Comparison of U.S. and International Prices for Top Medicare Part B Drugs by Total Expenditures

October 25, 2018

Executive Summary

The prices charged by drug manufacturers to wholesalers and distributors (commonly referred to as ex-manufacturers prices) in the United States are 1.8 times higher than in other countries for the top drugs by total expenditures separately paid under Medicare Part B. U.S. prices were higher for most of the drugs included in the analysis, and U.S. prices were more likely to be the highest prices paid among the countries in our study.

1. Introduction

Recently there has been increased interest in how U.S. drug prices compare to those of other developed countries. Much of this interest focuses on pricing for pharmacy-dispensed drugs, which account for about 72 percent of total prescription drug spending.[1] This paper, instead, focuses on prices for non-retail drugs, which are generally physician-administered.

In the fee-for-service Medicare program, outpatient prescription pharmaceuticals are covered under two separate voluntary benefits. Drugs dispensed by retail and specialty pharmacies to patients for self-administration are typically covered under the Medicare Part D program. Part D is operated by commercial insurance companies that negotiate formulary placement and prices with drug manufacturers and payment rates with pharmacies. This approach is one reason why spending growth under Part D has remained below its initial spending projections.

Drugs more typically administered to patients by healthcare practitioners, however, are covered and paid under Medicare Part B, which is part of the fee-for-service traditional Medicare benefit.[2] Under Part B, providers and suppliers "buy and bill" these types of drugs. Since 2005 for physicians, and 2006 for hospital outpatient departments, Medicare has paid suppliers and providers based upon the Average Sales Price (ASP) for each product, as reported by manufacturers to the Centers for Medicare & Medicaid Services (CMS).[3] Physician offices that buy and bill Part B drugs are paid 106% of the drug's ASP. Depending on a hospital outpatient department's participation in a safety

[1] U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation (ASPE). Observations on Trends in Prescription Drug Spending. March 2016. Available at https://aspe.hhs.gov/system/files/pdf/187586/Drugspending.pdf.

[2] Medicare Part B covers some self-administered drugs that were added to the benefit by Congress prior to the creation of Part D. These self-administered drugs are not the subject of this paper.

[3] Section 1847A of the Social Security Act governs payments to physicians for certain Part B drugs. Section 1833(t) governs payments to HOPDs, and allows the use of 1847A payment rates. By 2006, CMS cited this authority, and by 2014, was paying HOPDS based upon it.

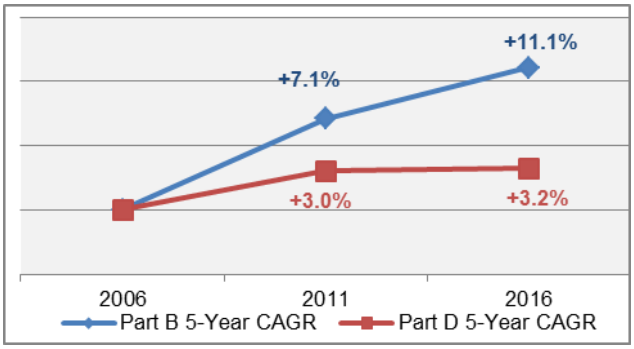
net drug pricing program, hospitals are reimbursed either 106 or 77.5 percent of ASP.[4]

ASP is reported by manufacturers to CMS as the total sales to all purchasers minus the price concessions granted to these purchasers and eventual end users, i.e. physicians and hospitals, with certain exceptions. For example, manufacturers may offer a rebate to physician specialists to prescribe and administer their product over a competitor's. The sale of the product to a wholesaler and the price concession granted to the physician are both accounted for in the ASP. Purchases and price concessions or rebates offered under federal discount programs (such as the Veterans Health Administration, the Medicaid Drug Rebate Program and State Supplemental Rebate Agreements, and the 340B Drug Discount Program) are excluded from the ASP calculation.[5]

Unlike the situation with traditional, pharmacy-dispensed drugs, payers are not typically involved in the prescribing, purchasing, or dispensing decision for physician-administered drugs, and there is therefore more limited private-payer negotiation for formulary coverage. Specifically, the Medicare program has not applied the types of formulary management practices that are commonly used to achieve better value for self-administered drugs by commercial insurers, including those sponsoring Medicare Advantage or Part D plans, which were recently granted new authority by CMS to use formulary management practices such as step therapy for Part B drugs.[6] However, this flexibility does not extend to the fee-for-service Medicare Part B. Many have also suggested that the 6 percent add-on payment currently in place for physician offices and some hospitals may incentivize the use of the highest priced clinically beneficial product.

Differences in coverage for drugs under Part B compared to Part D may have contributed to an acceleration in spending for physician-administered drugs, relative to spending growth under the approach taken under Part D. Specifically, spending for Part B drugs has doubled since 2006, despite overall low FFS enrollment growth.[7] In Part D, although enrollment continues to grow, annual and per-beneficiary expenditure growth rates are lower than in Part B. Put another way, per-beneficiary spending under Part B rose 7 percent and then 11 percent annually over two five-year periods (2006-2011 and 2011-2016) while Part D per-beneficiary spending increased only 3 percent per year in the same five-year intervals. See Figure 1.

Figure 1: Part B and D Per-Beneficiary Net Expenditures Growth Rates, 2006-2016[8]



Administration of coverage and payment of Part B drugs is delegated to regional Medicare

[4] HOPDs and off-campus locations that participate in the 340B Drug Discount Program are reimbursed a lower rate to account for significantly reduced acquisition costs. See 82 Fed. Reg. 52356.
[5] See SSA 1847A(c)(2) for exclusions.
[6] Source: CMS, "Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage," available at: https://www.cms.gov/Medicare/Health-Plans/HealthPlansGenInfo/Downloads/MA_Step_Therapy_HPMS_Memo_8_7_2018.pdf.

[7] While overall Medicare enrollment has grown, a growing proportion of beneficiaries have enrolled in Medicare Advantage plans, whose spending is not reflected in Figure 1.
[8] Source: Medicare Trustees Report from 2016 (for 2006) and 2018 (for 2011 and 2016); Part B annual National Summary Files; OPPS Final Rules from 2008, 2013, and 2018. Percent changes reported are annually over the five-year periods shown. Net payments exclude beneficiary cost-sharing.

Administrative Contractors (MACs). Broad rulemaking by CMS and ASP-based payment limits are applicable at the national level, while each MAC can determine for each patient if a Part B drug claim is reasonable and necessary.

While the Medicare program and MACs do not use formulary decision-making to restrict the coverage and payment of Part B drugs, a number of other economically comparable countries do for these types of drugs. Though these countries use their national health systems to negotiate lower prices in exchange for market access, drug manufacturers retain the choice whether to offer price concessions beyond those available to payers in the United States. To better understand the effect of these negotiations on prices paid for physician-administered drugs, ASPE compares in this paper the prices paid for physician-administered drugs in the U.S. to other selected countries.

