Commercial Importation of Prescription Drugs in the United States: Short-Run Implications

Patricia M. Danzon
University of Pennsylvania

Scott J. Johnson
Genia Long
Analysis Group

Michael F. Furukawa
Arizona State University

Abstract The option of legalizing the commercial importation of prescription drugs is of continued policy interest as a way to reduce U.S. drug spending. Using IMS data, we estimate potential savings from commercial drug importation under assumptions about percentage of drugs likely to attract imports; potential supply from foreign countries; and share of savings passed on to payers. Our base case estimate is that $1.7 billion per year, or 0.6 percent of total drug spending, would be saved by payers; sensitivity analyses range from 0.2 to 2.5 percent under plausible assumptions and up to 17.4 percent under unrealistic assumptions about unlimited foreign supply, costless trade, and zero profits for intermediaries. Estimated savings to payers are less than the average price differentials between the United States and foreign countries because proposed legislation exempts certain drugs from importation; foreign markets are small relative to the United States; regulatory and other constraints may limit the volume of exports; trade is costly; and intermediaries will retain some savings. Although savings to U.S. payers/consumers would likely be small and have minimal impact on total U.S. health care spending, costs to other countries could be significant, due to reduced access and possibly higher prices. In the long run, reduced investment in R&D could adversely affect consumers globally.

This research is based in part on data obtained under license from the IMS Health MIDAS (July 2004–June 2005) database. The conclusions and views expressed herein are not necessarily those of IMS Health or any of its affiliated or subsidiary entities. We would also like to thank the Pharmaceutical Research and Manufacturers of America for financial support. The analysis presented in this article was structured and executed entirely by the authors, and all conclusions and any errors or misstatements are ours alone.

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Introduction

The issue of prescription drug prices in the United States, especially relative to other countries, remains of keen interest; some observers note, "the same drugs, manufactured in the same factory, routinely sell for nearly two times as much in the US as they do in other countries" (Dorgan 2007). To address this apparent disparity, bills have been introduced in Congress to legalize commercial drug importation (also called parallel trade, which is legally permitted in the European Union), permitting wholesalers and other third parties to import on-patent prescription drugs from designated foreign countries into the United States. Proponents claim that allowing drug importation would enable Americans to "pay the same prices as the rest of the world" and save $50 billion over ten years (Dorgan 2007).

Recent bills not only propose to limit the traditional rights of patent holders to bar importation but also attempt to restrict manufacturers' potential responses in other countries. The Pharmaceutical Market Access and Drug Safety Act (S. 1232 or H.R. 1298, 111th Congress [2009], both based on similar legislation over the past six years),[1] for example, would authorize personal and commercial importation of "qualifying drugs" from thirty-two permitted countries, including Canada, Japan, and most European countries (S. 1232 [2009]). S. 1232 also includes several so-called forced-sale provisions. The first amends the U.S. patent code to provide for "international exhaustion," where a U.S. patent holder would lose its right to bar importation of products into the United States that have been sold in another country (S. 1232 [2009], §4[d]). The second deems it an "unfair and discriminatory" practice for manufacturers to charge importers into the United States prices that are higher than the government-controlled prices in the exporter's country, or to charge importers into the United States higher prices than those paid by anyone else in the exporting country. The third deems it unlawful to deny, delay, or restrict supplies to, or refuse to do business with, foreign exporters and domestic importers. The fourth deems it "unfair and discriminatory" to introduce in foreign countries a new drug that is different from the U.S. version of that product (S. 1232 [2009], §804[n][1][A–M]).

1. S. 1232, the Pharmaceutical Market Access and Drug Safety Act of 2009, was introduced on June 10, 2009, and reported out by the committee the following day. S. 1232 is similar to previous legislation introduced over the past six years, including S. 242 (110th Congress [2007]) and S. 334 and S. 1392 (109th Congress [2005]). As of May 15, 2010, it had not gone to a vote in the Senate, and its provisions were not reflected in the health care reform law signed by President Barack Obama in March 2010. Given the similarity of these past bills, it seems likely that any future proposals will have similar provisions.

This article estimates the likely savings to U.S. final payers, including insured and uninsured consumers, private third-party and government sector payers, and employers (which together we call "payers/consumers"), from S. 1232 or similar bills. Our estimates depend on which drugs would be eligible for importation, which is specified in S. 1232. The estimates also depend on other assumptions, particularly on the volume of potential import supply from foreign countries and the share of savings that would reach final payers/consumers. We focus on short-run savings for existing products and comment only briefly on importation's effects on safety, administrative costs, possible legal and policy response, and long-run effects on R&D. These are all important issues but are outside our research's scope.

