

The International Pharmaceutical Market as a Source of Low-Cost Prescription Drugs for U.S. Patients

Aaron S. Kesselheim, MD, JD, and Niteesh K. Choudhry, MD, PhD

In response to increasing prescription drug costs, more U.S. patients and policymakers are importing less-expensive pharmaceutical products from other countries. Large-scale prescription drug importation is currently illegal, but the U.S. Food and Drug Administration permits individuals to bring in 90-day supplies of drugs for personal use. As patient use of foreign-bought drugs has increased, federal legislators have continued to debate the full legalization of importation. Three factors help guide whether U.S. patients and policymakers can rely on other countries as sources of imported prescription drugs: whether the safety of the product can be ensured, how the import price compares with domestic prices, and how importation might affect the exporting country's pharmaceutical market. In wealthier countries with active regulatory systems, drug safety can be adequately ensured, and brand-name products

are usually less expensive than in the United States (although generic drugs may be more expensive). However, implementing large-scale importation can negatively impact the originating country's market and can diminish the long-term cost savings for U.S. consumers. In low- and middle-income countries, prices may be reduced for both brand-name and generic drugs, but the prevalence of unauthorized products on the market makes ensuring drug safety more difficult. It may be reasonable for individual U.S. consumers to purchase essential medicines from certain international markets, but the most effective way to decrease drug costs overall is the appropriate use of domestic generic drugs, which are available for almost every major therapeutic class.

Ann Intern Med. 2008;148:614-619.

www.annals.org

For author affiliations, see end of text.

The cost of prescription drugs remains an important domestic health policy issue for both payers and patients. Increasing drug-related expenses for government insurance programs have led to restrictions on services or changes in eligibility requirements (1). For patients, out-of-pocket payment for prescription drugs has been linked to non-adherence to treatment regimens (2) and worse health outcomes (3). Spending is largely driven by high prices for patent-protected, brand-name drugs (4).

In response, more Americans are obtaining less-expensive prescription drugs from other countries: In 2006, 11% reported importing pharmaceutical products—up from 5% in 2002 (5). Prescription drugs are being purchased from both foreign markets offering similar brand-name products and low- and middle-income countries. Canada reported \$1.2 billion in cross-border sales in 2004, and U.S. customers received numerous mail shipments from other countries, such as India, Thailand, and the Philippines (6). Meanwhile, federal legislators continue to debate whether to legalize large-scale importation.

Such practices allow U.S. patients easier access to essential medications, such as antiretroviral drugs for HIV and the antiplatelet agent clopidogrel (Plavix, Bristol-Myers Squibb, New York, New York) for cardiovascular disease. However, the U.S. Food and Drug Administration (FDA) restricts importation on safety grounds, and some commentators argue that importation can harm incentives for research and development (7).

Drugs from different international sources offer diverse trade-offs for policymakers and variable safety and affordability for consumers. This article reviews the legality of prescription drug importation and outlines the risks and benefits of foreign medications.

SUPPLIERS OF U.S. AND INTERNATIONAL PHARMACEUTICAL MARKETS

The U.S. prescription drug market is supplied by brand-name products and generic alternatives, which are usually manufactured independently and made available after expiration of the brand-name product's patent. All FDA-approved generic drugs must be bioequivalent to the original version. Generic drugs are much less expensive, in part because development costs are lower and because having more producers in the market helps lower prices (8).

Other countries with active prescription drug regulatory agencies, including Canada, Australia, and many European nations, offer similar brand-name and approved generic drug options (9). The drugs are produced by the same large, multinational manufacturers, often in the same FDA-approved plant; according to one report (10), 86% of domestic prescription medications are manufactured outside the United States. For example, both American and European consumers of the cholesterol-lowering agent atorvastatin (Lipitor, Pfizer, New York, New York) may receive tablets that were manufactured in Ireland and then shipped to local suppliers (11).