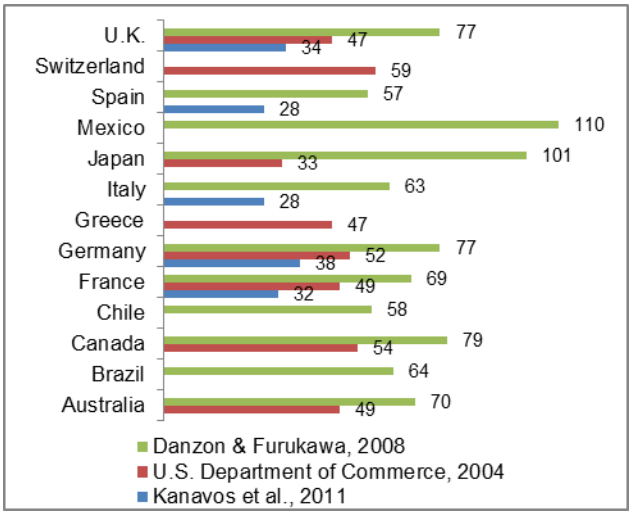
2. Background

The peer-reviewed literature assessing international drug prices has significant limitations, which we sought to address in our analysis. Namely, few of these analyses use data from after 2007, and there are no specific analyses of the exact set of drugs that we are interested in comparing.

Drug prices are generally higher in the U.S. based on price comparisons in the literature. In their recent systematic literature review, Kesselheim and Avorn (2016) estimate that U.S. prices were more than twice as high as those in other, similar countries. However, they include bilateral comparisons combined into a meta-analysis, which may overstate price differences.

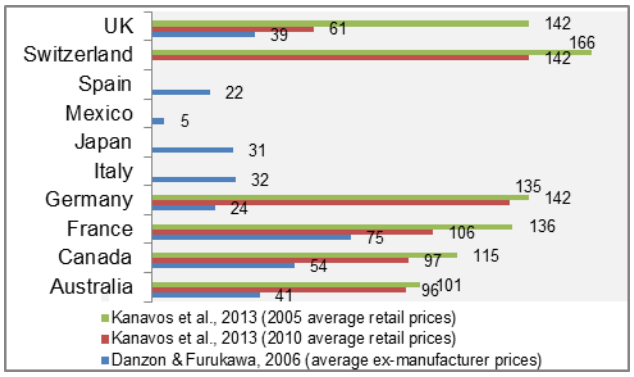
Instead, below and in Figures 2 and 3, we compare seminal original research publications. Comparing sample baskets of branded and generic prescription drugs in the U.S., all compared countries except Japan and Mexico had prices that were at least 20 percent less than those in the U.S. Prices in Japan were lower than U.S. prices in the 2004 Department of Commerce study but higher in Danzon and Furukawa (2003, 2005, 2006). This is likely due to methodological differences that result in different products being included in the study. For instance, package sizes in Japan differ significantly from elsewhere particularly because doses tend to be lower in Japan.

Figure 2: Reported Brand Drug Price Differentials from Price Index-Based Studies (U.S. = 100)



Narrowing to branded drugs, the literature demonstrates similar results, with prices higher in the U.S. than in all countries except Mexico among the three sources comparing branded drug prices. Two of the selected studies compared differences among biologics; these studies demonstrated mixed results for the drug class (Figure 3). We would note that Kanavos et al. (2013) compared a different price (average retail price per standard unit) than Danzon & Furukuwa (2006), which used ex-manufacturer prices, likely explaining the divergent results. Some of the variability may be related to product availability, per the authors' conclusions.

Figure 3: Reported Price Differentials from Studies Comparing Biologics (U.S. = 100)



There are important challenges in comparing drug prices across countries, including ambiguity in actual U.S. prices, assumptions and limitations related to available data on drugs sales and volume, and mismatches between drugs and dosage forms available in different markets. Despite these challenges, updated estimates of price differentials are needed.

3. Methods

In this paper, we calculate the price per gram of each included product in each selected country. We aggregate sales outside the U.S. and compare an average volume-weighted international price to the U.S. price. Below we describe each source underlying each aspect of this calculation in more detail.

Data Sources

International and Domestic Acquisition Cost Data. ASPE purchases licenses to several data products maintained by IQVIA (formerly known as Quintiles-IMS Institute for Healthcare Informatics or QIIHI). For this study, we used two products that contain acquisition pricing and volume information. First, MIDAS is IQVIA's international sales and volume database, which contains sales information (price and quantity) for more than 50 countries through the second quarter of 2018, from as early as 2013. Sales are stated in local and U.S. currency, as of the transaction date or current date, as desired.

For our analysis, we use ex-manufacturer prices[9] (sometimes called the ex-factory price) stated in U.S. currency on the transaction date. IQVIA also provides sales and volume information on U.S. domestic sales in its National Sales Perspective (NSP) database. We used this database to facilitate the accurate comparison of drug quantities in different package sizes and to account for how overfill is treated across the database. We describe how we make these corrections later in this section.

Medicare Program Data. In order to identify study drugs, we used two files that summarized Medicare program spending on Part B drugs. First, for physician offices, we used the Part B National Summary File for 2016, summing allowable charges and payments across all Health Care Procedural Coding System (HCPCS) J-codes and select Q-codes as appropriate. Second, for hospital outpatient departments, we used the CY 2018 Medicare Hospital Outpatient Prospective System's underlying cost statistics files to identify utilization and spending for separately payable drugs in 2016, and applied the listed payment rates to these. From each file we identified the 20 highest-spending products. Further discussion regarding drug selection is below.

We use Medicare's quarterly HCPCS ASP payment allowances for the third quarter of 2018 to compare prices paid in the U.S. and abroad through the first quarter of 2018. Since ASP is calculated based on the most recently available quarter's manufacturer's sales and is associated with a two quarter lag, third-quarter

[9] Ex-manufacturer price is the price received by manufacturers of a product, including discounts applied at the point of sale. In comparison, invoice price is the price paid by the dispenser of a product, including on-invoice discounts. To the extent that a product is sold through wholesalers, this price will differ by the wholesaler's markup.

2018 ASP is the best temporal approximation to the actual purchase prices paid in the first quarter of 2018. We also use these quarterly files to identify exactly which products are included in each selected drug's HCPCS code, which we describe in the section to follow. In all cases, the Medicare ASP payment files we use are publicly available. No manufacturer confidential information was collected for use in these analyses.

Drug Selection

ASPE compiled data on the top 20 drugs based on total Medicare reimbursement to either physician offices, hospital outpatient departments (HOPDs), or overall under Medicare Part B in 2016, which is the most recently available publicly accessible data (as described above). Drugs are defined in this study as each unique HCPCS code assigned by CMS. We included only U.S. single source[10] drugs[11] (as of July 1, 2018), biologicals, and biosimilars in our initial screening, and we specifically excluded vaccines and blood products, neither of which are paid under the ASP system. We also excluded contrast agents.