Commercial Importation and the U.S. Pharmaceutical Supply Chain

In the United States, as in most other countries, pharmaceutical manufacturers sell drugs to wholesalers who distribute to pharmacies and other outlets. Each stage of the distribution chain adds a margin based on its costs incurred and its market power relative to the next stage in the supply chain. Manufacturers sell to wholesalers at ex-manufacturer prices (roughly, the manufacturers' wholesale acquisition cost [WAC]), a list price, minus discounts for volume or prompt payment; wholesalers distribute drugs to outpatient and hospital pharmacies at ex-wholesaler prices; and outpatient pharmacies dispense the drugs to patients at retail (or "public") prices. Outpatient pharmacies are reimbursed by the patient's pharmacy benefit manager (PBM) or health plan, net of the patient's co-payment. PBMs do not observe the actual acquisition cost paid by pharmacies and therefore typically base their reimbursement on a published list price, such as average wholesale price (AWP) minus a percentage or WAC plus a percentage. In addition, PBMs often negotiate rebates from manufacturers in return for preferred formulary positioning that shifts share. Off-invoice rebates are confidential and transmitted electronically by the manufacturer directly to the PBM; hence, they do not affect the ex-manufacturer prices available to wholesalers. In this article, we refer to ex-manufacturer prices unless otherwise indicated.

If commercial importation were permitted, trading wholesalers would compare the ex-manufacturer prices in foreign countries to U.S. ex-manufacturer prices and source from abroad if the differential covered the costs associated with importation. Thus commercial importation

would impose a revenue loss on drug manufacturers equal to, in the first instance, the U.S.-foreign difference in ex-manufacturer prices times the share of U.S. volume that traders sourced from abroad. How much of this revenue loss to manufacturers would result in savings to U.S. payers/consumers would depend on the extent to which intermediaries along the supply chain, including wholesalers, pharmacies, PBMs, and health plans, were forced by competition to pass this savings along rather than capture it as profit.

Previous studies have generally concluded that savings from importation are modest. In a study of a bill similar to S. 1232, the Congressional Budget Office (CBO) concluded that drug importation would reduce drug spending by roughly 1 percent, or about $50 billion, over ten years beginning in 2006 (FTC Reauthorization Act, S. 1392, 109th Congress [2005]). However, this estimate used a review of the literature instead of primary data. Most analyses of parallel trade within the EU have found that payers see limited savings because traders capture most of the rents (Kanavos et al. 2004; Kanavos and Costa-Font 2005; Kyle, Allsbrook, and Schulman 2008; Kyle 2007). One exception is Ganslandt and Maskus (2004), who estimated a 12–19 percent ex-manufacturer price reduction for drugs subject to competition from parallel imports in Sweden. Given the much larger size of the U.S. market, we do not believe that this Swedish experience is a relevant precedent for the United States.

Methods

We used IMS MIDAS data[2] on the universe of pharmaceutical sales at ex-manufacturer prices in nine countries (Australia, Canada, France, Germany, Italy, Japan, Spain, the United Kingdom, and the United States) for the year ending June 2005. The data contain information at the presentation level (defined by molecule, dosage form, strength, and pack size) on the quantity sold in each country through outpatient, inpatient, and other channels. The data include the ex-manufacturer, ex-wholesale, and retail prices per standard unit measured in U.S. dollars at the current exchange rate in each quarter. IMS MIDAS data are the most comprehensive source of information on international drug prices and sales (Kyle, Allsbrook, and Schulman 2008; Danzon and Furukawa 2003, 2008). The eight non-

2. IMS MIDAS data report pharmaceutical sales in over seventy countries. IMS collects data primarily from wholesaler invoices at ex-wholesaler prices and then imputes ex-manufacturer prices by netting out the average wholesaler margin for that country/channel. IMS also estimates retail (or public) prices by adding the average pharmacy margin for that country/channel.

U.S. countries in our data represent 78.3 percent of total 2005 sales in the potential export countries permitted under S. 1232.

Importable Drugs

To identify drugs in the United States that could be imported under S. 1232, we select all sales through outpatient channels and nonfederal hospitals from the universe of 2005 U.S. sales reported in IMS MIDAS data.[3] S. 1232 explicitly excludes over-the-counter (OTC) products, controlled substances, biologics, multisource products (i.e., off-patent brands and generics), infused or injected drugs, and sterile ophthalmics (S. 1232 [2009–2010], §804[a][4][C][iv]). Previous proposed drug importation legislation, including S. 525 (111th Congress [2009]) and S. 242 (110th Congress [2007]), contained the same exclusions, while S. 334 (109th Congress [2005]) was similar but did not exclude sterile ophthalmics. Although not stated explicitly in the legislation, the rationale for these exclusions is presumably that these categories pose heightened safety risks or minimal savings potential.[4] Given the consistency of these product exclusions, with one addition (sterile ophthalmics) and no deletions, together with the solid reasons for the exclusions, our estimates based on the S. 1232 eligible classes should be reasonably robust for any importation proposals in the near future. We also exclude combination products and products sold in the "miscellaneous" channel or described as "miscellaneous category/formulation" due to lack of necessary information.

Presentation Matches across Countries

S. 1232, like previous legislation, allows for substitution between products "with the same active ingredient(s), route of administration, dosage form, and strength as the foreign drug" (S. 1232 [2009–2010], §804[a][4][C][i]). Accordingly, our base case savings estimate includes only products with identical presentations in the United States and at least one foreign country. In sensitivity analysis, we allow substitution (a) between tablet and capsule formulations of the same strength, and (b) where multiple

3. We exclude federal hospitals because they already receive large discounts based on the Federal Supply Schedule.

4. Biologics, controlled substances, infusions, injectibles, and sterile ophthalmics require special sterile supply conditions. Generics and OTC products are often unbranded and multisource, so controlling unlicensed versions may be more difficult. Moreover, generics and OTCs are already cheaper in the United States than in most other countries (Danzon and Furukawa 2003, 2008).

foreign products add up to the U.S. strength. For example, if a molecule is sold as a 150mg tablet in the United States, but Italy has only a 150mg capsule, or 50mg and 100mg tablets, the base case assumes no match and hence no importation. The first sensitivity analysis allows substitution of the 150mg Italian capsule for the 150mg U.S. tablet, and the second assumes that the two Italian tablets could substitute for the single U.S. tablet.

