

Cheaper Drugs in Foreign Markets Increase the Focus on Domestic Drug Prices

In 2003, the U.S. Food and Drug Administration (FDA) staked out postal facilities in major cities across the country for a few days at a time and examined any parcels that appeared to contain drug products. They discovered prescription drugs mailed from all over the world. Later, they released a report detailing what they found: non-FDA-approved, foreign versions of U.S. drugs such as sildenafil, simvastatin, tamoxifen, warfarin, and carbamazepine; controlled substances such as codeine, diazepam, lorazepam, and clonazepam; drugs that require close physician monitoring, such as isotretinoin (which can cause birth defects), lithium (which poses a toxicity risk), and metformin (which requires kidney function monitoring); and foreign versions of 2 asthma medications that had been recalled in some countries because of faulty drug delivery systems. Some drugs arrived damaged, some were packaged in plastic bags or envelopes, while others lacked proper labeling or contained only foreign-language instructions. Most of the drugs came from Canada, but some of the products shipped from Canada came from other foreign suppliers.

The thousands of drugs the FDA seized in just a few days represented only a handful of the hundreds of thousands of approved and unapproved prescription drugs imported to the United States every year. Patients—particularly Medicare beneficiaries and others who pay for medications out of pocket—can order medications over the Internet or through the mail from foreign pharmacies with and without legitimate prescriptions. Patients are also traveling over borders to purchase medications from Canadian and Mexican pharmacies. They're sometimes asking their physicians for help finding foreign sources to fulfill their prescriptions. And they're going to all this trouble far more often than they did just a few

years ago. Sales of prescription drugs imported from Canada reached \$1.1 billion in 2003, twice the sales from the year before, according to IMS Health, a drug tracking firm. (This is still just a small fraction of the \$216.4 billion total U.S. prescription drug sales in 2003.)

In most cases of importation from foreign sources, the reason is simple: cheaper drugs. The price of many U.S.-manufactured drugs under patent is 30% to 50% lower in Canada and other countries. A recent price comparison of a U.S. Internet pharmacy with a Canadian Internet pharmacy, for example, found that the price of 60 capsules of 100-mg celecoxib is \$92 in the United States and \$54 in Canada; the price of fluticasone propionate nasal spray is \$60 versus \$40; 90 tablets of 20-mg atorvastatin is about \$276 versus \$205, and 180 tablets of 10-mg generic tamoxifen is about \$140 versus \$45 (in U.S. dollars based on an exchange rate of \$1.34). Not surprisingly, many Americans want access to medications at the same low prices available to Canadians.

Americans are particularly comfortable turning to Canada because its regulatory controls over prescription drugs are similar to those in the United States. But FDA commissioner Mark B. McClellan, MD, PhD, has warned consumers of the risks associated with buying prescription medications from all foreign markets, including Canada. As the FDA's recent postal investigation showed, the drugs may not come from a Canadian pharmacy even if they appear to. Of greater concern, FDA research has found that imported drugs can have unpredictable drug potency, purity, and quality and therefore could complicate medical treatment by increasing the risk for dosing confusion, medication errors, and unnoticed drug interactions. According to Commissioner McClellan, "Unapproved drugs from foreign countries are out-

side of FDA's safety oversight, they could be outdated, contaminated, counterfeit or contain too much or too little of the active ingredient. In addition, foreign dispensers of drugs to Americans may provide patients with incorrect medications, or improper directions for use—things that can turn even a useful drug into a potentially harmful one. We are working hard to give Americans greater access to safe and affordable drugs, but illegal drugs that do not assure safety are no bargain." The past 11 FDA commissioners have also voiced concerns about the safety of drug importation, as have the leaderships of medical groups such as the American Medical Association, the American College of Physicians, and the American Pharmaceutical Association, and, not surprisingly, the pharmaceutical industry.

But many patients have called these safety issues scare tactics, and they remain largely undeterred. They have spurred an expanding movement that favors broader legalization for the importation of products from U.S. drug companies that are available from foreign suppliers. In their view, legalized importation would eliminate the unfair pricing system that makes the drugs more expensive in the United States. Many pharmaceutical experts caution that the implications of wide-scale drug importation would lead to disarray in the global pharmaceutical market and stifle pharmaceutical innovation. They have also warned that pharmaceutical companies would limit drug supplies abroad and increase drug prices globally before suffering the income losses that would come from discounting drugs for Americans. As consumers of 40% of the worldwide pharmaceutical supply, Americans have a lot at stake.