We compiled our list based upon the top 20 drugs by total spending from each segment—physicians and suppliers from the National Summary File and HOPDs using Final Rule data—because there are differences in patient conditions and acuity that may affect treatment patterns when aggregating total 2016 spending. These steps ensured there were at least 20 drugs for the comparison after any exclusions, such as those above. We also totaled spending across the two settings to include additional drugs that may not be in the top 20 in either segment, but were in the top 20 overall. We cross-checked this list against a 2017 publication from the U.S. Department of Health and Human Services Office of Inspector General (OIG) that compared price-inflation rates for top Part B drugs[12] to ensure that drugs the department has otherwise flagged with concerns about pricing were also included. No drugs needed to be added based upon the OIG report.

Appendix A lists all 32 products identified using this protocol. Among the 32 drugs identified in each payment system, we dropped Brovana (arformoterol tartrate) and Pulmicort (budesonide), because they are not physician-administered products. We also excluded Botox (onabotulinim toxin A) and Epogen (epoetin alfa) from the main analysis because within the IQVIA data they are not characterized as being sold using such mass-based measures such as milligrams or grams. However, we have included Epogen and Botox in the table examining prices per standard unit in Appendix C, since they are physician-administered.

To select products for comparison in other markets, we matched the HCPCS codes with National Drug Codes (NDCs) using the July 2018 ASP NDC-HCPCS Crosswalk file.[13] Using the identified NDCs, we examined which formulations of each product were included for each HCPCS code using IQVIA's NSP (described earlier) to identify other formulations of the same molecule. Based on this examination, we included formulations available in other countries that are not available

[10] In this paper, the single source status of a product was determined by the existence of a marketed product approved under an Abbreviated New Drug Application (ANDA). Some of the HCPCS codes included in this analysis contain multiple branded products marketed by different manufacturers. In addition, Velcade (bortezomib) is included in the analysis despite the recent approval of a generically named product that was approved under a New Drug Application (NDA) using the 505(b)2 pathway.

[11] Elsewhere and throughout this paper the term "drug" includes biological products and biosimilar products. Here we separate "drug" from "biological" to ensure clarity with statutory definitions.

[12] *See* HHS OIG, Calculation of Potential Inflation-Indexed Rebates for Medicare Part B Drugs 2017, available at https://oig.hhs.gov/oei/reports/oei-12-17-00180.asp.

[13] Crosswalk file available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2018ASPFiles.html.

in the United States if it appeared likely that these formulations would appear on the same HCPCS if available in the U.S. For example, Cimzia (certolizumab pegol) is sold as both a pre-filled syringe and a single-use vial formulation in the U.S. Both formulations are included in the HCPCS code and the calculated ASP. In Europe, an auto-injector formulation is available. We assume in this and other similar cases that an auto-injector formulation would be included in the same HCPCS code if approved in the U.S. under the same New Drug Application (NDA) or Biologics License Application (BLA). The technical appendix that accompanies this paper presents package size, formulation, and manufacturer-level detail on each included drug.

We reviewed our selection of drugs based on 2016 data, and identified one significant change in the market, requiring a further exclusion. In the U.S., Bendeka (bendamustine HCl) replaced Treanda in late 2015. Bendeka and Treanda are different formulations of the same active ingredient. Bendeka was assigned a unique HCPCS code by CMS as of January 1, 2017. We considered including both products in our analysis, but upon examining the dosage forms and strengths of the foreign formulations in MIDAS, we concluded that the foreign formulations more closely match Treanda than Bendeka. Bendeka is the fifth exclusion from the original list of 32 drugs, yielding 27 drugs for our main analysis, and 29 drugs for the standard unit analysis presented in Appendix C.

Country Selection

Not every drug product is available in every country, even among countries with similar economic conditions as the U.S. To ensure a broad representation of similar countries, we selected all countries in the G7[14] and all countries in Germany's external reference pricing market basket (15 countries).[15] We then excluded two countries (Denmark and the Netherlands) from this resultant list for lack of data in the IQVIA databases. This results in 17 countries including the U.S. to be included in our study. See Table 1. There is significant overlap among the G7 and Germany's market basket. While the absence of a drug in a given country may be related to the prices it could be sold for under that country's coverage system, this paper does not discuss access in these terms in any further detail.

Table 1: Countries Included in Analysis[16]

United States*	France*,**	Portugal**
Austria**	Germany*	Slovakia**
Belgium**	Greece**	Spain**
Canada*	Ireland**	Sweden**
Czech Republic**	Italy*,**	United Kingdom*,**
Finland**	Japan*	

Calculation of Price Ratios

Using IQVIA's MIDAS dataset, ASPE identified ex-manufacturer prices paid by wholesalers and distributors for identified drugs in the countries listed in Table 1. Based on discussions with the CMS, ASPE determined that ex-manufacturer price is preferable to gross price for cross-country comparisons, even while not directly comparable with ASP. Neither measure includes wholesaler margin, but only ASP includes price concessions to end users. We separately compared U.S. and foreign ex-manufacturer prices, and the ASP in the U.S. to foreign ex-manufacturer prices.

[14] See https://g7.gc.ca/en/g7-presidency/g7-members/.

[15] See Remuzat, C. et al. Overview of External Reference Pricing Systems in Europe. Journal of Market Access & Health Policy. 2015; 3: 27675.

[16] * indicates a member of the G7; ** indicates a member of Germany's external reference pricing market basket. See footnotes 14 and 15.

ASP Billing Unit Conversions

For this analysis, we also compared third quarter of the 2018 fiscal year ASP with the average ex-manufacturer prices paid in the first calendar quarter of 2018 derived from MIDAS (both domestically and internationally) and the invoice price paid in the U.S. derived for IQVIA NSP. As described above, ASP is published for the current quarter based on sales for the second preceding quarter to accommodate manufacturer reporting timelines. Therefore, the IQVIA price date range of Q1-2018 matches the Q3-2018 reimbursement rate's calculation date range in the U.S. Also, note that CMS publishes ASP+6 percent reimbursement rates. We removed the 6 percent to approximate purchase prices.

Package and Vial Configurations

Using MIDAS, we constructed prices in terms of price-per-equivalent quantity of drug or biologic. This resulted in prices per gram of the drug or biologic. For drugs not quantified by measures of mass, we report price ratios only in Appendix C by standard unit. For injectable drugs, the standard unit is typically one vial. For oral products, the standard unit is one pill. Standard units do not account for differences in strength. Using the price-per-gram, we calculated the price per HCPCS code billing unit, allowing us to compare the derived prices in IQVIA to Medicare's ASP reimbursement rate. This gram measure reports the total amount sold in each package of product and includes overfill.

