MarketWatch

Prices And Availability Of Biopharmaceuticals: An International Comparison

The United States might spend more on biologics, but prices are not noticeably higher than in nine other countries.

by Patricia M. Danzon and Michael F. Furukawa

ABSTRACT: This paper presents new evidence on availability, use, and prices of biopharmaceuticals in five major European Union (EU) markets, Canada, Australia, Japan, and Mexico, relative to the United States. Our data set from IMS Health includes all product sales in 2005. Per capita spending on biopharmaceuticals was at least twice as high in the United States as in the other countries. This difference reflects primarily greater availability and use of new, relatively high-price molecules and formulations. Prices for identical formulations are not higher on average in the United States. The broader price indexes, which do not control formulation, are also not higher in the United States, after adjusting for income. [*Health Affairs* 25, no. 5 (2006): 1353–1362; 10.1377/hlthaff.25.5.1353]

Biopharmaceuticals have attracted concern as the highest-price pharmaceutical products and the most rapidly growing component of drug spending in the United States and other countries.[1] For the year ending June 2005, U.S. spending on all pharmaceuticals, at manufacturer prices, was $921 per person; of this, $119 or 12.9 percent was on biopharmaceuticals. U.S. spending on these agents grew 127 percent from 2001 to 2005; in other countries, growth was more rapid but began from a lower starting point. Biologics account for a growing share of new drug approvals: Although only 6.3 percent of all molecules available in the United States in 2005 were biologics, 18 percent of new molecules approved in the United States since 1996 have been biologics.

The purpose of this paper is to compare spending on and availability, use, and prices of biopharmaceuticals in the United States relative to nine other countries: the major European Union (EU) markets (France, Germany, Italy, Spain, and the United Kingdom), Canada, Australia, Japan, and Mexico. In documenting price and volume differences, this analysis provides a detailed test, for one high-technology sector, of the hypothesis that differences between health care spending in the United States and other countries primarily reflect prices rather than use or availability.

Study Data And Methods

Our data are from the IMS Health MIDAS database for July 2004–June 2005, which reports sales by value and unit volume for all pharmaceutical and biologic products. We report price indexes based on the U.S. market basket, which provide the most relevant comparisons from a U.S. policy perspective. Our

Patricia Danzon (danzon@wharton.upenn.edu) is the Celia Moh Professor in the Health Care Department, Wharton School, at the University of Pennsylvania in Philadelphia. Michael Furukawa is an assistant professor in the School of Health Management and Policy, W.P. Carey School of Business, at Arizona State University in Tempe.

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comparisons of availability and use should be fully comprehensive, because our database reflects sales for all compounds in all countries through retail pharmacies and hospitals. In addition, the U.S. data include sales to clinics, physicians' offices, health maintenance organizations (HMOs), home health agencies, and long-term care facilities.

We defined the universe of biologics to include human therapeutics and vaccines available in all countries, not just the United States. Specifically, we included products that met at least one of the following criteria: approved by the U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Review (CBER); on a list of biologics approved by the European Agency for the Evaluation of Medicinal Products (EMEA) from the Tufts Center for Drug Development; listed in one of several papers that describe biologic approvals in the United States and the EU; on a list of biologics reported by the Japan Pharmaceutical Manufacturers Association (JPMA); or on a list of products from the Biotechnology Industry Organization (BIO) and reported by MIDAS in the same four-digit Anatomical Therapeutic Classification (ATC4) as a product that appears on one of the other lists, because products in the same ATC4 by definition have the same indication and mechanism of action.[2] The resulting sample includes 152 biologic molecules, of which 22 are available only in and 39 are not available in the United States. We followed the IMS classification of products by therapeutic class, such as antineoplastics, blood products, vaccines, and so on.[3]

All sales and prices are at ex-manufacturer levels, as reported by IMS.[4] These IMS ex-manufacturer prices should approximate the actual prices received by manufacturers, except to the extent of off-invoice discounts. As a check, we compared the IMS prices with the average sales price (ASP), which includes all discounts, as reported by the Centers for Medicare and Medicaid Services (CMS) for the corresponding quarter. On average, the IMS prices are similar to the ASPs for the products that we could compare, but with some variation.[5] We did not attempt to estimate public or reimbursement prices because our focus was on prices charged by manufacturers. Moreover, we lacked reliable data on the wholesaler and other distribution margins that account for the margin between manufacturer and public prices.[6]

Because IMS prices are gross of off-invoice discounts, which are common in the United States, we adjusted them by our best estimates of off-invoice discounts given by manufacturers.[7] For Germany, we adjusted the IMS prices for the mandatory rebates on drugs not included in the reference price system.[8] For other countries, we lacked data on the extent of discounting, if any, and therefore we used the prices as reported by IMS. To the extent that unmeasured discounts exist in other countries, their prices may be overestimated in the prices reported here.