IMPORTATION INCREASINGLY POPULAR

As of 1987, the law allows Americans to import up to a 90-day supply

of prescription medications for personal use. The same law bans larger-scale importation except by pharmaceutical manufacturers. Since 1987, people have become increasingly disgruntled over prescription drug costs, and they've turned importation into a higher-profile issue. The politicians have followed the lead of their constituency. In 2000, the U.S. Congress signed and President Clinton passed the Medicine Equity and Drug Safety (MEDS) Act, which lifted restrictions on large-scale wholesale importation of drugs and budgeted for FDA oversight. But the U.S. Department of Health and Human Services Secretary at the time, Donna Shalala, and her successor, Tommy Thompson, refused to implement the legislation because, they said, they could not certify, as required by the law, that importation would result in significantly lower prices without risking safety. In 2003, the House and Senate bills to reform Medicare included legislation modeled after the MEDS legislation to permit large-scale drug importation from Canada with certification by the Department of Health and Human Services. Then the House passed, with bipartisan support, a separate bill that would permit wholesale importation from more than 20 countries without requiring certification by the Department of Health and Human Services. The Senate has not yet ruled on the bill.

Not all the action is happening in Washington, DC. Officials in many state and local governments have voiced interest in offering discounted drugs from Canada with their employee health plans. So far, only Springfield, Massachusetts, and Montgomery, Alabama, have actually done so. Officials in Montgomery have estimated that by allowing its 4100 city employees and retirees to buy drugs from Canada for about a year, the city has saved up to \$500 000. In late 2003, Illinois Governor Rod Blagojevich requested permission from the Department of Health and Human Services to allow the state to import discounted U.S.-manufactured prescription drugs from Canada. If the

program served 230 000 state employees and retirees, Blagojevich estimated, the substitution of imported drugs from Canada would save the state up to \$56.6 million per year and state employee and retirees could save up to \$34.2 million in out-of-pocket costs.

Already, some drug manufacturers are trying to thwart such large-scale importation by limiting shipments to Canada, particularly shipments to Canadian mail-order pharmacies. The pharmaceutical trade industry's lobbying group, Pharmaceutical Research and Manufacturers of America (PhRMA), spent millions of dollars last year working to deter importation legislation. Meanwhile, the FDA has dissuaded some cities and states from importing pharmaceuticals from Canada by arguing for other ways to reduce prescription drug costs (such as by promoting the use of generics) and by threatening legal action.

PRICING, PRICING, PRICING

Why do Americans foot a higher bill for products from U.S. pharmaceutical companies than other developed countries? The answer is complicated. Canada, for instance, negotiated special rates with the U.S. pharmaceutical industry when it passed a patent reform law in 1992. In return for Canada's agreeing to honor drug patents, the U.S. companies agreed to discounted drug pricing controls. Because Canada is a relatively small player in the global pharmaceutical market, the companies did not expect these discounts to hurt their bottom line. Over the years, almost all other western governments, except the United States, have also negotiated deals to control drug prices based on their individual political and health insurance environments, said Judith L. Wagner, a scholar in residence at the Institute of Medicine. According to research by University of Pennsylvania economist Patricia M. Danzon, PhD, drug price differences tend to reflect income differences between countries as well.

In a recent report comparing prices in 8 countries relative to the United

States, Danzon determined that Japan paid more for prescription drugs than U.S. consumers, while the other countries—Canada, Chile, France, Germany, Italy, Mexico, and the United Kingdom—paid 6% to 33% less. Canadian consumers paid the least. When Danzon converted foreign currencies at gross domestic product purchasing power parities (an economic standard that accounts for cost-of-living differences), rather than exchange rates, the differential between Japan and the United States disappeared and the differential between Canada and the United States decreased from 33% to 14%. Overall, Danzon concluded, while the United States pays more for new drugs, the country benefits more than other countries from a competitive, low-priced generic market once patents expire. This structure, she said, appears to favor pharmaceutical innovation (2).

Indeed, price differences may not be as dramatic or as widespread as commonly believed, according to Wagner. "The United States foots the highest bill, but the price differentials are not nearly as substantial as many people think. This big difference in drug prices is pretty much an artifact of the past," said Wagner, who recently published a paper on international drug prices (1). New drugs that are clinically significant—not just substitutes for existing molecules on the market—are typically priced similarly throughout the world, for instance. Older drugs and drugs in crowded therapeutic categories, on the other hand, are more likely to be significantly cheaper in foreign countries, according to Wagner. Some U.S. health plans are believed to have negotiated price concessions that are similar to those obtained by national governments. She noted that U.S. consumers receive some new medications years before they're available in other countries.