However, Medicare's ASP does not include overfill,[17] so we adjusted by using the price per kilogram in the MIDAS database to the price per kilogram in a different IQVIA database – NSP – which we described above. NSP accounts for only the labeled amount of drug per package, not the overfill. So, for example, if a vial is labeled with 100 mg at $100 apiece, but has 10 mg overfill, the NSP price would be $1,000 per gram while the MIDAS price would be $909.10 per gram. ($100 divided by 110 mg times 1,000 mg per gram equals $909.10.) This ratio is calculated for each product where applicable. We assume in our analysis that overfill among identical package configurations is standard regardless of country sold, but if products are overfilled by different amounts between countries, this may introduce a source of variability in the ratio of prices.[18]

Federal Discount Programs

The MIDAS and NSP invoice prices include all sales through all distribution channels to all categories of end purchasers. In the U.S., this means IQVIA estimates include sales to 340B Drug Discount Program covered entities at that program's ceiling price (or a negotiated subceiling price). Similarly, sales to federal VHA facilities, at the program's mandatorily reduced prices, are included. This has the effect of depressing average prices in the U.S. relative to purchases made outside of these two mandated discount programs. Undiscounted sales to 340B covered entities were approximately $16 billion in 2016,[19] out of $450 billion in total pharmaceutical sales, but these sales are concentrated among drugs typically reimbursed under Part B rather than Part D.[20]

[17] See 75 Fed. Reg. 73466.

[18] We make one exception to this methodology for Eylea based on the high ratio of overfill to labeled drug volume in the U.S. relative to overfill outside the U.S. (0.28 mL compared to 0.05 mL). While we are unable to verify each country's labeled dosage, we assume 0.05 mL, rather than holding the ratio constant. Both the NSP and MIDAS prices account for this assumption.

[19] HRSA, Fiscal Year 2019 Justification of Estimates for Appropriations Committees, p. 255. Available at https://www.hrsa.gov/sites/default/files/hrsa/about/budget/budget-justification-fy2019.pdf.

[20] MedPAC's reported that the share of payments for Part B drugs made to 340B covered entities was 48% in 2013 and increasing year over year. See Chapter 3 of the June 2015 Report to Congress, available at http://www.medpac.gov/docs/default-source/reports/chapter-3-part-b-drug-payment-policy-issues-june-2015-report-.pdf.

VHA spent approximately $7 billion in 2017,[21] but not similarly concentrated among drugs reimbursed under Part B. For these reasons, the MIDAS and NSP estimated prices per gram will typically be below the Part B ASP. We do not adjust for these price differences in our analysis.

Biologics, Biosimilars, and Generics

Many of the products we include in the analysis are biologics. While biologics do face competition from biosimilars in the U.S., there are far more biologics facing biosimilar competition outside of the U.S. Because we restate ex-U.S. pricing in terms of per-HCPCS-billing code amounts, our analysis does not include prices for biosimilars with the reference biologics, in part because the Medicare Part B reimbursement system treats biosimilars distinctly under current law and regulation. In our main analysis we include biologics that outside the U.S. face biosimilar competition, even if biosimilars are not available in the U.S. For these products, we use only the prices for the reference biologics, as we do for U.S. sales.

Which drugs are subject to generic competition can differ between countries, as patents and other exclusivities may expire earlier in one country compared to another. In addition, a generic company may successfully challenge a patent in one country, but not succeed in another, or a country may not have granted a patent in the first place. Since this study is assessing U.S. and ex-U.S. pricing for single source drugs, we exclude all U.S. products with generic competition as of July 1, 2018 from our analysis. However, single source status may be related to U.S.-only patent or other exclusivity terms, so our main analysis combines the generic sales with brand sales, outside the U.S., if generics are available in another country.

[21] Mike McCaughan. Health Affairs Policy Brief: Prescription Drugs; Veterans Health Administration. Available at https://www.healthaffairs.org/do/10.1377/hpb20171008.000174/full/healthpolicybrief_174.pdf.

We are interested in understanding the effect of the U.S.'s prices on Medicare Part B spending, relative to prices paid elsewhere. To better understand these differences, we calculate additional spending under Medicare Part B assuming that drugs are reimbursed at the international average price rather than ASP+6 percent. This spending difference is calculated as total Medicare allowed charges divided by the average international price ratio. Effectively, the new payment rate is ASP reduced to the average international price plus 6 percent of ASP, also reduced by the same ratio.

Considerations for Weighting for Aggregation

For our main analysis, we aggregated country specific ratios into an international ratio. In addition, we aggregated product ratios into an overall ratio for the analysis. When aggregating within a product across countries, we generated an international average price that was weighted by the amount of grams sold. When aggregating into categories, we calculated an average ratio by weighting by total U.S. sales dollars as measured in MIDAS.

4. Results

We identified 32 Medicare Part B drugs among the top 20 drugs in spending for each setting (physician offices or HOPDs) or overall in the U.S. in 2016.[22] See Appendix A for a full list of these drugs, ranking by setting of care, and setting-specific and total spending by drug. These 32 drugs accounted for $18 billion in spending, out of a total of $27 billion on Part B drugs across these settings (67 percent). The 27 drugs included in the main analysis account for $17 billion (64 percent). The top product by expenditures in physician offices was Eylea (aflibercept), at $2.1 billion. This drug is the

[22] We included Zaltrap (ziv-aflibercept) in the analysis to ensure it was separated from Eylea (aflibercept), because IQVIA codes these products as the same molecule.

22nd-ranked drug in HOPDs with $138 million in spending in that setting. The top product in HOPDs by expenditures was Rituxan (rituximab), at $826 million, which was the second-ranked drug in physician offices with $840 million in expenditures.

In our main analysis we report on 27 Part B drugs. As described above, we excluded two drugs that are not physician-administered (Brovana and Pulmicort). Further, we exclude one drug (Bendeka) for lack of international sales data for comparison. In addition, Epogen (J0881) and Botox (J0585) are not sold in measures of mass and are excluded from the main analysis, but are included in the standard unit analysis as presented in Appendix C. These five drugs comprised only 5 percent of Part B drug spending for our study's drugs in 2016.

Only 11 of the 27 drugs in our main analysis were sold in all 16 comparator countries in the first quarter of 2018. Specific brands of intravenous immunoglobulin drugs (IVIG), as one example, are not uniformly available in each country. Finally, sales data for one drug indicated for a rare disease, Soliris (eculizumab), was available in IQVIA in 10 of the 16 countries. Prices for Soliris in these 10 countries were similar to U.S. prices. This suggests that rather than getting price concessions from the manufacturers, some countries simply choose to not cover the product. Sales data for the remaining products were available for most of the 16 countries.

Across the 27 drugs in our study, U.S. ex-manufacturer prices are 1.8 times that of the average international ex-manufacturer price in the first quarter of 2018. Table 2 (see page 13) presents Q1-2018 price ratios for the U.S. and the countries with the highest, median, and lowest prices for the selected products and groupings. We do not find that any one country consistently has the highest or lowest prices compared to the U.S. In this paper we do not report individual country price index ratios beyond the highest, median, and lowest prices that we present in Table 2.