Low- and middle-income countries feature a more heterogeneous drug market. Brand-name manufacturers avoid the poorer populations in these countries partly because revenues can be lower. Nonetheless, a range of pharmaceutical choices exists, because regulatory systems are not as active, and these countries, until recently, did not allow

See also:

Web-Only

Conversion of graphics into slides

patents on drug products. For example, Intas Pharmaceuticals in India sells its version of atorvastatin as Lipicure, despite the fact that the chemical structure is currently protected by patents in the United States (12). Even after the 2005 implementation of the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights agreement, which set worldwide standards and mandated that patents be permitted on drug products, numerous disputes have arisen about whether preexisting patents covering brand-name products are enforceable (13).

Well-established, local manufacturers in some of these countries, such as Ranbaxy and Cipla in India, produce authorized products and seek government marketing approval. These manufacturers also frequently obtain licenses to supply generic products to the United States (14). However, other suppliers may market unauthorized prescription drugs of varying quality. In Russia, for example, pharmaceutical products were marketed by certain unregulated producers. However, they were of high-enough quality that law enforcement authorities did not pursue the cases (15).

THE LEGAL STATUS OF PRESCRIPTION DRUG IMPORTATION

The FDA approval of a drug is attached to an individual manufacturer's version, including the label and packaging. As a result, imported prescription drugs may not meet FDA requirements when produced by a different manufacturer—even if the products are chemically identical—or when produced by the same manufacturer in different packaging for a non-U.S. market. The FDA also restricts “reimportation” of drugs produced by U.S. manufacturers and sold elsewhere. However, the FDA generally refrains from taking legal action against individuals importing limited (up to 90 days) supplies of products for personal use.

Recent legislation has addressed prescription drug importation (Table 1). In 2000, Congress passed a bill authorizing imports from some foreign countries if the Secretary of the U.S. Department of Health and Human Services certified that the provision would “pose no additional risk to the public's health and safety” (16). Although the Secretary never provided such certification, Congress revisited the issue in 2003, allowing importation from certain Canadian pharmacies and formalizing the FDA's 90-day personal use policy (17). Again, however, implementation required certification from the Secretary, which has not been granted (18). Nevertheless, some state governments set up programs to import prescription drugs for state employees and Medicaid recipients. In 2004, the Illinois I-SaveRx program allowed consumers to use licensed, inspected pharmacies in Canada and the United Kingdom. However, state programs have struggled with administration of the licensing process and have not been as popular as anticipated (19), in part because the federal government continues to consider these programs illegal.

Table 1. Recent Federal Legislation Addressing Importation of Prescription Drugs

Legislation Title	Year	Major Provisions Related to Drug Importation*
Medicine Equity and Drug Safety Act	2000	Allowed pharmacists and wholesalers to import prescription drugs from a group of foreign countries with certain safety conditions Permitted manufacturers to contract with distributors and limit the supply or set the price of imported drugs
Medicare Prescription Drug, Improvement, and Modernization Act	2003	Allowed pharmacists and wholesalers to import prescription drugs from Canadian sources who met certain safety conditions Authorized the U.S. Food and Drug Administration to allow individuals to import prescription drugs for personal use
Pharmaceutical Market Access and Drug Safety Act†	2007	Permitted importation from registered importers from some countries (gives priority to significant Canadian exporters in registration process) or for personal use Prohibited manufacturers from discriminating against registered exporters or importers or attempting to restrict or delay importation

* All legislation required certification by the Secretary of the U.S. Department of Health and Human Services before implementation of importation provisions.

† Approved by the U.S. Senate only (as Title VIII of the Food and Drug Administration Revitalization Act).

Interest in fully legalizing prescription drug importation has persisted. In 2007, the U.S. Senate passed a bill allowing pharmacies and drug wholesalers to import medications from authorized international markets (20), potentially leading to 35% to 55% savings over current prices (21). However, an amendment once again required certification as to the products' safety. Because such certification is unlikely in the current political environment, this amendment has ironically been called a “poison pill” for the program (22).