Biopharmaceutical Spending And Availability

Aggregate sales of biopharmaceuticals in the United States are about six times the next-largest biologics market, Japan, and the United States has the highest biopharmaceutical share (12.9 percent) of total drug spending among all countries studied (Exhibit 1). U.S. per capita spending on biopharmaceuticals is almost twice as great as in the next-highest-ranked country, France. Among the EU countries, although the United Kingdom has the highest per capita income, followed by France, Germany, Italy, and Spain, per capita spending on biologics is highest in France and lowest in the United Kingdom (26 percent of the U.S. level). Whereas Japan's per capita spending on pharmaceuticals overall is 80 percent of the U.S. level, its spending on biologics is only 33 percent of the U.S. level.

However, from 2001 to 2005 spending on biologics grew more rapidly in other countries than in the United States (except in Japan and Mexico). If these trends continue, the gap between foreign and U.S. per capita spending on biologics could narrow over time.

Total per capita spending on biopharmaceuticals depends on the compounds available

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EXHIBIT 1
Biopharmaceutical Spending And Availability In Ten Countries, 2005

	US	CAN	FR	GER	IT	SP	UK	JP	AUS	MEX
Biologic sales, ex-manufacturer ($US millions)	$34,957	$1,142	$3,828	$3,736	$2,106	$2,009	$1,864	$5,051	$553	$65
Percent of universe of Rx sales	12.9%	7.4%	9.7%	8.7%	8.5%	10.9%	7.8%	5.4%	6.6%	0.5%
Percent change in biologic sales 2001–2005	127%	213%	227%	235%	189%	190%	158%	82%	230%	82%
Pharmaceutical sales per capita[a]	$921	$481	$658	$518	$432	$447	$400	$734	$415	$123
Biologic sales per capita	$119	$36	$63	$45	$37	$47	$31	$40	$27	$0.62
Universe of molecules[a]	1,872	1,341	2,344	2,581	1,811	1,840	1,678	2,104	1,837	1,664
New[b] molecules	301	173	227	282	227	231	236	181	259	198
Biologic molecules	117	74	102	104	98	101	101	74	83	61
New[b] biologic molecules	55	26	47	44	39	43	44	19	31	20
Anti-neoplastics	18	9	15	13	12	12	12	7	10	9
Blood products	8	5	8	5	7	7	8	3	7	2
Vaccines	1	1	2	2	1	1	2	0	1	0
Insulins	4	3	5	6	3	5	5	4	4	4
Anti-rheumatics	3	3	3	3	3	3	3	1	3	2
Growth hormones	1	0	1	1	1	1	1	0	0	0
Other biologic classes	20	5	13	14	12	14	13	4	6	3
Percent of 69 new global biologics available	80%	38%	68%	64%	57%	62%	64%	28%	45%	29%
New biologics as percent of all new molecules	18%	15%	21%	16%	17%	19%	19%	10%	12%	10%
New biologics launch lag (months)	5.6	22.1	18.5	6.7	19.2	17.0	11.7	35.1	19.2	28.5

SOURCE: Authors' calculations based on data from the IMS Health MIDAS database, 2005.

NOTES: Countries are as follows: CAN is Canada; FR is France; GER is Germany; IT is Italy; SP is Spain; UK is United Kingdom; JP is Japan; AUS is Australia; MEX is Mexico.

[a] Includes all molecules (drugs and biologics) with nonzero sales.