- U.S. prices are lower: For two products (Gammagard and Soliris), U.S. prices were lower than the average international price ratio
- Prices are similar: For five products, while the U.S. price is higher, it is within 20 percent of the international price (Gamunex-c & Gammaked, Keytruda, Privigen, Remicade, and Velcade).
- U.S. prices are higher: For the remaining 20 products, U.S. prices exceed the average international price by more than 20 percent. This includes three products (Lucentis, Prolia & Xgeva, and Treanda) with U.S. prices more than four times the international average.

In addition to comparisons of the U.S. price to the international average, we also evaluated price ratios at the country-specific level.

- U.S. prices are higher than any other country: For 19 of the 27 products, the highest price among comparison countries is in the U.S. (In Table 2, the column for highest price has a value above 1.0, meaning the U.S. price is the highest.)
- U.S. prices are within range of other countries' prices: For the eight other products, the average international price may be lower than the U.S. price, but at least one other country's price exceeded the price in the U.S. Spain, Germany, and Japan had these highest prices (exceeding the U.S. price) for two drugs each. Finland and Sweden were the highest (in excess of the U.S. price) for one product each.

We also assessed which countries have uniformly higher or lower prices.

- Highest prices: Excluding the U.S., which has the highest price for 13 drugs as noted above, among all 27 products both Germany and Canada had the highest prices for six drugs, and Japan for five drugs. No other country had the highest price for more than three drugs.
- Lowest prices: For four products each, France and the United Kingdom have the lowest price measured outside the U.S. Japan, Sweden, and Slovakia have the lowest prices for three drugs each. No other country has the lowest price on more than two products.

We also restated international and domestic prices in terms of HCPS billing units to facilitate comparisons of the IQVIA-derived prices to ASP. We also restated two U.S. prices derived from two IQVIA data sets to caveat the direct comparisons between ASP and IQVIA derived prices. Table 3 provides comparisons to ASP overall.

Finally, we calculated that the Medicare program and its beneficiaries spent an additional $8.1 billion (or 47 percent more) on these 27 products than it would have, if payments based upon ASP were scaled by the international price ratios we calculated. Recognizing that the plus 6 percent add-on is an often-discussed topic, we made this comparison solely to illustrate the effects of the price differences we calculated. See Table 4.

5. Discussion

Overall, prices and reimbursement rates for Part B drugs are significantly higher for U.S. providers than purchasers outside the U.S. Except in a few outlier cases, this conclusion holds for each drug, and regarding each international comparator. Medicare could achieve significant savings if prices in the U.S. were similar to those of other large market-based economies.

One of the products for which this is not the case is an IVIG product. In addition, Soliris prices are approximately the same in the U.S. and our comparison countries. Soliris treats a rare disease and has no competitors, which may reduce the ability for any country to obtain price concessions.

Limitations

There are several limitations to this data, which may apply to some products more than others. Namely, product presentations (dosage forms and strengths) and manufacturing standards may differ significantly. Further, the design choices we made in our analysis may affect the point estimates we calculate. We describe these limitations below.

Meaningful Differences across Countries

The products available in other countries do not perfectly align with products available in the United States. The technical appendix that accompanies this paper provides product specific information that explores differences in products by country.

We found that the responsible manufacturer differs between the U.S. and other countries. For example, no fewer than five manufacturers sell branded Treanda across our comparison countries. Remicade (infliximab) is sold by Merck Sharp & Dohme in at least 11 countries and by Johnson & Johnson in the U.S. and at least four other countries. In this case (and in others), Japan has a different manufacturer than all other countries. Different manufacturers may have different marketing strategies, which may make it difficult to fully compare the pricing between countries.

In addition, available formulations may differ between countries. These differences in formulations may alter the usage pattern of the drug. For instance, as we discussed above, an auto-injector version of Cimzia is available in Europe. Auto-injectors help facilitate self-

administration of a product. While the pre-filled syringe formulation of Cimzia sold in the U.S. is also self-administered, Cimzia may have a larger share of spending through self-administration outside the U.S. Thus, it may be inappropriate to compare the U.S. and European versions.

Third, there may be broad differences in clinical indications for these products, or different regulatory approval standards. For instance, Cimzia's self-administered formulations were approved much earlier in European markets than they were in the U.S. As with overall approval, indications for use may differ widely, as well as may typical dosages even for the same indicated uses. To the extent that pricing may differ based on clinical indication or expected dosage, we did not account for it.

Overfill

For injectable products, the manufacturer may decide to include more product in a vial than is administered to the patient. Some products have more overfill than other products. Within MIDAS, the price-per-gram data includes the total amount of drug in the physical product. We used IQVIA NSP to attempt to address this concern by only including the amount of drug typically dispensed. As a result, we included NSP prices in Table 3. Given that we are mostly concerned about the ratio of prices between the U.S. and other countries, overfill would be only an issue in cases in which vial sizes differ between countries.

Data reporting

The data available in MIDAS is collected at different levels in each country. For example, in some countries data is collected at the hospital level, while at others only at a higher level such as the wholesale level. IQVIA then uses its own proprietary methods to estimate whole-country sales volumes and prices. IQVIA does not have specific information on discounts for any given unit including rebates, volume-based discounts, or prompt-pay discounts.

Further, IQVIA data reporting may be subject to limitations by manufacturers. If a manufacturer restricts IQVIA's ability to publish data, the pricing numbers in IQVIA may be incorrect. For instance, for some drugs in the U.S., IQVIA only receives data from federal facilities. As a result, the prices for drugs may not be representative overall prices paid. For example, IQVIA's data products underestimate the sales volume and price for Eylea due to data restrictions from the manufacturer. Based on examining distribution channel data in IQVIA NSP, we estimate that the U.S. price should be higher. IQVIA's Eylea data reflects mostly sales to federal facilities, which are able to purchase the product at a lower price relative to the rest of the market. We still included Eylea in this analysis despite this issue, because the ratio itself was not an outlier and it underestimates the difference between U.S. and international prices.

Ex-manufacturer Price versus Net Price

This analysis compared the U.S. and other countries at the ex-manufacturer level. This price may not accurately reflect the actual amount paid in the U.S. or abroad.

In other countries, there may be additional rebates and value-based agreements that are not captured in the ex-manufacturer price. Similarly, the U.S. ex-manufacturer prices do not include potential rebates and after sale discounts. To the extent that these impacts differ by country, our results will be biased. While this is an important limitation, as we explained above, we considered this issue to be less important for drugs administered by physicians compared to drugs dispensed through retail pharmacies. Some of the drugs included in this study also have notable distribution through pharmacies for self-administration, which may result in greater bias in the results, if pricing

strategies differ based on whether consumers face direct costs at the pharmacy point of sale for example.