Before prescription drug importation can be implemented, policymakers must resolve some details, such as how to monitor the shipments of products, how to manage manufacturers' patent rights (23), and how to adapt risk management strategies currently in place for certain drugs known to cause dangerous side effects (24). However, federal legislators' interest in reducing domestic spending on prescription drugs remains strong. As a result, authorizing large-scale importation is likely to be one of many strategies considered as the 2008 presidential elections approach.

THE RISKS AND BENEFITS OF IMPORTING PRESCRIPTION DRUGS

Three types of factors help determine whether U.S. consumers and policymakers can rely on prescription drugs

from different international markets: the integrity of the product; the product's relative cost; and other considerations, such as the effect of exports on local production and supply of the product (Table 2).

Drug Product Integrity

Imported prescription drugs must be as safe and effective as those available on the domestic market. Although specific data are scant, the FDA estimates that less than 1% of the U.S. drug supply is counterfeit (25) and asserts that once a product leaves our borders and changes hands, its safety can no longer be guaranteed (26). Medications may be unsafe if patients receive the wrong dose of a drug, a different drug altogether, or an inert or even harmful substance (27). For example, the FDA reported that versions of the muscle relaxant carisoprodol and the cholesterol-lowering agent simvastatin bought in Mexico were less potent than described on the label and some lacked any active ingredient (28).

The ability of U.S. regulators to ensure the integrity of a drug product varies in different markets. Many other countries effectively ensure the safety of products sold through legitimate pharmacies: In Canada, for example, Health Canada takes longer on average to release drugs than the FDA (29). In Europe, it may be even easier to identify counterfeit drugs than in the United States, because patients can receive drugs in containers sealed at the point of manufacture (30). As a result, concerns about the integrity of imported brand-name and generic drugs from these markets are often exaggerated, and U.S. regulators should be able to readily ensure the safety of imported products.

Ensuring medication integrity may be more difficult in low- and middle-income countries, where the prevalence of misbranded products is higher (31). In addition to local regulatory authorities, the World Health Organization offers a Prequalification Programme to certify the quality of reproductive health drugs and products aimed at treating HIV/AIDS, malaria, and tuberculosis (32). Reducing the

manufacture and sale of illegitimate prescription drugs will require time and investment in stronger enforcement of counterfeiting laws and better regulation of pharmaceutical dissemination. Still, U.S. policymakers and consumers can rely on certain manufacturers in these countries that work closely with local authorities to ensure the integrity of their products and even export approved generic drugs to the United States. Although there is little empirical evidence on this point, most counterfeit medications seem to be sold in rural and extremely poor regions and usually in stores that stock a wide range of goods and often do not have a trained pharmacist on hand (33).

Savings from Imported Drugs

Lower drug prices arise when foreign governments engage in negotiations with pharmaceutical manufacturers or use formal price controls (34). However, costs can differ substantially between brand-name and generic products. A recent study found that Canadian brand-name drugs are, on average, 24% cheaper per unit than prices in the United States (35). The brand-name product of the migraine medication sumatriptan (Imitrex, GlaxoSmithKline, London, United Kingdom) costs approximately \$21 to \$25 per dose in the United States in 2005 but could be purchased in Canada for as low as \$10 to \$13 per dose (36). On the other hand, prices for generic drugs are lower on average in the United States (37).

In countries like India, both brand-name and generic drugs cost less than in the United States. In these environments, unauthorized products are likely to cost less than drugs produced by manufacturers that have better safety and efficacy standards and have registered their products with drug regulatory authorities.

Other Policy Implications of Importation

Large-scale U.S. importation can have important effects on foreign prescription drug markets. For example, formalizing a process of importing drug products from Canada could be problematic because the Canadian mar-

Table 2. Policy Considerations When Deciding Whether U.S. Patients Can Rely on International Markets as an Alternative to Domestic Brand-Name Drugs

Consideration	Brand-Name Product		Authorized Generic Product			Unauthorized Generic Product
	United States	International	United States	International: Well-Regulated Market	International: Other	
Example	Lipitor*	Lipitor	None†	None‡	Lipicure§	Atorvastatin
Legal to produce?	Yes	Yes	Yes	Yes	Yes	No
Legal to import for personal use?	–	Yes	–	Yes	Yes	Yes
Product integrity	Yes	Yes	Yes	Yes	Possible	Cannot ensure
Cost	++++	+++	++	+++	+	+
Should U.S. patients rely on it?	–	No	Yes	Yes	Case-by-case basis	No

* Pfizer, New York, New York.