[b] Molecule launch date post-1996.

and on the use and prices of those compounds. Although the total number of molecules available is greater in Germany, France, and Japan than in the United States, the latter has had more pharmaceuticals approved since 1996 (Exhibit 1). The United States also leads in the availability of biopharmaceutical molecules, followed by Germany, France, and Spain and the United Kingdom. Similarly, of the sixty-nine new biologics launched since 1996, the United States has the highest percentage (Exhibit 1). Biologics' share of all post-1996 new drug launches is slightly higher in France, Spain, and the United Kingdom than in the United States, which suggests that post-1996 biologics have been somewhat more successful than other new drugs in obtaining approval or reimbursement, or both, in regulated markets, and the evidence on prices reported below is consistent with this.[9] Among these new biologics, the United States has more availability of anti-neoplastics and the category for all other biologics, whereas some other countries have slightly more insulins and vaccines (Exhibit 1).

Exhibit 1 also reports the average lag in the launch of new biologics. We measured this as the difference between the country-specific launch date and the first launch of each molecule in any country as reported by MIDAS. The mean launch lag is shortest for the United States and longest for Japan. Thus, launch delay is a major contributor to the relatively low availability of new biologics in Japan. Within the EU, mean launch lag is 6.7 months for Germany and 11.7 months for the United Kingdom, the two countries that do not require price approval prior to reimbursement. By contrast,

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mean launch lags are longer for Italy, France, and Spain, all of which require price approval. Because post-1996 biologics have been approved through the EMEA, which grants EU-wide registration, these launch-lag differentials between EU countries plausibly reflect reimbursement delay, not registration delay.

Price Comparisons

■ **Methods.** *Matching.* Calculating price indexes for biologics, as for other drugs, implies a trade-off between matching precision and sample size. There are various possible definitions of matching products, ranging from broadest to narrowest definition as follows: "molecule" defines products by their active ingredient; "molecule-ATC4" distinguishes products within a compound if they are listed by IMS in different therapeutic categories (ATC4); and "molecule-ATC4-form-strength" distinguishes different formulations or strengths, or both.[10] For most countries, there are three or four different formulation-strengths per molecule-ATC4. If we match products based on molecule-ATC4, then 76–98 percent of each country's biopharmaceutical sales matches with that of the United States and can be included in the price comparisons; the percentage of doses (standard units) matched is lower than the share of sales, which indicates that the matching molecule-ATC4s are relatively high-price products. By contrast, when we restrict the price comparisons to products that match on molecule-ATC4-form-strength, less than 44 percent of products match. With the exception of Canada, these matching products account for 15–45 percent of sales and a lower share of doses, ranging from 2 percent in Japan to 48 percent in Germany. Although Canada has only 75 of the 134 biologics available in the United States, formulations are similar, such that the molecule-ATC4-form-strength comparison includes 59 percent of sales and 77 percent of doses in Canada.

Given these trade-offs, no single set of price indexes is both representative and precise. We therefore report two indexes: The molecule-ATC4 indexes include the most comprehensive share of products and sales, while the molecule-ATC4-form-strength indexes include only those products that have the same form and strength and thus provide a less representative but more apples-to-apples comparison.[11]

Weights. The indexes reported here use U.S. consumption weights; that is, each index provides a measure of the cost of the U.S. market basket of products at foreign prices relative to U.S. prices; values greater (less) than 100 imply that on average foreign prices are higher (lower) than U.S. prices. Since consumption patterns vary greatly across countries and price indexes are sensitive to the volume weights, these U.S.-weighted price indexes are appropriate for the United States; other countries should use indexes based on their own market baskets.

Currency conversion. Most of the comparisons reported here use exchange rates to convert currencies to U.S. dollars. Exchange rates are appropriate for measuring revenues to manufacturers or potential for parallel trade and international reference pricing. We also report some results using gross domestic product (GDP) purchasing power parities (PPPs).

■ **Price indexes.** *Molecule/ATC4 and form-strength indexes—all classes.* In Exhibit 2, the first two bars in each grouping show the two alternative price indexes using exchange rates for currency conversion. The more comprehensive molecule-ATC4 price indexes show prices in Canada and France 3–8 percent higher than U.S. levels, whereas prices in Japan, Australia, Germany, Spain, the United Kingdom, Italy, and Mexico are 5–44 percent lower than in the United States. However, the molecule-ATC4-form-strength indexes, which include only the strictly matching products, indicate that all countries except Canada, Mexico, and Spain have higher prices than does the United States.

Exhibit 2 also shows the molecule-ATC4 price comparisons with foreign currencies converted to U.S. dollars at GDP PPPs (third bar in each grouping), which in theory provide a more accurate measure of the purchasing power of different currencies. Using PPPs generally reduces foreign prices relative to U.S. prices, particularly for the EU markets: U.K.