Generics and Biosimilars

This analysis included only single-source U.S. drug products. Thus, if the product has generic or biosimilar products available elsewhere, but not in the United States, it is included. When calculating international prices, we included generic products outside the US as part of the price of the product. While this choice reduced prices paid outside the U.S., it reflected current HCPCS policy had we included U.S. multiple source drugs, and it allowed us to better understand the role that longer patents or exclusivities in the U.S. may play in price differences. On the other hand, biosimilars are not included in the same HCPCS code as their reference biologic. As a result, this analysis did not include biosimilars in the U.S. or outside the U.S. in the analysis. Even though biosimilars are not included in the analysis, it is possible that the existence of biosimilars in other countries reduces the price of the reference biologic in those countries. Due to these pricing impacts some may suggest that such products should be removed from the analysis.

6. Conclusion

In this paper, we found that overall, the prices paid for Medicare Part B drugs with the greatest expenditures in the U.S. exceeded the prices paid in countries with similar economic conditions. The amount by which U.S. prices exceeded those of international comparators varied significantly by product, and there was no clear pattern as to which countries were consistently paying lower prices. We find these higher U.S. prices mean that the Medicare program pays nearly twice as much as it would pay for the same or similar drugs in other countries.

Table 2. Comparisons of Price per Gram, U.S. and International Ex-Manufacturer Prices, Q1 2018.

Product	U.S. Price per Gram	U.S. Price Divided by Average International Price (U.S. = 1)	Country with Lowest Price	Country with Median Price	Country with Highest Price
Alimta (pemetrexed sodium)	$4,690	2.0	39.7 (Canada)	1.8 (Japan)	1.3 (Austria)
Aranesp (darboepoetin alfa)	$3,517,653	2.1	3.4 (Portugal)	2.4 (France)	1.3 (Belgium)
Avastin (bevacizumab)	$6,504	2.0	2.4 (France)	2.2 (Japan)	1.5(Belgium)
Cimzia (certolizumab pegol)	$8,197	3.0	4.2 (France)	3.3 (Sweden)	2.2 (Germany)
Eligard/ Lupron (leuprolide acetate)	$37,814	1.3	5.8 (Greece)	1.4 (Sweden)	0.95 (Japan)
Eylea (aflibercept)	$775,994	1.7	3.1 (Belgium)	1.6 (UK)	1.4 (Canada)
Gammagard (IVIG)	$68	0.95	1.8 (Japan)	1.0 (France)	0.69 (Spain)
Gamunex-c/ Gammaked (IVIG)	$67	1.1	1.8 (Sweden)	1.1 (Italy)	1.0 (Finland)
Herceptin (trastuzumab)	$7,688	2.2	2.7 (Japan)	2.4 (Portugal)	1.5 (Germany)
Kadcyla (ado-trastuzumab emtansine)	$26,249	1.3	1.6 (Canada)	1.2 (France)	1.0 (Spain)
Keytruda (pembrolizumab)	$40,036	1.2	1.5 (Slovakia)	1.3 (UK)	0.91 (Spain)
Lucentis (ranibizumab)	$3,270,469	5.4	9.8 (Greece)	6.9 (France)	1.4 (Japan)
Neulasta (pegfilgrastim)	$588,937	3.2	4.7 (Portugal)	3.3 (France)	1.8 (Canada)
Opdivo (nivolumab)	$22,856	1.4	1.9 (Germany)	1.5 (Sweden)	0.86 (Japan)
Orencia (abatacept)	$4,381	2.3	3.2 (Slovakia)	2.5 (France)	1.6 (Germany)
Privigen (IVIG)	$65	1.2	1.8 (Sweden)	1.3 (Belgium)	0.91 (Finland)
Prolia/Xgeva (denosumab)	$15,575	4.6	5.9 (France)	4.8 (Japan)	3.4 (Canada)
Remicade (infliximab)	$7,108	1.2	1.9 (Slovakia)	1.2 (Japan)	0.84 (Sweden)
Rituxan (rituximab)	$6,597	2.7	4.3 (UK)	2.8 (Spain)	2.1 (Japan)
Sandostatin LAR (octreotide acetate)	$111,548	2.7	6.1 (Spain)	3.1 (UK)	1.5 (Germany)
Soliris (eculizumab)	$16,720	0.99	1.3 (UK)	1.0 (Italy)	0.86 (Germany)
Treanda (bendamustine)	$24,138	6.9	34.2 (Sweden)	10.8 (France)	2.5 (Canada)
Tysabri (natalizumab)	$18,674	2.9	4.1 (UK)	2.8 (France)	2.1 (Canada)
Velcade (bortezomib)	$359,040	1.1	5.9 (Czech Republic)	1.0 (Italy)	0.82 (Germany)
Xolair (omalizumab)	$6,128	2.2	2.9 (UK)	2.2 (Italy)	1.8(Canada)
Yervoy (ipilimumab)	$121,862	1.5	1.7 (Japan)	1.6 (Germany)	1.2 (Belgium)
Zaltrap (ziv-aflibercept)	$7,413	1.7	2.1 (France)	1.6 (Italy)	1.3 (Japan)
All Products Total	**N=27**	**1.8**			

Source: IQVIA MIDAS. Analysis based on data released August 17, 2018.

Table 3. Comparison of ASP (Q3 2018) to IQVIA U.S. Invoice, IQVIA Ex-Manufacturer, and, international Ex-Manufacturer Average (Q1 2018)

U.S. Brand Name	HCPCS Dosage	U.S. ASP, per HCPCS unit, July 2018	U.S. IQVIA NSP, Q1 2018	U.S. IQVIA MIDAS, Q1 2018	Ex-U.S. IQVIA MIDAS International (Average)
Alimta	10 MG	$63.64	$53.23	$46.90	$23.54
Aranesp	1 mcg	$3.62	$3.63	$3.52	$1.70
Avastin	10 MG	$74.39	$66.94	$65.04	$32.69
Cimzia	1 MG	$7.57	$11.99	$8.20	$2.71
Eligard/ Multiple Products	7.5 MG	$205.82	$214.20	$303.78	$210.38
Eylea	1 MG	$912.90	$792.73	$775.99	$462.50
Gammagard	500 MG	$43.71	$34.98	$33.99	$35.70
Gamunex-c/gammaked	500 MG	$38.88	$34.34	$33.37	$29.12
Herceptin	10 MG	$97.86	$79.16	$76.86	$35.42
Kadcyla	1 MG	$28.95	$27.02	$26.25	$20.62
Keytruda	1 MG	$45.82	$51.51	$40.04	$33.75
Lucentis	0.1 mg	$352.36	$360.16	$327.05	$60.05
Neulasta	6 MG	$4,453.63	$3,637.41	$3,533.62	$1,103.33
Opdivo	1 MG	$25.62	$23.52	$22.86	$16.91
Orencia	10 MG	$48.71	$45.07	$43.81	$19.40
Privigen	500 MG	$37.42	$33.48	$32.53	$26.76
Prolia/Xgeva	1 MG	$17.34	$16.02	$15.58	$3.39
Remicade	10 MG	$79.15	$73.14	$71.08	$60.52
Rituxan	100 MG	$863.49	$679.14	$659.53	$240.72
Sandostatin LAR	1 MG	$187.77	$131.18	$111.55	$41.25
Soliris	10 MG	$217.43	$172.05	$167.20	$169.08
Treanda	1 MG	$29.01	$24.83	$24.14	$3.49
Tysabri	1 MG	$18.77	$19.22	$18.67	$6.51
Velcade	0.1 MG	$44.10	$36.94	$35.90	$33.00
Xolair	5 MG	$34.28	$31.54	$30.64	$13.80
Yervoy	1 MG	$140.22	$125.39	$121.86	$81.76
Zaltrap	1 MG	$7.63	$7.63	$7.41	$4.42