† Generic atorvastatin expected to be available in the United States in 2011.

‡ Generic atorvastatin may be available in Canada before 2010.

§ Intas Pharmaceuticals, Gujarat, India.

|| Number of plus signs indicates likely relative cost.

ket is smaller. Brand-name drug makers have already imposed restrictions on Canadian pharmacies engaged in sales to U.S. consumers (38). Manufacturers may respond by further limiting supply to Canadian pharmacies engaged in substantial cross-border sales, which can also prevent Canadians from obtaining their own prescriptions. Prices to Canadians would probably rise from the increased demand, bringing drug prices closer to those in the United States and reducing or eliminating the potential savings (39). Considerations about limited supply are not applicable to generic drug products because they come from many different manufacturers.

Finally, some have argued that U.S. prescription drug importation will decrease innovation because large international manufacturers rely on U.S. consumers to fund pharmaceutical research (40). However, there is no direct connection between revenues of for-profit companies and their level of innovation. In fact, a report indicated that the largest pharmaceutical companies spend more of their revenues (about 30%) on promotion, marketing, and administration than on research and development (from 11% to 14%) (41), whereas another study also suggested that pharmaceutical manufacturers spend about twice as much on promotion as they do on research and development (42).

LESSONS FOR PATIENTS, PHYSICIANS, AND POLICYMAKERS REGARDING IMPORTATION OF PRESCRIPTION DRUGS

Brand-name drug products sold in wealthier countries may be safe and less expensive, but any savings from importation are likely to be short-lived.

Importing brand-name drugs from countries with active regulatory agencies can provide cost savings to individual U.S. consumers, and physicians should advise their patients that valid safety concerns can be addressed with prudent purchasing practices. However, system-wide adoption of this practice would probably diminish its benefits over time, because governments and the global pharmaceutical suppliers adjust their policies to account for the additional demand. Accordingly, U.S. policymakers should not rely on this strategy.

Generic drug products sold in countries with active drug regulatory agencies are valid options only if no cheaper generic alternatives exist in the United States.

Consumers in the United States should not consider importing domestically available generic products because, even though safety considerations can be accommodated, U.S. prices for these products tend to be lower. However, because intellectual property laws may be applied differently among countries, generic versions of essential drugs may become available sooner in other similar markets. For example, although many generic cholesterol-lowering agents are available for U.S. consumers, atorvastatin can provide more substantial reductions in low-density lipoprotein levels and may be required by a small number of

patients to achieve their target lipid level. Although U.S. patents lasting until at least 2010 will protect atorvastatin's brand-name status in the U.S. market, a Canadian court recently held that the patent in that country does not cover one manufacturer's generic version (43). The Canadian generic version could be available before 2010 (although the case is currently under appeal). In that case, U.S. patients requiring this specific product for their cardiovascular health who cannot afford local prices may consider importing a generic version, and U.S. policymakers may ensure that our regulatory systems support the efforts of such patients.

Brand-name drug products sold in low- and middle-income countries for which no generic equivalent exists may be viable options for U.S. consumers if safety can be ensured, but widely available generic drugs and unapproved products in these markets, while less expensive, are not worth the risk.