Necessary Economic Conditions

Previous research found that the key determinants of parallel trade in Europe are the price difference between the importing and exporting countries and aggregate sales value in the import market (Kanavos et al. 2004; Kanavos and Costa-Font 2005; Kyle, Allsbrook, and Schulman 2008; Kyle 2007; Ganslandt and Maskus 2004). This is consistent with the assumption that trade occurs only if traders' expected revenue from importation (arbitrage price difference times volume traded) is sufficient to cover fixed costs of entry (e.g., obtaining an import license, establishing repackaging and relabeling facilities) and variable costs per unit traded (e.g., transportation, packaging and labeling, insurance). The CBO estimated that fee receipts alone from importers and exporters of imported pharmaceuticals would be about $2.2 billion over a ten-year period (S. 1392 [2005]).

In the absence of data on entry costs and margins that would be necessary to attract commercial importers into the United States, we estimate importation volumes under three alternative assumptions about margins necessary to attract trade:

- Entry condition 1: The foreign price of a presentation is lower than the U.S. price.
- Entry condition 2: The foreign-U.S. price differential is at least 5 percent, and U.S. sales at the molecule level (i.e., all presentations with the same active ingredient or molecule) are at least $5 million.
- Entry condition 3: The foreign-U.S. price differential is at least 10 percent, and U.S. sales at the molecule level are at least $15 million.

U.S.-foreign price differentials depend on exchange rates. To approximate recent conditions, we convert foreign prices in the data to U.S. dollars at January 2009 exchange rates (Federal Reserve Bank of St. Louis n.d.) and report sensitivity analysis using 2005 rates.

Potential Volumes Available for Export

Because the U.S. market is relatively large, another key factor in our estimate is how much supply could be diverted to the United States without causing unacceptable shortages in each potential exporting market. Although S. 1232 attempts to prohibit manufacturers from restricting supply to potential importers into the United States, legal or logistical constraints may nevertheless limit exports. We report the total quantity of doses consumed in each foreign country and the share of U.S. volume that these foreign sales represent. We calculate the import volume to the United States under alternative assumptions about the proportion of each country's supply available for importation. The base case assumes that 20 percent of the national supply in each foreign country would be exported and would displace the same number of doses in the United States. Whereas the CBO assumed that only 10 percent of a foreign country's supply would be available for export (S. 1392 [2005]), we chose 20 percent as a generous but plausible base case estimate.[5] We also report sensitivity analysis using the CBO's 10 percent assumption (S. 1392 [2005]). To provide an upper bound that we believe is highly unrealistic, we also report estimated savings assuming that unlimited import supply is available at the lowest price of any permitted country for each presentation. Effectively, this assumes that 100 percent of U.S. consumption for each imported presentation is sourced from a single lowest-price country, ignoring local supply disruptions such exportation would likely entail.

Potential Savings to Payers/Consumers

The estimated importable volume times the price differential yields the estimated *potential* savings to purchasers from importation. The *potential* savings overstates the ultimate savings for final payers/consumers to the extent that trade entails costs and some fraction of potential savings is retained as profit by intermediaries. These costs include costs of licensure, repackaging and labeling, transportation, and other expenses, as discussed above. Given the potential savings net of costs, the fraction of net savings

5. Congressional Budget Office (2004) states: "Many foreign governments would have incentives to limit the volume of drugs diverted to the United States, given both their interest in preventing shortages or higher prices in their own countries and the drugmakers' ability to limit supply. Depending on domestic circumstances, governments might simply influence purchasing arrangements by agreeing to export restrictions by contract, for example, or by imposing statutory restrictions on imports." Furthermore, foreign wholesalers may have incentives to limit exports to the extent that wholesaler licenses require the ability to meet local demand.

passed on to final payers/consumers depends on there being a sufficient number of importers and a supply of product to create competitive supply conditions. Specifically, pharmacy purchasers are likely to extract savings from wholesalers/importers only if either there is sufficient competition between importers or the pharmacy purchasers could credibly threaten to import directly. These conditions are plausible for the large pharmacy chains and mass retailers (such as Walmart), provided that foreign supply is sufficiently large and stable. The smaller, independent pharmacies are unlikely to realize significant savings unless foreign supply is abundant, which we believe is unlikely for the reasons cited above.