Furthermore, generics tend to be significantly less expensive and more available in the United States than in other countries. Once drugs hit the market, they typically go off patent after about a dozen years (the clock on

the 20-year patents starts to tick while a drug is still in trials), and once the patent expires, generic versions frequently follow quickly thereafter. Patent expiration on many popular drugs in recent years has meant that many expensive name-brand drugs now cost a lot less, including generic versions of fluoxetine, loratadine, and omeprazole. Commonly used and expensive drugs such as the lipid-lowering agent simvastatin (Zocor), the antibiotic amoxicillin-clavulanate (Augmentin), the antidepressant agent sertraline (Zoloft), and the arthritis drug nabumetone (Relafen) are all scheduled to go off patent in the next few years. "Drugs are going generic at an average rate of roughly 10% of the market each year. Between 30% to 40% of spending in 2000 was for drugs that will be generic by end of 2004," said John E. Calfee, PhD, at the American Enterprise Institute in Washington, DC. The total annual savings from substituting generic drugs for patented drugs typically runs into the billions of dollars.

ASSESSING SAFETY AND FEASIBILITY

Few Americans would complain about cheaper drugs, but they would certainly have a problem with unsafe drugs. Concern over safety is the most frequently raised reason for opposing importation, but whether this concern is legitimate remains a matter of debate. People on both sides of the issue have called safety concerns a smoke screen for larger, more complicated issues related to importation. "The notion that we all have to fear the low quality of Canadian drugs is ludicrous. The Canadians have the same kind of controls as we have, they often are using exactly the same drug as we have in the United States made by the same people probably side by side in the same manufacturing plant," said Marilyn Moon, PhD, at the American Institute for Research in Silver Spring, Maryland. It is certainly possible that people could import drugs that were not well made, without the normal FDA oversight, according to Brian L.

Strom, MD, MPH, a pharmacology and preventive medicine expert at the University of Pennsylvania. But Strom noted that these fears remain largely theoretical. "The concern makes sense for drugs from countries like India or countries in Africa where there have been some documented problems, but it is theoretical only with countries with good regulation, like Canada or many countries in Europe," Strom said. If current legislation is any guide, importation law is unlikely to allow importation from countries outside of Canada and specific European countries with strong prescription drug regulation.

Regardless of the safety issue, many people believe that widespread importation will never achieve the goal of lower drug prices for Americans. "The most convincing argument against importation that it is just not feasible to do," Moon said. In short, what works on a relatively small scale today—with a million or so Americans importing prescription drugs for personal use—would not work if practiced on a larger scale—with wholesalers importing much larger quantities for distribution throughout the United States, according to Moon and other experts. Canada-only importation poses some immediate problems. The Canadian drug market is about a tenth of the U.S. market, and so U.S. importation from Canada would deplete the Canadian drug supply far before making a dent in U.S. drug demands. Ultimately, drug manufacturers would probably limit supply to staunch revenue loss from Canadian drug importation to the United States, according to Moon. Some pharmaceutical companies have already threatened to stop sales of their medicines in Canada unless Canadian pharmacies stop selling to U.S. consumers. According to Wagner, "the reduced pricing system in Canada won't go on if the United States tries to piggyback onto it, because the pharmaceutical companies will do whatever they have to do to stop it." Should the pharmaceutical companies go so far as to sharply limit drug shipments to Canada, the result would be massive

shortages as supply is drained off to the United States, according to Calfee. Regaining the Canadian drug supply would probably require that Canadians accept prices closer to those in the United States rather than U.S. prices going down, Calfee said.

Importation might be more feasible if the United States could draw from dozens of countries to fill its demand for discounted drugs. But by making the supply chain more complex and less predictable, importation from many foreign sources might increase the risk for adulterated or unofficial drug products and decrease safety oversight. Regulatory authorities seeking to prevent threats to the U.S. pharmaceutical market are also likely to institute onerous rules, restrictions, quotas, and monitoring on imported drugs, Calfee said. And before long, pharmaceutical companies are likely to push back by limiting supply, he added, so discounts on imported drugs would be unlikely to last long.