Source: CMS quarterly ASP files for Q3-2018 and IQVIA MIDAS and IQVIA NSP. Analysis based on data released August 17, 2018 (MIDAS) and July 29, 2018 (NSP).

Table 4. Changes in Medicare Part B Spending Based on International Comparator Price

HCPCS Code	U.S. Brand Name	2016 Total Medicare Part B Allowed Charges	Medicare Part B Spending if Paid at the International Volume-Weighted Average Price[23]	Difference in Spending
J0178	Eylea	$2,208,730,192	$1,152,867,398	($892,314,629)
J9310	Rituxan	$1,665,667,931	$639,603,352	($1,057,851,434)
J2505	Neulasta	$1,375,670,111	$424,641,010	($946,133,518)
J1745	Remicade	$1,338,726,195	$1,134,829,514	($198,877,939)
J9299	Opdivo	$1,220,839,260	$933,097,337	($317,397,205)
J9035	Avastin	$1,111,678,364	$567,128,402	($552,964,027)
J0897	Xgeva/ Prolia	$1,086,664,418	$234,454,406	($849,982,901)
J2778	Lucentis	$1,044,324,413	$187,779,622	($852,588,112)
J9355	Herceptin	$703,556,755	$339,667,923	($379,373,082)
J9305	Alimta	$511,822,437	$253,797,147	($254,960,126)
J0129	Orencia	$586,532,902	$255,021,785	($326,803,388)
J9041	Velcade	$490,438,068	$452,011,950	($39,651,249)
J2353	Sandostatin LAR	$411,511,792	$154,824,669	($259,319,716)
J9217	Eligard	$289,060,099	$215,839,009	($74,636,177)
J1561	Gamunex	$299,752,172	$261,524,159	($38,228,013)
J0881	Aranesp	$290,619,828	$141,366,296	($150,572,598)
J9271	Keytruda	$327,322,225	$285,984,921	($51,358,260)
J1569	Gammagard	$282,939,607	$297,155,879	$14,216,272
J1459	Privigen	$237,597,939	$195,414,760	($42,183,179)
J2357	Xolair	$328,046,394	$146,959,018	($180,282,725)
J2323	Tysabri	$305,983,047	$103,995,559	($199,303,326)
J9033	Treanda	$263,809,341	$41,215,343	($225,623,458)
J1300	Soliris	$267,076,579	$269,976,437	$3,003,237
J9228	Yervoy	$236,636,161	$168,272,373	($77,863,939)
J0717	Cimzia	$235,364,188	$77,115,101	($157,589,093)
J9354	Kadcyla	$113,231,486	$89,670,721	($24,273,582)
J9400	Zaltrap	$6,188,170	$3,686,556	($2,501,614)
Grand Total, Top 20 PO or HOPD (N=27)		**$17,239,790,075**	**$9,104,376,292**	**($8,135,413,782)**

Source: CMS and IQVIA MIDAS. Analysis based on data released August 17, 2018.Numbers may not add up due to rounding.

[23] Deflation is based upon the ratios in Table 2. We take the total amount paid for these Part B drugs in 2016 as presented Appendix A and divided them by the ratios that were the results of our analysis in Table 2.

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Appendix A: Top Part B Drugs in Physician Offices or Hospital Outpatient Departments, 2016

	HCPCS Code	U.S. Brand Name	Molecule	Physician Office Allowed Charges, 2016	Physician Office Rank	HOPD Allowed Charges, 2016	HOPD Rank	Total Spend	Total Rank
	J0178	Eylea	Aflibercept	$2,071,052,178	1	$137,678,013	21	$2,208,730,192	1
	J9310	Rituxan	Rituximab	$839,577,817	3	$826,090,112	1	$1,665,667,931	2
	J2505	Neulasta	Pegfilgrastim	$681,665,008	6	$694,005,097	2	$1,375,670,111	3
	J1745	Remicade	Infliximab	$832,050,751	4	$506,675,440	5	$1,338,726,195	4
	J9299	Opdivo	Nivolumab	$580,636,482	7	$640,202,771	3	$1,220,839,260	5
	J9035	Avastin	Bevacizumab	$561,491,122	8	$550,187,233	4	$1,111,678,364	6
	J0897	Xgeva/Prolia	Denosumab	$683,404,048	5	$403,260,364	6	$1,086,664,418	7
	J2778	Lucentis	Ranibizumab	$1,005,623,707	2	$38,700,704	56	$1,044,324,413	8
	J9355	Herceptin	Trastuzumab	$334,464,920	10	$369,091,825	7	$703,556,755	9
	J0129	Orencia	Abatacept	$406,895,619	9	$179,637,275	15	$586,532,902	10
	J9305	Alimta	Pemetrexed	$235,992,292	12	$275,830,133	8	$511,822,437	11
	J9041	Velcade	Bortezomib	$263,115,549	11	$227,322,508	10	$490,438,068	12
	J2353	Sandostatin	Octreotide acetate	$179,163,663	22	$232,348,111	9	$411,511,796	13
	J2357	Xolair	Omalizumab	$155,367,158	26	$172,679,213	17	$328,046,398	14
	J9271	Keytruda	Pembrolizumab	$115,235,357	40	$212,086,833	12	$327,322,229	15
	J2323	Tysabri	Natalizumab	$121,603,932	38	$184,379,082	14	$305,983,051	16
	J1561	Gamunex	IVIG	$113,441,522	41	$186,310,613	13	$299,752,176	17
*	J0585	Botox	Onabotulinumtoxin A	$203,050,245	16	$92,436,264	29	$295,486,525	18
*	J0885	Epogen	Epoetin alfa	$208,040,284	15	$83,413,376	30	$291,453,675	19
	J0881	Aranesp	Darboepoetin alfa	$166,314,575	24	$124,305,233	24	$290,619,832	20
	J9217	Eligard	Leuprolide acetate	$224,381,941	13	$64,678,145	38	$289,060,099	21
	J1569	Gammagard	IVIG	$124,326,865	36	$158,612,710	18	$282,939,611	22
	J1300	Soliris	Eculizumab	$88,680,008	50	$178,396,526	16	$267,076,583	23
	J9033	Treanda	Bendamustine	$125,105,469	35	$138,703,842	20	$263,809,345	24
*	J9034	Bendeka	Bendamustine		#N/A		#N/A		
	J1459	Privigen	IVIG	$24,580,466	95	$213,017,381	11	$237,597,943	25
	J9228	Yervoy	Ipilimumab	$96,651,726	47	$139,984,392	19	$236,636,165	26
	J0717	Cimzia	Certolizumab Pegol	$197,956,992	18	$37,407,181	57	$235,364,191	27
*	J7605	Brovana	Arformoterol tartrate	$211,074,241	14		#N/A	$211,074,255	28
*	J7626	Pulmicort	Budesonide	$196,567,537	19		#N/A	$196,567,556	29
	J9354	Kadcyla	Ado-trastuzumab emtansine	$47,500,452	67	$65,730,971	37	$113,231,490	30
	J9400	Zaltrap	ziv-Aflibercept	$4,326,085	170	$1,861,918	152	$6,188,174	234
Drugs Excluded from Main Analysis			**N=5**	**$610,692,023**		**$92,436,264**		**$703,128,287**	
Drugs Included in Main Analysis			**N=27**	**$10,488,645,988**		**$7,042,597,002**		**$17,531,242,990**	