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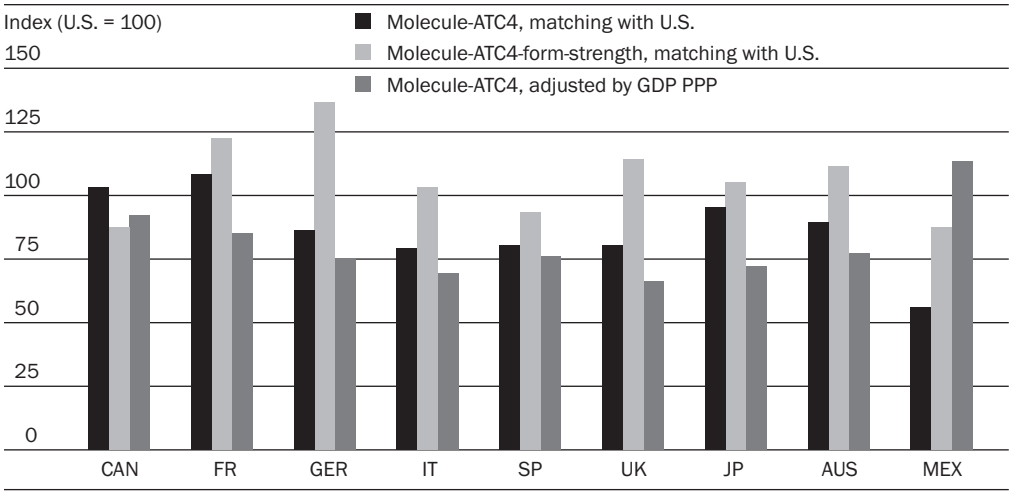
EXHIBIT 2
Biopharmaceutical Price Indexes In Nine Countries, Relative To U.S. Prices, 2005



SOURCE: Authors' calculations based on data from the IMS Health MIDAS database, 2005.
NOTES: For explanation of biopharmaceutical categories, see text. ATC4 is four-digit anatomical therapeutic category. GDP is gross domestic product. PPP is purchasing power parity. Countries are as follows: CAN is Canada; FR is France; GER is Germany; IT is Italy; SP is Spain; UK is United Kingdom; JP is Japan; AUS is Australia; MEX is Mexico.

prices drop from 20 percent to 34 percent lower than U.S. prices; French prices drop from 8 percent higher to 15 percent lower than U.S. prices; and prices for Spain, Germany, and Italy are 24–31 percent lower than those for the United States at PPPs. This finding—that biopharmaceutical prices appear lower in the EU compared to the United States when we use PPP conversion—may partly reflect the fact that PPPs are based on consumer-level prices that include a value-added tax (VAT) of 16–20 percent in EU countries, whereas the United States has no VAT and only modest sales taxes. Thus, when our manufacturer-level prices for drugs are compared with these consumer-level prices inclusive of VAT, drug prices would appear relatively cheap in the EU. Because the PPPs are intended for comparison of consumer-level prices but our drug prices are at ex-manufacturer levels, we use exchange rates for subsequent analysis.

New versus old compounds. Exhibit 3 reports price indexes for new versus old molecules. "New" includes molecules with launch dates in any country after 1996; "old" is all other molecules. For the comprehensive product definition (molecule-ATC4 indexes), most countries' prices are lower relative to U.S. prices for new products than for old products. This evidence suggests that new biologics are launched at lower prices relative to older products in the EU compared to the United States. By contrast, in Mexico the new molecule index is 101, whereas the old molecule index is 71, which suggests a sizable increase in relative prices for new molecules in Mexico, although the small samples make conclusions tentative.