Uneven distribution of savings across pharmacies will likely limit the ability of payers to extract savings. In the United States, most PBMs, Medicaid, and other third-party payers reimburse pharmacies for the drugs that they dispense based on a discounted list price that is adjusted to reflect the payers' estimate of the pharmacies' actual acquisition cost. If payers perceive that the average pharmacy acquisition cost declined because some fraction of supply can be imported at a lower foreign price, U.S. payers would likely reduce their reimbursement to pharmacies, similar to the so-called clawback approach used in the Netherlands and the United Kingdom (Kanavos et al. 2004). Such clawback mechanisms reflect the payers' estimate of the savings realized by pharmacies on a particular molecule, in order to preserve incentives for pharmacies to seek out cheaper products, while being administratively practical. However, aggressive clawback based on *average* acquisition cost of all pharmacies likely would penalize systematically the small, independent pharmacies that are least able to obtain cheap imports. Even larger chains may be squeezed sporadically if their access to cheaper imports is limited or unreliable. Thus the smaller, less pervasive, and less reliable the savings realized by pharmacies, the less likely are health plans and PBMs to capture all savings realized by pharmacies. Cash-paying patients are likely to realize even smaller savings, because they lack leverage relative to pharmacies, especially if supply of imported drugs is limited or sporadic.

Accordingly, we assume that the share of potential savings captured by payers/consumers increases with the share of a given molecule that can be imported.[6] Specifically, we aggregate doses from the presentation level to the molecule level and assume that payers capture 50 percent of savings for molecules when imported doses are at least 40 percent of U.S. total domestic supply (in doses); 25 percent of savings when imported doses are

6. That is, all formulations and strengths of a given molecule.

20 to 40 percent of U.S. supply; and 10 percent when imported doses are below 20 percent of U.S. supply.[7] As an unrealistic upper bound, we also report savings assuming payers capture 100 percent of potential savings for all tradable molecules, noting that the implicit assumptions of costless trade and zero margin for intermediaries are implausible.

As a final step, we express estimated payer savings as a percentage of current expenditures on pharmaceuticals at average retail or public prices paid by payers, net of off-invoice rebates as estimated by Danzon and Furukawa (2008).[8]

Drug Matching and Availability

Table 1 reports doses and sales for the U.S. market in 2005. Total U.S. sales are $246.8 billion at ex-manufacturer prices and $336.7 billion at retail prices, before off-invoice rebates, which are estimated at approximately 11 percent of ex-manufacturer prices. S. 1232 excludes OTC drugs, biologics, controlled substances, infused or injected drugs, sterile ophthalmics, and multisource drugs, which we estimate (nonmutually exclusively) at $11.4, $29.1, $12.2, $55.7, $3.2, and $61.0 billion, respectively. After excluding these products, combination products, miscellaneous drugs, and sales to federal hospitals and the miscellaneous channel, we estimate the market subject to commercial importation to be $103.6 billion at ex-manufacturer prices or $120.6 billion at retail prices net of off-invoice rebates, which is 40.3 percent of total $299.4 billion retail expenditures by payers/consumers for drugs reported by IMS MIDAS (i.e., the denominator in our savings analysis).[9] Thus almost 60 percent of pharmaceutical expenditures is ineligible for importation under S. 1232.[10]

The $103.6 billion of pharmaceutical sales (at ex-manufacturer prices)

7. These assumptions are consistent with the 2004 report of the HHS Task Force on Drug Importation (U.S. Department of Health and Human Services 2004), which concludes: "Under any safe, legalized commercial importation program, when the scope is limited, intermediaries would likely capture a large part of the price differences. (This is based on evidence from European countries where some form of importation is legal)" (xi). The report adds, "Intermediaries will likely capture at least half of any savings between the United States and price-controlled countries and potential quantity constraints imposed by foreign governments and manufacturers will likely further limit the supply of these drugs to U.S. consumers" (xiii).

8. For hospital products, we assume that IMS MIDAS ex-manufacturer prices already reflect discounts.

9. Our estimate exceeds the National Health Expenditure's because we include more retail and hospital channels and miscellaneous/combination products.

10. We omit federal hospitals because their Federal Supply Schedule discounts would likely exceed any savings from importation.

Table 1 Total U.S. Market and Commercially Importable Market in Doses and at Ex-manufacturer and Retail Prices in 2005

	Doses[a] (billion)	At ex-manufacturer prices ($ billion)	At retail prices ($ billion)
Total U.S. pharmaceutical sales (before off-invoice rebates)	350.4	246.8	336.7
Total U.S. pharmaceutical sales (net of off-invoice rebates)[b]	350.4	219.4	299.4
S.1232–excluded drugs (before rebates)[c, d]			
OTC drugs	138.6	11.4	15.6
Biologics	0.4	29.1	39.7
Controlled substances	21.7	12.2	16.7
Infused or injected drugs	2.0	55.7	76.0
Sterile ophthalmics	26.7	3.2	4.3
Multisource (generic and off-patent brand)	269.2	61.0	83.3
Federal facilities/miscellaneous channel	11.2	4.4	6.0
Combination products	9.5	15.2	20.8
Miscellaneous categories/forms	25.6	7.1	9.6
Sales at risk from commercial importation (before rebates)[d]	42.9[e]	103.6[f]	141.3[f]
Sales at risk from commercial importation (after rebates)[b, d]	42.9[e]	88.4	120.6

Source: Author estimates based on IMS MIDAS data for year ending June 30, 2005

Notes:

[a]IMS standard units

[b]The methodology for estimating off-invoice rebates is described in the text and appendix of Danzon and Furukawa 2008. The average discount across all products and purchasers is 15 percent.

