugs requiring close physician monitoring, and drugs containing addictive controlled substances. The FDA determined that approximately 80% of the parcels were exported from Canada, approximately 16% were from Mexico, and the remaining 4% were from Japan, the Netherlands, Taiwan, Thailand, and the United Kingdom. Some of the imported drugs identified during this inspection included warfarin, clomiphene, metformin, tamoxifen, and lithium, all of which can be dangerous without appropriate monitoring.¹⁷

Difficult-to-Read, Inaccurate, or Insufficient Product Labeling

The FDA is also concerned about drugs manufactured overseas because of problems with the product's labeling.¹¹ When a drug is imported from a country where English is not the main language, the language of the label or the package insert may be difficult to read or understand. The label might also make claims that have not been supported by clinical studies, or it may suggest uses that have not been confirmed to be safe or effective. These shortcomings may lead to the improper use of the medication and to serious ADEs.

If patients experience ADEs after taking an imported drug, they may be at an increased risk for complications because the product might not contain the information needed to quickly counteract or avoid the reaction.¹¹ It may also be difficult to track recalled products that have been imported into the U.S.

The spot inspection performed in November 2003 found

that American patients were receiving GlaxoSmithKline's salmeterol xinafoate (Serevent® Diskus) and fluticasone propionate (Flovent® Diskus) from Canada. Shortly after this inspection, certain lots of the Canadian versions of both Diskus products were recalled in Canada because of a possible malfunction of the drug-delivery system, with the potential to result in insufficient delivery of the active ingredients and subsequent lack of therapeutic effect. Canadian patients were advised to return the product to the pharmacy or physician's office in order to obtain a replacement. If the FDA had not released a Talk Paper to alert patients in the U.S. of this problem, the

American public might not have learned of this situation.^{17,18}

INTERNET PURCHASES

Although shopping online for medications can provide several benefits, including convenience and time savings, considerable potential dangers may result from ordering medications via the Internet. The Internet's distinctive traits include the relative anonymity afforded to creators of Web sites, the accessibility to individuals and groups around the world, and the ease of creating and removing old Web sites. These aspects make the enforcement of federal laws regulating drug importation more challenging. Investigations of Internet sites have been impeded by the difficulty in determining and locating the individuals responsible for posting content in "cyberspace." This difficulty usually results in more complex investigations, for which additional time and resources are necessary.

One reason why ordering drugs via the Internet is risky is that patients may have difficulty distinguishing legitimate Web sites from those that sell counterfeit medications, subpotent or superpotent products, or unapproved prescription drug products. Patients can check with the National Association of Boards of Pharmacy¹⁹ to determine whether a Web site is a licensed pharmacy in good standing.²⁰

HOW THE FDA EDUCATES THE AMERICAN PUBLIC

The FDA's Web site contains information developed by the Center for Drug Evaluation and Research (CDER) to alert patients about counterfeit medications, buying medications via the Internet, and FDA-approved drugs.⁹ These public service campaigns provide guidance by informing the public about the dangers of medications acquired outside the U.S. In addition, the FDA recently announced plans to create an independent Drug Safety Board to oversee the management of drug safety problems.²¹

Patients may also speak to Consumer Safety Officers at the FDA by calling 888-INFO-FDA (888-463-6332).

Dangers of Drug Importation

HOW HEALTH CARE PROFESSIONALS CAN INFORM PATIENTS ABOUT IMPORTED DRUGS

Educating American patients about the safety concerns associated with drug importation should be considered a duty of all health care professionals. We should help patients understand the safety risks involved each time they use a foreign drug, and we should advise patients of the possibility that some imported medications may be counterfeit or may contain ingredients that have not been evaluated by the FDA.

Patients should be informed about alternatives to purchasing imported drugs, such as using less expensive generic drug products, participating in state-sponsored programs, and applying for the federal Medicare Drug Benefit Discount Card.

Generic drugs account for most prescription drugs used in the U.S., and their costs are often lower than international prices for similar drugs.⁵ State-sponsored programs are another alternative; as of May 2004, 39 states offered pharmaceutical assistance programs to qualifying low-income individuals.²²

The Medicare card is a temporary measure that provides an average discount of 12% to 21% for prescription drugs compared with national average prices. However, this program will end in 2006, when Medicare will implement a comprehensive new prescription drug benefit.^{23,24}

Health care professionals can also educate patients about assistance programs sponsored by drug firms. Four Internet sites (www.needymeds.com, www.rxassist.org, www.helping-patients.org, and www.rxhope.com) provide information on patient medication assistance programs.²⁵ Many of these programs are administered by individual drug manufacturers and may require completed paperwork from the patient's physician. However, the Together Rx Access Card Program includes more than 175 prescription products from 10 different manufacturers, and physician-completed forms are not necessary. This free program provides a 25% to 40% discount on prescriptions to patients without prescription drug coverage.^{26,27} Pharmacists can assist their patients who cannot afford their prescription medications by initiating discussions with their doctors about potential generic alternatives as well as programs that minimize consumers' costs for prescription drugs.

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