However, when we compare prices for the smaller sample of strictly matching formulations, prices are quite similar across countries, with the United States roughly in the middle: Six countries have prices ranging up to 18 percent higher than U.S. prices, and in the remaining three countries (Canada, Mexico, and Japan), prices are within 11 percent lower than U.S. prices. For older products with matching formulations, the United States is again in the middle, but the range of prices is wider: Prices are highest in Germany and France, followed by Japan and the United Kingdom; prices are lowest in Canada and Spain. Thus, the relatively higher U.S. prices for the molecule-ATC4 comparisons could reflect more higher-price formulations in the United States than in other

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EXHIBIT 3
Biopharmaceutical Price Indexes In Nine Countries, By Molecule Age And Class, Relative To U.S. Prices (U.S. = 100), 2005

	CAN	FR	GER	IT	SP	UK	JP	AUS	MEX
Old[a] biologic molecules[c]	118	123	88	78	75	91	92	93	71
Old[a] biologic presentations[d]	84	148	156	105	76	125	132	107	90
New[b] biologic molecules[c]	90	96	84	79	84	71	100	84	101
New[b] biologic presentations[d]	89	101	118	101	103	105	97	116	94
Anti-neoplastics[c]	103	98	84	78	83	68	109	81	112
Blood products[c]	126	139	60	80	78	85	63	85	55
Vaccines[c]	86	65	87	76	67	67	77	56	58
Insulins[c]	73	53	53	59	45	57	91	58	90
Anti-rheumatics[c]	77	107	128	102	102	92	70	124	76
Growth hormones[c]	79	112	143	73	60	136	320	232	86
Other biologic classes[c]	132	126	131	69	92	99	98	66	69

SOURCE: Authors' calculations based on data from the IMS Health MIDAS database, 2005.

NOTES: Countries are as follows: CAN is Canada; FR is France; GER is Germany; IT is Italy; SP is Spain; UK is United Kingdom; JP is Japan; AUS is Australia; MEX is Mexico.

[a] Molecule launch date pre-1996.

[b] Molecule launch date post-1996.

[c] Matching by identical molecule-ATC4 (four-digit anatomical therapeutic category).

[d] Matching by identical molecule-ATC4-form-strength.

countries, especially for new products.

Price indexes by therapeutic class. Exhibit 3 also shows price indexes by therapeutic class. The considerable variation across classes within countries precludes strong generalizations. For the anti-neoplastics class (which includes immunomodulating products), prices are somewhat lower in the EU countries than in the United States (ranging from 2 percent lower in France to 32 percent lower in the United Kingdom) and mixed for the other countries, with Canada, Japan, and Mexico higher than the United States. For insulins, which are an older, cheaper category on average, all countries have lower prices than the United States. Recall that these molecule-ATC4 indexes might reflect differences in formulations as well as differences in prices for the same formulations. Thus, the general pattern of higher relative prices for the United States, based on the comprehensive molecule-ATC4 indexes than the form-strength indexes, again suggests that the United States has more higher-price formulations within matching molecules than other countries have.

■ **Price and volume indexes adjusted for income.** Differences in per capita income are often suggested as an appropriate basis for drug price differentials. Exhibit 4 reports the price indexes normalized by per capita income. The results are striking. Prices adjusted for income are higher in nearly all countries than in the United States, ranging from 5 percent higher in Japan to 243 percent higher in Mexico. The lone exception is the United Kingdom, which has adjusted prices that are 12 percent lower than U.S. prices. These effects of normalizing by income as a measure of affordability are different from the effects of converting at PPPs (Exhibit 2) as a measure of affordability based on general price levels rather than per capita income. As noted earlier, PPP comparisons could be biased by the VAT that is included in EU retail prices.

Exhibit 4 also reports volume normalized by per capita income. We do not suggest that use should vary with income; in fact, if prices varied with income while medical need and other determinants of use were uniform across countries, then use would be unrelated to income. In fact, use (volume of doses) adjusted for per capita income shows considerable variation, with very high use in Spain and very low use in Mexico, which is not surprising, given Mexico's high prices, relative to income.