* Indicates drug is excluded from main analysis. Source: CMS program data.

Appendix Table B: Selected Drugs and Generic or Biosimilarity Availability.

	HCPCS Code	U.S. Brand Name	Molecule	Total Part B Allowable Charges	Total Part B Rank	Physician Administered	Generic Available (year)	Biosimilars Available in U.S. (year)	Biosimilars Available ex-U.S. (year)
	J0178	Eylea	Aflibercept	$2,208,730,192	1	Yes	N/A	No	No
	J9310	Rituxan	Rituximab	$1,665,667,931	2	Yes	N/A	No	Yes
	J2505	Neulasta	Pegfilgrastim	$1,375,670,111	3	Yes	N/A	Yes (2018)	No
	J1745	Remicade	Infliximab	$1,338,726,195	4	Yes	N/A	Yes (2016)	Yes
	J9299	Opdivo	Nivolumab	$1,220,839,260	5	Yes	N/A	No	No
	J9035	Avastin	Bevacizumab	$1,111,678,364	6	Yes	N/A	No, but approved in 2017	No, but approved in 2017
	J0897	Xgeva/ Prolia	Denosumab	$1,086,664,418	7	Yes	N/A	No	No
	J2778	Lucentis	Ranibizumab	$1,044,324,413	8	Yes	N/A	No	No
	J9355	Herceptin	Trastuzumab	$703,556,755	9	Yes	N/A	No, but approved in 2017	Yes, 2018
	J0129	Orencia	Abatacept	$586,532,902	10	Yes	N/A	No	No
	J9305	Alimta	Pemetrexed	$511,822,437	11	Yes	No	N/A	N/A
	J9041	Velcade	Bortezomib	$490,438,068	12	Yes	N/A	N/A	N/A
	J2353	Sandostatin LAR	Octreotide acetate	$411,511,796	13	No	No	N/A	N/A
	J2357	Xolair	Omalizumab	$328,046,398	14	Yes	N/A	No	No
	J9271	Keytruda	Pembrolizumab	$327,322,229	15	Yes	N/A	No	No
	J2323	Tysabri	Natalizumab	$305,983,051	16	Yes	N/A	No	No
	J1561	Gamunex	IVIG	$299,752,176	17	No	N/A	No	No
*	J0585	Botox	Onabotulinumtoxin A	$295,486,525	18	Yes	N/A	No	No
*	J0885	Epogen	Epoetin alfa	$291,453,675	19	Yes	N/A	No, but approved in 2018	Yes, 2007
	J0881	Aranesp	Darboepoetin alfa	$290,619,832	20	Yes	N/A	No	Yes, 2007
	J9217	Eligard	Leuprolide acetate	$289,060,099	21	Yes	Yes (2009)	N/A	N/A
	J1569	Gammagard	IVIG	$282,939,611	22	No	N/A	No	No
	J1300	Soliris	Eculizumab	$267,076,583	23	Yes	N/A	No	No
	J9033	Treanda	Bendamustine	$263,809,345	24	Yes	No	N/A	N/A
*	J9034	Bendeka	Bendamustine	N/A	N/A	Yes	Yes (2018)	N/A	N/A
	J1459	Privigen	IVIG	$237,597,943	25	No	N/A	No	No
	J9228	Yervoy	Ipilimumab	$236,636,165	26	Yes	N/A	No	No
	J0717	Cimzia	Certolizumab Pegol	$235,364,191	27	Yes	N/A	No	No
*	J7605	Brovana	Arformoterol	$211,074,255	28	No	No	N/A	N/A
*	J7626	Pulmicort	Budesonide	$196,567,556	29	No	Yes (2013)	N/A	N/A
	J9354	Kadcyla	Ado-trastuzumab emtansine	$113,231,490	30	Yes	N/A	No	No
	J9400	Zaltrap	ziv-Aflibercept	$6,188,174	234	Yes	N/A	No	No

Appendix Table C: Comparisons of Price Per Standard Unit, U.S. and International Ex-Manufacturer Prices, Q1 2018

Product	U.S. Price per Standard Unit	U.S. Price Divided by Average International Price (U.S. = 1)
Alimta	$1,494.65	1.8
Aranesp	$205.66	2.5
Avastin	$1,611.05	2.0
Botox	$792.69	3.2
Cimzia	$1,639.42	3.1
Eligard/ Other products	$944.66	2.1
Epogen	$253.08	3.4
Eylea	$1,540.91	1.6
Gammagard	$918. 83	2.1
Gamunex-c/gammaked	$909.32	2.1
Herceptin	$1,153.17	1.4
Kadcyla	$3,070.00	1.3
Keytruda	$4,003.59	1.6
Lucentis	$1,635.17	1.8
Neulasta	$3,533.62	3.6
Opdivo	$2,206.09	1.7
Orencia	$862.33	2.8
Privigen	$1,019.83	1.4
Prolia/Xgeva	$1,262.77	4.8
Remicade	$710.84	1.2
Rituxan	$1,756.93	1.5
Sandostatin LAR	$3,308.19	2.5
Soliris	$5,016.08	0.99
Treanda	$1,691.81	6.4
Tysabri	$5,602.42	2.9
Velcade	$1,256.63	1.1
Xolair	$919.29	2.3
Yervoy	$12,610.53	1.5
Zaltrap	$1,124.65	1.7
Source: IQVIA MIDAS. Analysis based on data released August 17, 2018.		