[c]See S. 1232 (2009), §804(a)(4)(C)(iv). We did not exclude "drugs inhaled during surgery," which are also excluded, as they are not separately identifiable in the data.

[d]We assume that all channels except federal facilities and miscellaneous channels would be susceptible to commercial importation.

[e]S. 1232–excluded categories are not mutually exclusive, hence the sales at risk from commercial importation are greater than total sales minus the sum of the exclusions.

[f]42.9 billion doses from 609 unique presentations

at risk for importation corresponds to 609 different U.S. presentations. Of these, 439 match an identical presentation in at least one foreign country (table 2). Germany, Canada, and the United Kingdom have the most matches and Japan the fewest, consistent with previous findings that countries differ in their preferred drug forms (Danzon and Furukawa 2003, 2008).

Table 2 also shows the number of matching presentations that meet our entry conditions. Of the S. 1232–eligible U.S. presentations, 68.5 percent are available in at least one foreign country at a lower price. If traders require at least a 5 percent U.S.-foreign price differential and U.S. sales of at least $5 million to import a given presentation, 54.0 percent of the eligible presentations would be subject to imports. This falls to 43.3 percent if a 10 percent price differential and $15 million market are required.

Foreign markets are much smaller than the U.S. market, which limits the quantity each country could export without disrupting local availability. Table 3 shows doses and sales for S. 1232–eligible presentations as a proportion of U.S. doses and sales of those same presentations. Under the least restrictive entry condition, 100 percent of U.K. doses would supply 12.2 percent of total U.S. doses. Varying entry conditions has little effect on the share of total doses and sales that could be supplied by each country, because more stringent entry requirements eliminate primarily low-volume products. The last row in table 3 shows the percentage of doses that have a match in any foreign country by entry condition. Under the implausible assumption that any country with a matching presentation priced below the U.S. price could supply unlimited exports to the United States, these imports would displace at most 75.5 percent of the 42.9 billion doses, or 81.5 percent of the $103.6 billion sales at risk for commercial importation.

In table 4, we estimate potential savings on S. 1232–eligible drugs at ex-manufacturer prices under alternative assumptions about foreign supply constraints. For each entry condition, the first column shows the percentage of S. 1232–eligible U.S. doses that could be imported. The second shows the implied reduction in U.S. expenditures at ex-manufacturer prices, which is the first-instance potential revenue loss to manufacturers and savings to payers/consumers from S. 1232. For comparison, the first row shows results assuming that unlimited volume could be imported from the lowest-price country for each presentation. In this "unlimited supply" scenario, if the lowest price for a given presentation were in, say, Australia, we assume that 100 percent of U.S. demand could be sourced from Australia, even though Australia's consumption is only 3.9 percent of

Table 2 Number of S. 1232–Eligible Matching Presentations under Alternative Entry Assumptions

Entry condition	•Presentation match only		•Presentation match •Foreign price lower than U.S. price		•Presentation match •Foreign price < 95 percent of U.S. price •U.S. sales[a] > $5 mil.		•Presentation match •Foreign price < 90 percent of U.S. price •Presentation match •U.S. sales[a] > $15 mil.	
	Number[b]	Percent matched with U.S.[c]	Number[b]	Percent matched with U.S.[c]	Number[b]	Percent matched with U.S.[c]	Number[b]	Percent matched with U.S.[c]
Australia	234	38.4	212	34.8	172	28.2	149	24.5
Canada	308	50.6	166	27.3	136	22.3	100	16.4
France	239	39.2	197	32.3	164	26.9	131	21.5
Germany	305	50.1	253	41.5	210	34.5	177	29.1
Italy	233	38.3	212	34.8	178	29.2	155	25.5
Japan	115	18.9	72	11.8	55	9.0	39	6.4
Spain	244	40.1	221	36.3	185	30.4	155	25.5
United Kingdom	314	51.6	298	48.9	250	41.1	205	33.7
United States[d]	439	72.1	417	68.5	329	54.0	264	43.3

Source: Author calculations based on IMS MIDAS data for year ending June 30, 2005
Notes: U.S. and foreign prices are per dose, at ex-manufacturer prices converted into U.S. dollars at January 2009 exchange rates.
[a]Sales-based entry conditions are at the molecule rather than the presentation level.
[b]Number of presentations in each country with a match
[c] Proportion of total U.S. presentations available in each country. The total number of S. 1232–eligible U.S. presentations is 609. See table 1.
[d]Presentations available in the United States with a match in any foreign country

Table 3 S. 1232–Eligible Foreign Doses and Sales of Matching Presentations as a Percentage of Eligible U.S. Doses and Sales under Alternative Entry Assumptions

Entry condition	• Presentation match • Foreign price lower than U.S. price		• Presentation match • Foreign price < 95 percent of U.S. price • U.S. sales[a] > $5 mil.		• Presentation match • Foreign price < 90 percent of U.S. price • U.S. sales[a] > $15 mil.	
	Percent of U.S. doses[b]	Percent of U.S. sales[c]	Percent of U.S. doses[b]	Percent of U.S. sales[c]	Percent of U.S. doses[b]	Percent of U.S. sales[c]
Australia	3.9	3.9	3.7	3.8	3.6	3.7
Canada	5.6	5.4	5.2	5.1	4.8	4.7
France	10.3	10.0	10.0	9.8	8.8	9.0
Germany	9.5	9.5	9.4	9.3	8.8	9.0
Italy	7.0	7.2	6.5	6.7	6.2	6.5
Japan	9.3	7.2	7.9	6.5	5.5	5.5
Spain	6.2	6.1	5.8	5.8	5.4	5.6
United Kingdom	12.2	12.0	11.0	11.6	10.6	11.3
United States (doses with unlimited supply)	75.5	81.5	75.1	81.1	73.5	79.1

Source: Author calculations based on IMS MIDAS data for the year ending June 30, 2005

Notes: U.S. and foreign prices are per dose, at ex-manufacturer prices converted into U.S. dollars at January 2009 exchange rates.