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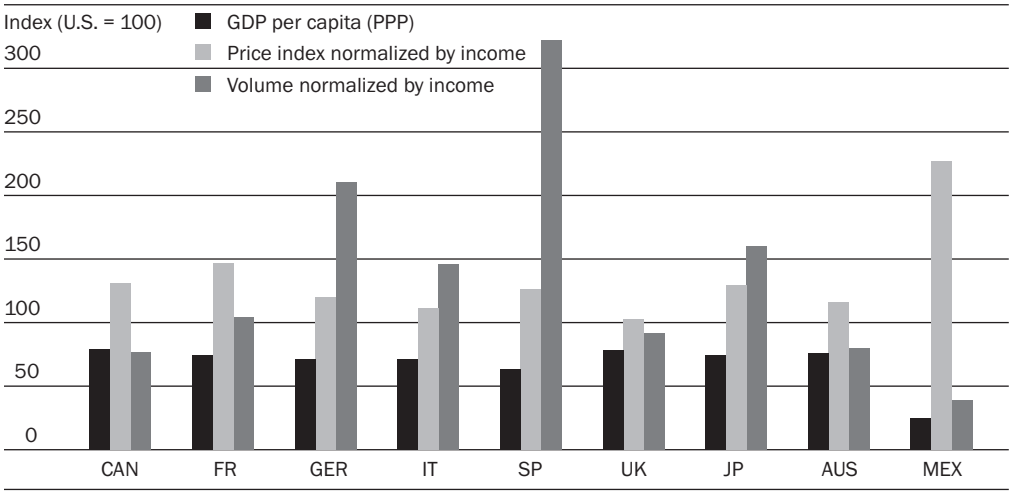
EXHIBIT 4
Biopharmaceutical Price And Volume In Nine Countries, Relative To The United States, Normalized By Income, 2005



SOURCES: World Bank World Development Indicators, 2005; and authors' calculations based on data from the IMS Health MIDAS database, 2005.
NOTES: GDP is gross domestic product. PPP is purchasing power parity. Countries are as follows: CAN is Canada; FR is France; GER is Germany; IT is Italy; SP is Spain; UK is United Kingdom; JP is Japan; AUS is Australia; MEX is Mexico.

Average Use And Prices By Therapeutic Class

The findings reported above show that the United States has much higher per capita spending on biopharmaceuticals but that prices for specific formulations are comparable with prices in other countries. Exhibit 2 suggests that one contributor to the higher U.S. per capita spending is greater use of high-price formulations. Other possible contributors are greater use of high-price molecules or higher total use, or both.

To shed light on the latter issues, Exhibit 5 reports relative use (number of doses per capita, compared with the United States) and average price per dose, by therapeutic class. Note that each country's average price per dose in Exhibit 5 is effectively weighted based on its consumption of molecules and formulations; thus, differences across countries in price per dose reflect these use differences in addition to price differences for the same formulations. By contrast, the price indexes reported in Exhibits 2–4 reflect price differences based on U.S. consumption patterns.

Averaged over all classes, per capita use is not unusually high in the United States: Spain, Germany, Japan, and Italy all have higher per capita use than the United States. However, the decomposition by class shows that U.S. use is considerably higher for the highest-price categories—anti-neoplastics and anti-rheumatics—whereas other countries have higher use levels for insulins and vaccines, which tend to be older and relatively cheap. Spain is an outlier for growth hormones.

The United States has a relatively high mean price per dose for some classes, especially anti-neoplastics, which indicates relatively high use of the more expensive products within a class. For other classes, the pattern of relative price per dose varies across countries; no countries are consistently highest-price, which reflects the different mix of drugs, formulations, and use patterns in different countries. The mean price per dose overall is higher in the United States than in other countries, reflecting this higher weighting of U.S. utilization by the relatively high-price classes and products, especially anti-neoplastics and anti-rheumatics.

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EXHIBIT 5
Biopharmaceutical Use And Average Price Per Dose, By Therapeutic Class, 2005

	US	CAN	FR	GER	IT	SP	UK	JP	AUS	MEX
All biologic classes										
Use relative to US[a]	100	61	77	150	104	203	71	118	61	10
Avg. price per dose[b]	$59	$32	$44	$14	$19	$13	$23	$18	$24	$3
Anti-neoplastics										
Use relative to US[a]	100	61	63	63	63	69	46	44	78	0.3
Avg. price per dose[b]	$355	$226	$250	$138	$167	$181	$119	$189	$138	$254
Blood products										
Use relative to US[a]	100	44	30	17	40	44	17	113	18	0.2
Avg. price per dose[b]	$133	$76	$300	$78	$110	$112	$155	$46	$147	$57
Vaccines										
Use relative to US[a]	100	47	123	152	208	26	32	68	59	0.2
Avg. price per dose[b]	$33	$31	$17	$19	$5	$27	$19	$15	$14	$6
Insulins										
Use relative to US[a]	100	146	136	334	97	222	227	84	183	4
Avg. price per dose[b]	$17	$7	$9	$8	$8	$7	$9	$15	$7	$15
Anti-rheumatics										
Use relative to US[a]	100	40	23	20	12	26	35	0.4	12	0.06
Avg. price per dose[b]	$187	$122	$205	$234	$189	$198	$161	$117	$201	$120
Growth hormones										
Use relative to US[a]	100	32	15	5	6	143	3	7	1	1
Avg. price per dose[b]	$10	$8	$34	$106	$76	$6	$100	$127	$19	$11
Other biologic classes										
Use relative to US[a]	100	3	87	230	235	588	27	396	4	48
Avg. price per dose[b]	$32	$111	$34	$4	$7	$4	$42	$4	$46	$1

SOURCE: Authors' calculations based on data from the IMS Health MIDAS database, 2005.