Officially sanctioned, brand-name products may continue to be available at substantially reduced prices in low- and middle-income countries. Some governments have used compulsory licenses to prevent patents from interfering with public health goals and have reduced the costs of essential medications by authorizing large-scale purchase or local manufacture of these products. Brazil used the threat of a compulsory license to negotiate low prices on a heat-stable form of the antiretroviral agent lopinavir–ritonavir (Kaletra, Abbott Laboratories, Abbott Park, Illinois), and Thailand recently used a compulsory license to permit local production of clopidogrel and lopinavir–ritonavir. However, while regulatory systems in those countries continue to develop, physicians should warn their patients to be wary about pursuing these purchases on their own. Systematic importation of these products will be possible if U.S. policymakers ensure the products' integrity by examining manufacturers' quality control measures on a case-by-case basis. Products from unauthorized manufacturers, despite their extremely low cost, are never worth the risk.

Greater use of domestically sold generic drugs, where available, is the safest and most cost-effective policy option for U.S. consumers and policymakers.

Although some essential medications may be available only in brand-name form, domestically sold generic products currently exist in almost every major therapeutic class. Cost savings would be substantial if physicians prescribed generic products, according to established treatment guidelines, that are already sold on the U.S. market (44). Such cost savings may also help improve patient outcomes: One recent study suggested that patients who begin using generic drugs are more likely to adhere to their therapeutic regimens (45). As a result, legislative proposals or judicial decisions in the United States that extend a pharmaceutical product's market exclusivity by delaying the approval of a generic alternative should be strictly limited (46). If national and state health care reform efforts promoting timely approval and rational prescription of generic drugs are im-

plemented, many U.S. consumers may no longer need to consider importing foreign prescription drugs.

CONCLUSION

The increasing cost of prescription drugs has inspired U.S. policymakers and consumers to turn to international markets as sources of lower-priced products. In cases in which essential medicines are unaffordable and no domestic generic alternatives are available, certain international markets can be reasonable sources of lower-priced products. However, the safest way to control U.S. drug prices is by promoting consumer demand for and appropriate prescription of domestic generic drugs.

From Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts.

Acknowledgment: The authors thank Kevin Outterson, Michael Reich, Rahul Rajkumar, and Frank May for their comments on earlier drafts of the manuscript.

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Aaron S. Kesselheim, MD, JD, Division of Pharmacoepidemiology and Pharmacoeconomics, 1620 Tremont Street, Suite 3030, Boston, MA 02120; e-mail, akesselheim@partners.org.

Current author addresses are available at www.annals.org.

References

1. Soumerai S. Unintended outcomes of medicaid drug cost-containment policies on the chronically mentally ill. *J Clin Psychiatry*. 2003;64 Suppl 17:19-22. [PMID: 14680423]
2. Choudhry NK, Avorn J, Antman EM, Schneeweiss S, Shrank WH. Should patients receive secondary prevention medications for free after a myocardial infarction? An economic analysis. *Health Aff (Millwood)*. 2007;26:186-94. [PMID: 17211028]
3. Tamblyn R, Laprise R, Hanley JA, Abrahamowicz M, Scott S, Mayo N, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001;285:421-9. [PMID: 11242426]
4. Kaiser Family Foundation. Prescription drug trends. November 2005. Accessed at www.kff.org/insurance/upload/3057-04.pdf on 4 March 2008.
5. Cummings J, ed. Eighty percent of U.S. adults favor allowing importation of prescription drugs, according to Wall Street Journal Online/Harris Interactive Health-Care Poll. Wall Street Journal Online/Harris Interactive Health-Care Poll. 15 September 2006:5. Accessed at www.harrisinteractive.com/news/letters/wsjhealthnews/WSJOnline_HI_Health-CarePoll2006vol5_iss15.pdf on 19 February 2008.
6. Hearing Before the Senate Judiciary Committee on Examining the Implications of Drug Importation (14 July 2004) (testimony of William K. Hubbard, Associate Commissioner for Policy and Planning, U.S. Food and Drug Administration. Accessed at www.fda.gov/ola/2004/importeddrugs0714.html on 19 February 2007.
7. Outterson K. Pharmaceutical arbitrage: balancing access and innovation in international prescription drug markets. *Yale J Health Policy Law Ethics*. 2005; 5:193-291. [PMID: 15742578]
8. Frank RG. The ongoing regulation of generic drugs. *N Engl J Med*. 2007; 357:1993-6. [PMID: 18003956]
9. U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation. Washington, DC: U.S. Department of Commerce International Trade Administration; December 2004. Accessed at www.ita.doc.gov/td/chemicals/drugpricingstudy.pdf on 19 February 2008.