The United States might learn from the European drug market, which legalized importation about 15 years ago. Licensed drug trade is a legal and well-established business in Europe, according to Jim Furniss, director of pricing and reimbursement at Bridgehead Technologies in Leicestershire, United Kingdom. Since most European countries have some form of state-run health care system, the consumers are not interested in drug prices, but pharmacists and in some cases the health care systems improve their profit margins or save money by dispensing cheaper drugs. One concern about importation was that countries with significantly cheaper drugs, such as Greece and Portugal, might experience shortages of drugs, but there has been little evidence of this, Furniss said. Pharmaceutical companies reacted with legal challenges to importation, most of which failed, he added. One new tactic, not yet ruled illegal, is limiting supply to source markets such as Greece and Portugal, which restricts the wholesalers' ability to divert large quantities of product into trade with other European countries. Because of

these adjustments, importation has offered few benefits in the European drug market except to make some money for the importing wholesalers at the expense of pharmaceutical companies, Furniss said.

IMPORTATION AS THE ROAD TO FREE TRADE?

For importation to impel lasting reductions in U.S. drug prices, other countries may face higher prices. “The greatest change in American prices would come if all the large European nations dismantled their price controls. That would allow prices in the wealthiest nations to converge at a single international level, which would presumably be somewhat lower than current prices here and significantly higher than current prices abroad,” Calfee reported in a recent article (3). Roger Pilon, PhD, JD, from the Cato Institute in Washington, DC, agrees that the threat of importation into the United States would lead drug companies to raise their prices in the rest of the world, but he doesn’t think that this would be a bad thing.

Free trade advocates such as Pilon are in favor of such a global pricing readjustment as a way to spread the costs of drug research and development more evenly around the world. For instance, experts have noted that Germany, the third largest economy in the world with a population 30% the size of the United States, paid just 5% of the global bill for prescription drugs in 2002, while the United States paid almost 50% of the bill. “Importation would certainly unsettle the drug market worldwide, but that’s good. If it goes through, removing the barrier on reimportation will mean cheaper drugs for Americans and more expensive drugs for Europeans. Canadians and Europeans will scream, but Americans should not stand for a regime that

forces them, in effect, to bear the lion’s share of drug research and development costs,” Pilon said.

But while replacing price controls with free trade sounds democratic and fair, importation is unlikely to result in a workable free trade, Calfee noted. Poorer nations would suffer because pharmaceutical companies would be less willing to charge them lower prices—a practice that works only if the drugs stay where they are delivered instead of being shipped to Europe and the United States. International displeasure against the increases in the cost of health care costs resulting from rising pharmaceutical prices, especially in socialized health care systems, may cause a global uprising against the United States, Calfee added. Besides paying increased prices for their prescription drugs, the countries’ main alternative would be to exert intense diplomatic pressures on the United States while also threatening to break the drug company patents and make the drug compounds themselves, which has occurred with HIV/AIDS drugs. So, rather than force this situation, the United States would probably first establish domestic price controls of its own and force pharmaceutical companies to accept discounted drug payments, Calfee said. He warned that the effects of such price controls could endanger pharmaceutical innovation. “There’s no way to know what you’re losing in research and development when you cut down the pay-off from a big, expensive drug,” Calfee said. Not everyone thinks that his concerns are valid. And some experts think that allowing global free trade for drugs would encourage the drug companies to focus more on unique, life-saving drug compounds that people would be willing to pay top dollar for and less on spin-off versions of drug treatments that are already available.

REARRANGING PHARMACEUTICAL PRIORITIES

It remains unclear whether the importation debate will reduce drug prices in the United States, but it just might. Should pharmaceutical companies try to divert attention from importation, they may increasingly offer limited drug discounts in the United States. In a possible effort to deflect the importation effort, Pfizer, GlaxoSmith-Kline, Eli Lilly, and other pharmaceutical companies have already offered a few drugs at steeply discounted prices to poor Americans. Meanwhile, the impending Medicare prescription drug benefits are sure to relieve some of the pressure on the pharmaceutical industry by allowing more elderly Americans to afford their medications. Ultimately, Americans may never feel comfortable with the price of prescription drugs. “The American consumer wants all drugs at a virtually free price—ultimate choice at extremely low price. And they don’t want economics to come into the choice among medical therapies,” Wagner said. “But these are economic goods just like everything else, and we make choices.”

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