NOTES: Countries are as follows: CAN is Canada; FR is France; GER is Germany; IT is Italy; SP is Spain; UK is United Kingdom; JP is Japan; AUS is Australia; MEX is Mexico.

[a] Doses (standard units) per 1,000 population.

[b] Weighted average price, weighted by total doses (standard units).

Discussion And Conclusions

■ **Caveat.** The conclusions of this study have one caveat: Although our analysis draws on a comprehensive database for all countries (including products dispensed in U.S. physicians' offices), if MIDAS does not fully capture all channels of distribution for biologics, our estimates of utilization would be biased downward. Similarly, if there is off-invoice discounting that is not captured by MIDAS or by our discount adjustments, our price measures would be biased upward.

Overall, these data indicate higher per capita spending on biopharmaceuticals in the United States than in other countries, primarily as a result of greater availability of new molecules and greater use of more-costly products and formulations, most evident with anti-neoplastics, rather than higher prices for the same product. Thus, for this high-technology sector, our data suggest that "it's the availability and utilization mix, not the prices." Although the broader molecule-ATC4 indexes, which do not control for formulation, show the United States with higher prices than seven of the nine other countries, when we adjust for per capita income, all countries have higher prices than in the United States.

■ **Areas of future research.** These findings suggest several important areas for future research. One important issue is the extent to which the differences in use reflect reimbursement incentives, spending controls in regulated markets, or simply differences in prescribing norms. Second, whether the higher U.S. use of more-costly products yields bene-

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fits commensurate with costs is an important issue that is not addressed here.

■ **Differences with nonbiologics.** Finally, these price comparisons for biopharmaceuticals differ in important respects from the price comparisons for nonbiologic drugs.[12] Specifically, prices for biologics are more uniform across countries than prices for other drugs, and U.S. prices for biologics with identical formulations are not higher, on average, than prices for the same products in other countries. Rigorous analysis of the factors that lead to relatively higher prices for biopharmaceuticals than for nonbiologic drugs in regulated markets is beyond the scope of this paper. Here we simply suggest possible contributing factors.

Although price regulatory systems do not explicitly distinguish biologics from other drugs, in practice, biopharmaceutical prices might be less stringently regulated for several reasons. First, some countries exempt drugs used in hospitals from price regulation, on the grounds that hospitals can negotiate prices with manufacturers and have incentives to be price-sensitive.[13] Biologics might be used disproportionately in hospitals and hence be less subject to the price regulation that applies to drugs dispensed through retail pharmacies. Second, to the extent that biologics have novel mechanisms of action or indications, or both, their prices are less likely than those of nonbiologics to be constrained by prices of older products in the same class in regulatory systems that benchmark prices of new drugs to prices of existing products (for example, France). Allowable cost-effectiveness thresholds might also be higher for biologics that treat incurable diseases for which no good treatments exist. Alternatively, biologics that target relatively small disease classes, such as rare cancers, might be able to "fly under the regulatory radar" in countries where price regulation targets classes with high budget impact. Some biologics also qualify for orphan drug status, which conveys market exclusivity and hence even greater market power than patent protection. Third, most countries have industrial policies designed to encourage local biotech investment, which could lead to less stringent price controls of biologics. Finally, patient advocacy groups might be influential in advocating for new drugs that treat incurable conditions, such as multiple sclerosis.

Whatever the reasons, this evidence suggests that prices for biologics are relatively low in the United Kingdom (where prices are constrained only indirectly by profit and cost-effectiveness screens) and relatively high in France (with strict price regulation), contrary to the conventional wisdom, for pharmaceuticals, that France has among the lowest prices and the United Kingdom, among the highest prices in the EU.