10. Statement of the Nathan Jacobson, President of MagenDavidMeds.com, to the U.S. Department of Health and Human Services Secretary’s Task Force on Drug Importation. 14 May 2004. Accessed at www.hhs.gov/importtaskforce/session6/presentations/MagenDavidMeds.pdf on 19 February 2008.
11. Pfizer. Patient information: Lipitor. New York: Pfizer; June 2006. Accessed at www.pfizer.com/pfizer/download/ppi_lipitor.pdf on 19 February 2008.
12. Intas Pharmaceuticals lipid lowering agents. Accessed at www.intaspharma.com/pharmaceuticals_products_therapeutic_segment.php?thera_seg=45 on 19 February 2008.
13. Mueller JM. Taking TRIPS to India—Novartis, patent law, and access to medicines. *N Engl J Med*. 2007;356:541-3. [PMID: 17287473]
14. Wal-Mart in talks to directly source generic drugs from India. AFX News Limited. 1 May 2007. Accessed at www.forbes.com/markets/feeds/afx/2007/05/01/afx3670846.html on 19 February 2008.
15. Kramer AE. Drug piracy: a wave of counterfeit medicines washes over Russia. *New York Times*. 5 September 2006:C1.
16. Medicine Equity and Drug Safety Act, Pub. L. No. 106-387 (2000).
17. Medicare Prescription Drug, Improvement and Modernization Act, Pub. L. No. 108-173 (2003).
18. U.S. Department of Health and Human Services Task Force on Drug Importation. Report on Prescription Drug Importation. Washington, DC: U.S. Department of Health and Human Services; December 2004. Accessed at www.hhs.gov/importtaskforce/Report1220.pdf on 19 February 2008.
19. State of Illinois Office of the Auditor General. Management Audit of the Flu Vaccine Procurement and I-SaveRx Program. Springfield, IL: Office of the Auditor General; September 2006. Accessed at www.auditor.illinois.gov/Audit-Reports/Performance-Special-Multi/Performance-Audits/FY06-Flu-Vaccine-ISaveRX-MGMT-digest.pdf on 19 February 2008.
20. Pharmaceutical Market Access and Drug Safety Act of 2007, H.R. 380 (2007).
21. Baker C. Would prescription drug reimportation reduce U.S. drug spending? Economic and budget issue brief. Washington, DC: Congressional Budget Office; 2004.
22. Pear R. Senate vote upholds drug import limits. *New York Times*. 8 May 2008:A1.
23. Thomas JR. Patents and drug importation. Washington, DC: Congressional Research Services; 25 May 2004.
24. Hearing Before the U.S. Senate Subcommittee on Interstate Commerce, Trade, and Tourism, Committee on Commerce, Science, and Transportation, Implications of Importing Drugs into the United States (7 March 2007) (statement of Randall W. Lutter, PhD, Acting Deputy Commissioner for Policy, U.S. Food and Drug Administration). Accessed at http://commerce.senate.gov/public/index.cfm?FuseAction=Hearings.Testimony&Hearing_ID=1829&Witness_ID=6533 on 19 February 2008.
25. Rudolf PM, Bernstein IB. Counterfeit drugs. *N Engl J Med*. 2004;350:1384-6. [PMID: 15070787]
26. Outterson K, Smith R. Counterfeit drugs: the good, the bad and the ugly. *Albany Law Journal of Science & Technology*. 2006;16:525-43.
27. Liang BA. Fade to black: importation and counterfeit drugs. *Am J Law Med*. 2006;32:279-323. [PMID: 16927613]
28. U.S. Food and Drug Administration. FDA warns consumers about counterfeit drugs purchased in Mexico. Silver Spring, MD: U.S. Food and Drug Administration; 30 July 2004. Accessed at www.fda.gov/bbs/topics/answers/2004/ans01303.html on 19 February 2008.
29. Safety of canadian drugs. *Med Lett Drugs Ther*. 2003;45:100. [PMID: 14657804]
30. Barry P. States defy FDA on drug importation: governors from both sides fight for savings. *AARP Bulletin*. October 2004. Accessed at www.aarp.org/bulletin/prescription/a2004-10-08-fda_importation.html on 19 February 2008.
31. Cockburn R, Newton PN, Agyarko EK, Akunyili D, White NJ. The global threat of counterfeit drugs: why industry and governments must communicate the dangers. *PLoS Med*. 2005;2:e100. [PMID: 15755195]
32. World Health Organization Prequalification Programme. Accessed at <http://mednet3.who.int/prequal/> on 19 February 2008.
33. World Health Organization. Counterfeit medicines: some frequently asked questions. 6 May 2005. Accessed at www.wpro.who.int/media_centre/fact_sheets/fs_20050506.htm on 19 February 2008.
34. Frank RG. Prescription-drug prices. *N Engl J Med*. 2004;351:1375-7. [PMID: 15459294]
35. Quon BS, Firszt R, Eisenberg MJ. A comparison of brand-name drug prices