[a]Sales-based entry conditions are at the molecule rather than the presentation level.

[b]The numerator is the total volume of doses in each foreign country meeting the entry condition. The denominator is the number of U.S. doses in S. 1232–eligible categories at risk for commercial importation (42.9 billion; see table 1).

[c]The numerator is total sales of matching foreign doses, converted to U.S. dollars at January 2009 exchange rates. The denominator is total U.S. sales at risk from commercial importation ($103.6 billion; see table 1).

Table 4 Potential Payer Savings at the Ex-manufacturer Level from S. 1232 by Supply Constraint and Alternative Entry Assumptions

Entry condition	• Presentation match • Foreign price lower than U.S. price		• Presentation match • Foreign price < 95 percent of U.S. price • U.S. sales[a] > $5 mil.		• Presentation match • Foreign price < 90 percent of U.S. price • U.S. sales[a] > $15 mil.	
	Percent of U.S. doses at risk[b]	Percent reduction in U.S. ex-manufacturer sales[c]	Percent of U.S. doses at risk[b]	Percent reduction in U.S. ex-manufacturer sales[c]	Percent of U.S. doses at risk[b]	Percent reduction in U.S. ex-manufacturer sales[c]
Unlimited supply	75.5	50.3	75.1	50.1	73.5	48.8
20% supply constraint	12.8	5.6	11.9	5.6	10.7	5.5
10% supply constraint	6.4	2.8	5.9	2.8	5.4	2.7

Source: Author calculations based on IMS MIDAS data for the year ending June 30, 2005

Notes: U.S. and foreign prices are per dose, at ex-manufacturer prices converted into U.S. dollars at January 2009 exchange rates.

[a]Sales-based entry conditions are at the molecule rather than the presentation level.

[b]The numerator of the percentage of U.S. doses affected is the supply of foreign doses meeting the supply constraint at U.S. prices. For example, the 20 percent supply constraint implies that 20 percent of each country's supply can be exported. The denominator of the percentage of U.S. doses affected is the number of U.S. doses that are at risk of commercial importation based on the language of S. 1232, which is 42.9 billion, per table 1.

[c]The numerator of the percentage reduction in U.S. ex-manufacturer sales is the difference in foreign and U.S. prices multiplied by the supply of foreign doses meeting the supply constraint. Prices are converted to U.S. dollars at January 2009 exchange rates. The denominator is the total in sales at ex-manufacturer prices without rebated discounts of products at risk from commercial importation based on the language of S. 1232 ($103.6 billion, per table 1) meeting the entry conditions and supply constraints.

U.S. consumption. Under this implausible assumption, commercial importation reduces expenditures on S. 1232–eligible products by roughly 50 percent, or 17.3 percent of total sales.

If, more plausibly, exports to the United States are restricted to 20 percent of the doses consumed in each foreign country, the maximum percentage of S. 1232–eligible doses that can be imported drops from 75.5 to 12.8 percent, and potential savings fall from 50.3 to 5.6 percent of ex-manufacturer sales for S. 1232–eligible drugs, or 1.9 percent of total sales. Assuming the CBO's 10 percent constraint, potential U.S. savings are roughly halved again.[11] Again, these potential savings estimates ignore pass-through issues.

Base Case Estimate and Sensitivity Analysis

Table 5 presents our final savings estimates for payers/consumers. The base case assumes that identical presentation matching is required; U.S.-foreign price differentials are at least 5 percent, and U.S. molecule-level sales are at least $5 million; 20 percent of foreign supply can be exported; and payers/consumers capture an average of 23.3 percent of potential savings (given our assumptions that the share of savings captured by payers/consumers rather than intermediaries depends on drug-specific import volume relative to total U.S. demand). Under these assumptions, payer/consumer savings are $1.4 billion annually from our sample countries. Extrapolating from our sample to all S. 1232–eligible countries yields a final base case savings estimate of $1.7 billion, or approximately 0.6 percent of the $299.4 billion of 2005 expenditures on pharmaceuticals at retail prices paid by payers, net of off-invoice discounts.[12] Plausible sensitivity estimates range from 0.2 to 2.5 percent of total retail drug sales.

This finding that proposals for drug importation will, under reasonable assumptions, yield very small savings in total drug costs to payers reflects several characteristics of drugs and drug markets. One major factor limiting importation-based savings is the exclusion of OTC products, controlled substances, biologics, off-patent brands, generics, infused and injected drugs, and sterile ophthalmics, which together with combination

11. The volume of exports exceeds U.S. supply for 1.8 percent of sales. In these cases, we assume that each sample country exports an amount proportional to the ratio of its national supply to the total permitted country supply.