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NOTES

1. C.D. Mullins et al., "Variability and Growth in Spending for Outpatient Specialty Pharmaceuticals," *Health Affairs* 24, no. 4 (2005): 1117–1127.
2. Papers describing biologic approvals include M.E. Gosse and M. Manocchia, "First Biopharmaceuticals Approved in the U.S.: 1980–1994," *Drug Information Journal* 30, no. 4 (1996): 991–1001; J.M. Reichert, "New Biopharmaceuticals in the USA: Trends in Development and Marketing Approvals 1995–1999," *Trends in Biotechnology* 18, no. 9 (2000): 364–369; J.M. Reichert and E.M. Healy, "Biopharmaceuticals Approved in the EU 1995–1999: A European Union–United States Comparison," *European Journal of Pharmaceutics and Biopharmaceutics* 51, no. 1 (2001): 1–7; G. Walsh, "Pharmaceutical Biotechnology Products Approved within the European Union," *European Journal of Pharmaceutics and Biopharmaceutics* 55, no. 1 (2003): 3–10; and G. Walsh, "Biopharmaceuticals: Approvals and Approval Trends in 2004," *BioPharm International* (May 2005): 58 ff. For the list of products from BIO, see Biotechnology Industry Organization, "Approved Biotechnology Drugs," December 2005, http://www.bio.org/speeches/pubs/er/approveddrugs.asp (accessed 2 February 2006).
3. The products included in these major categories are listed in Appendix Exhibit A1, available online at http://content.healthaffairs.org/cgi/content/full/25/5/1353/DC1.
4. IMS collects data on sales and pack prices by auditing the wholesaler invoices of various distribution channels. See IMS Health, "Guide to Pack Prices on IMS Midas Quantum" (Fairfield, Conn.: IMS Health, 24 May 2005). IMS adjusts the ex-wholesaler prices by the average wholesale margin to obtain the ex-manufacturer prices reported here.
5. Differences between IMS ex-manufacturer prices and ASPs might reflect differences in dosage forms, off-invoice discounts, and IMS sampling of channel outlets.
6. For the United States, public prices for biologics dispensed in physicians' offices reflect reimbursement policy under Medicare Part B and other payers. Medicare changed from 85 percent of average wholesale price (AWP, a list price reported by pricing services) in 2004 to 1.06 percent of average sales price (ASP) in 2005. Some private payers follow Medicare reimbursement for Part B drugs; others use different rules, and these are in flux. Thus, the standard IMS margins for projecting from ex-manufacturer to retail/public prices are unlikely to be accurate for biologics in 2004–05.
7. For the United States, we adjusted prices in all channels except federal hospitals by the product-specific difference between the MIDAS price and the ASP as reported by the Centers for Medicare and Medicaid Services (CMS) for the corresponding quarter. ASPs are supposed to reflect average selling price to private-sector buyers, net of all discounts. For products where ASP is greater than the MIDAS price, we made no adjustment. For federal hospitals, the MIDAS prices appear to reflect the mandatory discounts to federal purchasers.
8. For Germany, the mandatory rebate for non-reference-price drugs was 16 percent for 2004 and 6 percent for 2005. We assumed that all biologics were not included in the reference price system.
9. Nonavailability of new molecules might reflect decisions by regulatory authorities to deny market authorization or reimbursement or decisions by manufacturers not to seek approval or accept the regulated prices offered.
10. Online Appendix Exhibit A2 shows two of these definitions; see Note 3.
11. For many biologics the strength (grams per dose) is not reported. These molecule-ATC4-form-strength indexes include products that match on molecule-ATC4-form but with strength unreported in both countries. None of these indexes require that products be produced by the same manufacturer in the comparison countries. As of 2005 there was no true generic regulatory approval process for biologics in the EU or the US. Thus the great majority of biologics are classified by MIDAS as either originator, licensed, or branded generics (including copy products).
12. See, for example, P.M. Danzon and M.F. Furukawa, "Prices and Availability of Pharmaceuticals: Evidence from Nine Countries," *Health Affairs* 22 (2003): w521–w536 (published online 29 October 2003; 10.1377/hlthaff.w3.521). See also U.S. Department of Commerce, International Trade Administration, "Pharmaceutical Price Controls in OECD Countries" (Washington: ITA, December 2004).
13. France recently extended price regulation to hospital drugs that are reimbursed separate from diagnosis-related group (DRG) reimbursement.

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