between Canadian-based Internet pharmacies and major U.S. drug chain pharmacies. *Ann Intern Med.* 2005;143:397-403. [PMID: 16172438]

36. **Consumer Reports Best Buy Drugs.** Treating headaches: the triptans. Yonkers, NY: Consumers Union; 2006. Accessed at www.crbestbuydrugs.org/PDFs/triptanFINAL.pdf on 19 February 2008.

37. In re Canadian Import Antitrust Litigation, 470 F.3d 785 (8th Cir. 2006).

38. **U.S. Food and Drug Administration.** Generic drug prices in the U.S. are lower than drug prices in Canada. Silver Spring, MD: U.S. Food and Drug Administration; November 2003. Accessed at www.fda.gov/oc/whitepapers/drugprices.html on 19 February 2008.

39. **Choudhry NK, Detsky AS.** A perspective on US drug reimportation. *JAMA.* 2005;293:358-62. [PMID: 15657329]

40. **Hollis A, Ibbott P.** How parallel trade affects drug policies and prices in Canada and the United States. *Am J Law Med.* 2006;32:193-217. [PMID: 16927610]

41. **Families USA.** Profiting from pain: where prescription drug dollars go.

Washington, DC: Families USA; 2002.

42. **Gagnon M-A, Lexchin J.** The cost of pushing pills: a new estimate of pharmaceutical promotion expenditures in the United States. *PLoS Med.* 2008;5:e1. [PMID: 18177202]

43. **Johnson A.** Pfizer is handed set-back in Canada on Lipitor patent. *Wall Street Journal.* 27 January 2007:A4.

44. **Fischer MA, Avorn J.** Economic implications of evidence-based prescribing for hypertension: can better care cost less? *JAMA.* 2004;291:1850-6. [PMID: 15100203]

45. **Shrank WH, Hoang T, Ettner SL, Glassman PA, Nair K, DeLapp D, et al.** The implications of choice: prescribing generic or preferred pharmaceuticals improves medication adherence for chronic conditions. *Arch Intern Med.* 2006;166:332-7. [PMID: 16476874]

46. **Kesselheim AS, Fischer MA, Avorn J.** Extensions of intellectual property rights and delayed adoption of generic drugs: effects on Medicaid spending. *Health Aff (Millwood).* 2006;25:1637-47. [PMID: 17102189]

READERS' COMMENTS

Readers wishing to comment on published articles should use the "Send comment/rapid response letter" option at www.annals.org. While this service is free to *Annals* subscribers, readers without subscriptions who wish to comment on articles may purchase temporary access.

Current Author Addresses: Drs. Kesselheim and Choudhry: 1620 Tremont Street, Suite 3030, Boston, MA 02120.