12. $1.4 billion divided by 78.3 percent yields $1.73 billion.

Table 5 Estimated Savings from S. 1232 to Payers/Consumers under Base Case and Alternative Assumptions

Assumptions	U.S. dollars ($ billion)	Percent savings for payers/ consumers[a]
Base Case		
Entry conditions: Identical presentation, 5% lower foreign price, $5 million U.S. molecule sales Foreign supply constraint: 20% of each foreign country's national supply is tradable Percentage savings realized by payers: 23.3%, based on assumptions in Methods section Other: January 2009 currency exchange rates	1.730	0.6
Sensitivity Analyses[b]		
—10% foreign supply constraint (rather than 20%)	0.538	0.2
—2005 exchange rates	1.762	0.6
—10% price difference, $15 million U.S. market size (rather than 5% and $5 million)	1.696	0.6
—lower price and no minimum market size (rather than 5% price difference and $5 million minimum market size)	1.740	0.6
—substitution between tablet and capsule formulations of the same strength	1.923	0.6
—substitution of multiple foreign products that add up to the U.S. strength	2.406	0.8
—100% of savings captured by payers, none retained by traders / wholesalers and pharmacies	7.413	2.5

Notes: U.S. and foreign prices are per dose, at ex-manufacturer prices converted into U.S. dollars at January 2009 exchange rates.

[a]Savings as a percentage of total payer expenditures at retail prices, net of off-invoice discounts, in 2005, estimated at $299.4 billion (see table 1).

[b]Figures in sensitivity analyses are comparative, not additive (i.e., they represent the alternative savings estimate that would result if only the enumerated changes in assumptions were applied).

products account for approximately 59 percent of total sales. Some of these exclusions (biologics, controlled substances, infusions and injected drugs) are likely to be preserved in any importation legislation, given heightened safety concerns regarding these drugs. Even if generics and OTC drugs were eligible for import, the fact that their prices are usually

lower in the United States than in other countries (Danzon and Furukawa 2003, 2008) precludes significant savings on these categories.[13]

A second factor limiting savings is that potential exporting countries often use different formulations even for matching S. 1232–eligible molecules. For example, fewer than 20 percent of eligible presentations match between the United States and Japan, and 71 percent of eligible U.S. presentations have a match in at least one exporting country (table 2). Sensitivity analysis shows that allowing substitution of tablets for capsules or aggregating foreign tablets of different strengths to match U.S. doses would increase potential savings only modestly, to $1.9 billion and $2.4 billion, respectively. Future trends in harmonization of presentations across countries are uncertain. Legalization of importation would create incentives for manufacturers to further differentiate presentations; although legislation may attempt to curtail this practice, differences in medical norms may make such an effort impractical.

A third factor limiting potential savings is the fact that the import volume required to meet U.S. needs far exceeds normal supply for each potential export country, based on their domestic consumption. Our "unlimited supply" assumption requires that manufacturers sell unlimited supply in the lowest-priced countries, which then act as conduits for unlimited exports to the United States. Given these unrealistic conditions, if the entire U.S. demand for each S 1232–eligible presentation with a cheaper foreign match could be sourced from the cheapest matching country without limitation, and 100 percent of savings were passed on to payers/consumers, then an estimated $52.1 billion could in theory be saved as a direct transfer from manufacturers.

Under the more realistic assumption that 20 percent of each country's domestic supply is exportable and intermediaries retain some share of potential savings, the estimated savings to payers/consumers is $1.7 billion. Using the CBO's assumption of a 10 percent supply constraint reduces projected savings to $0.5 billion.

Results are also sensitive to the savings payers/consumers could extract from intermediaries. Our base case assumes that payers would attempt to claw back some share of savings in drug acquisition costs realized by pharmacies but that this share would be modest if import volume is small. Based on the import volumes implied in our analysis, the predicted payer

13. Previous research found that price differences for U.S. biologics, OTCs, and generics were limited and usually lower, respectively, than in foreign countries. For price differences for biologics, see Danzon and Furukawa (2006). For generics, see Danzon and Furukawa (2008).

share of savings is approximately one-quarter (23.3 percent), depending on supply conditions. Assuming that payers capture all savings (i.e., intermediaries neither incur costs nor retain profit, but other base case assumptions are maintained) increases payer/consumer savings to $7.4 billion. Our predicted payer share of savings is broadly consistent with evidence from the EU, which has found small or no savings accrued to public payers; most or all potential savings have been captured by parallel traders as arbitrage rents, with one exception (Kanavos et al. 2004; Kanavos and Costa-Font 2005; Kyle, Allsbrook, and Schulman 2008; Kyle 2007; Ganslandt and Maskus 2004). However, our savings estimate is not based on these EU findings because differences in scale, statutory, legal, and reimbursement rules, and competition limit the relevance of EU supply-chain experience for the United States.

Stakeholder Responses

The EU experience with parallel trade suggests that foreign governments could adopt policies to prevent supply disruptions to their citizens that would reduce exports to the United States. Also, in assuming that 10 percent of each country's supply would be exportable, the CBO stated that "some foreign countries would act to restrict the export of prescription drugs to the United States to maintain sufficient domestic supply. . . . Canadian officials have already announced that they may limit drug exports if parallel trade presents a threat to the availability of affordable drugs in Canada" (S. 1392, 2005). Foreign policies could include mandatory export caps and shelters for manufacturers and their subsidiaries to avoid S. 1232's forced-sale provisions and associated local supply disruptions.

Foreign court decisions could also reduce exports to the United States. A recent European Court of Justice ruling indicated that manufacturers can limit supplies to wholesalers if parallel trade has an adverse impact on local supply. At issue was the Greek subsidiary of a manufacturer that stopped shipping to parallel-trading wholesalers and reestablished supply directly to Greek hospitals and physicians after it became aware of shortages. After supply had been reestablished, the manufacturer capped supply to wholesalers at the national supply plus 18 percent. The European Court of Justice found that "a producer of pharmaceutical products must be in a position to protect its own commercial interests if it is confronted with orders that are out of the ordinary in terms of quantity" (Court of

Justice of the European Communities 2008). Other EU cases have reached different decisions about the conditions under which manufacturers may limit supply to exporters, and it remains to be seen how conflicts would be resolved between foreign governments' efforts to ensure local supply and S. 1232's goal of promoting maximal importation to the United States.

Other stakeholders, such as small pharmacies, hospitals, physicians, or patient advocacy organizations, may also support restrictions on exports—for example, supply limits or dual pricing strategies (where sales for export are at a higher price). These policies, adopted to assure local supply, could significantly reduce export volume. Strategic changes to presentation mix may also reduce matching (Kyle 2007). While S. 1232 seeks to bar such practices, in practice it would be difficult to distinguish them from changes in local preferences or medical norms. At a minimum, S. 1232's forced-sale provisions are likely to prove contentious, given traditional intellectual property and commercial interest prerogatives and potential for conflict between S. 1232 and the interests of foreign consumers and governments.

Rising Drug Prices, Delayed Launches, and Structural Changes in the Industry

In the long run, prices or restrictions in access to drugs could increase, depending on countries' budget constraints and reimbursement policies. Because many foreign countries constrain launch prices and do not permit postlaunch price increases, new drugs may be delayed or not launched; evidence of these effects as a result of referencing or parallel importation within the EU already exists (Danzon, Wang, and Wang 2005; Kyle 2007; Danzon and Epstein 2008). Foreign consumers' loss of access and manufacturers' loss of foreign revenues has no offsetting benefit to U.S. payers/consumers. In fact, in the longer run, lower global revenues will reduce incentives for R&D and new drugs for U.S. consumers.

The estimated savings reported in table 5 are based on 2005 U.S. consumption patterns, ignoring any start-up costs of adapting to importation. Extracting savings from importation would take time: importers must be licensed, intermediaries must secure reliable supply, and payers must monitor price changes and renegotiate contracts with PBMs and pharmacies. Although these start-up costs would presumably decline over time, potential savings will also likely decline due to structural changes in pharmaceutical markets. While sales of biologics, other specialty products,

and generics grew between 2007 and 2008, the sales of on-patent, high-volume, chemical drugs, which comprise the majority of sales vulnerable to S. 1232, declined. Since these trends are expected to continue, the potential savings from importation will likely decline over time as the share of drugs amenable to importation declines (Aitken, Berndt, and Cutler 2009).

Under S. 1232, our estimates imply at most small savings to U.S. payers/consumers, whereas global total costs and inequity in health care access could increase for several reasons. First, trade in pharmaceuticals will not yield the efficiencies normally associated with free trade, because lower foreign prices for drugs primarily reflect government-imposed price regulation or lower per capita incomes, not lower real marginal costs of production. Moreover, importation would add costs associated with transportation, repackaging, and monitoring product safety. Second, intermediaries may capture a significant share of any savings that are available. Third, consumers in foreign countries will likely face higher prices or reduced access to new drugs, which could be viewed as inequitable. Importation that attempts to equalize prices between the United States and foreign countries could undermine price differences that simply reflect per capita income differences, which would be inconsistent with static and dynamic efficiency. Fourth, lower global revenues of pharmaceutical companies will reduce incentives for R&D and the rate of new product development for everyone, including U.S. consumers. Within R&D portfolios, incentives may be distorted toward products that are exempt from importation, even if the latter are more costly.

Under plausible assumptions, savings to U.S. payers/consumers would likely be in the range of 0.2 to 2.5 percent of current drug spending, which implies a minimal impact on aggregate U.S. health care spending. These figures may underestimate savings: if potential exporting countries are willing to provide unlimited supply for export to the United States and forced-sale provisions can be fully enforced, savings may be higher. These estimates may also overestimate savings: if major export sources permit higher launch prices or experience launch delays, and if the supply of new drugs shifts toward products that are exempt from importation, savings may be lower. Revenue losses to manufacturers will significantly exceed savings to U.S. payers/consumers, because importation entails real additional costs; savings that are captured by intermediaries represent real revenue loss to manufacturers; and loss of sales to foreign consumers could be significant, due to disruptions and spot shortages that result from exporting local supplies, higher prices, and/or delays in access to new

drugs. In the long run, U.S. consumers may be worse off due to lower investment in R&D and distortions toward import-exempt products.

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