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COMPARING INTERNATIONAL DRUG PRICES TO PRICES IN THE UNITED STATES

MAKING INDIVIDUALIZED DRUG PRICE COMPARISONS

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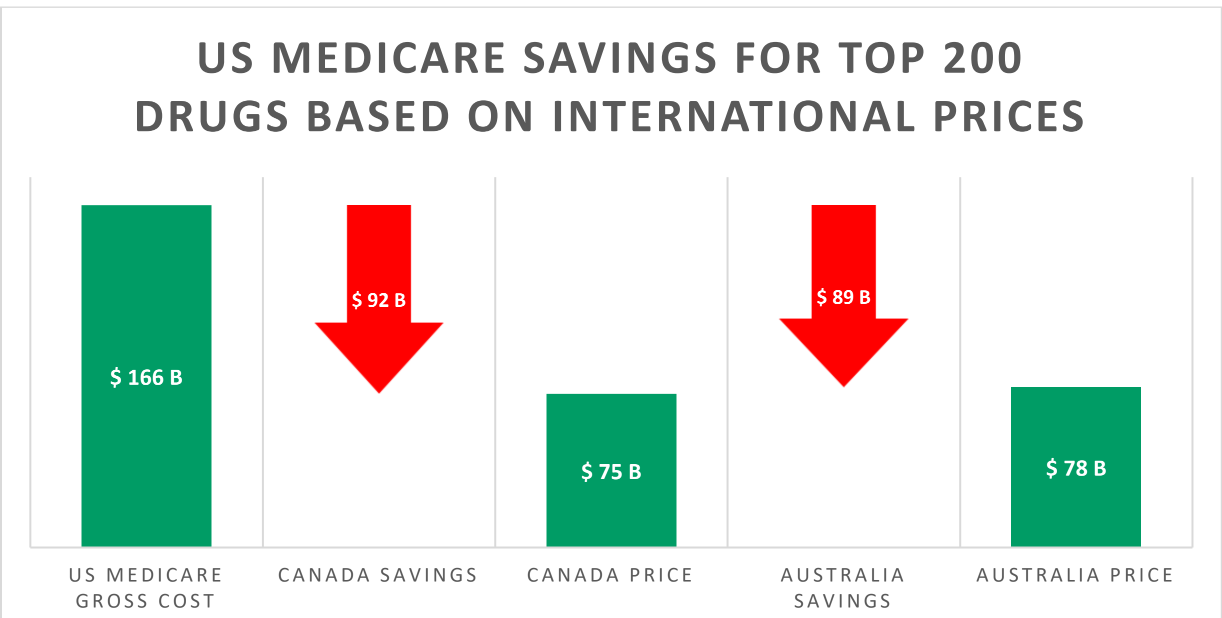
Executive Summary

Many studies have examined the pricing differences in prescription drugs between the United States and other countries around the globe. Those studies have consistently found that the U.S. is paying more for prescription medications than our global peers. For years, policy proposals at both the federal and state levels have sought to address the affordability of prescription medications in the U.S. by accessing international prices. At times, these proposals have been to benchmark U.S. drug prices to international prices. Other proposals have sought to directly source the medications internationally at their lower cost rather than through using the existing U.S. distribution system. Overwhelmingly, studies of international prices have resulted in aggregate figures of savings but have been sparse on which drug prices are actually producing the savings.

In this report, we undertook a study of international drug prices that sought to not only confirm that international prices remain cheaper than the prices incurred by prescription drug programs in the United States (like Medicare), but to provide transparency around price differentials on a product-to-product basis. To that end, we developed a tool to enable interested individuals to directly compare prices to Australia and select Canadian provinces. While we gathered pricing information across a broad spectrum of products, we limited this report to the Top 200 drugs by cost within the Medicare program. Overall, we found that international prices are associated with potentially significant savings (i.e., greater than 50%) for this subset of products (based on comparisons to list prices in the U.S.). Our results are consistent with prior studies on this topic.



And while we acknowledge that our study cannot readily account for the substantial retrospective price concessions that exist within U.S. programs like Medicare, we should acknowledge that current drug manufacturer price concessions produce a 22% savings to Medicare. Our prior work found that other federal programs, such as the Federal Supply Schedule (FSS) can produce retrospective rebates equivalent to 30% of gross brand spending.[I] As a result, even if we could account for rebates, it seems highly likely that international prices would be associated with significant savings to the Medicare program.

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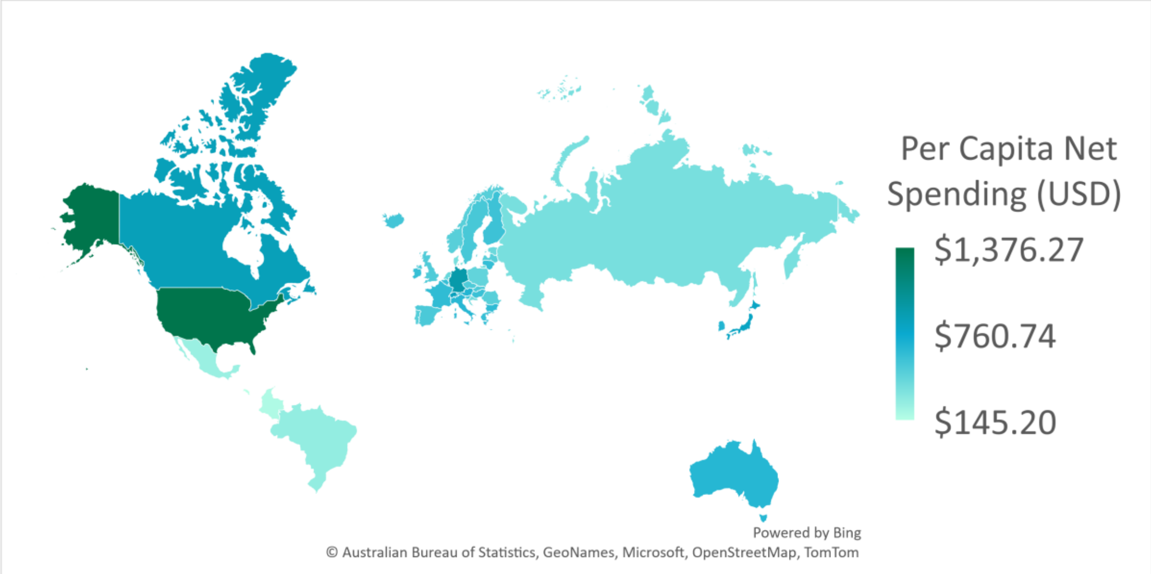
Background

Prescription medications are the standard of care for treating many medical ailments across the globe. As a result, many spend a great deal of their income to obtain medications to extend or improve their quality of life. Spending on retail prescription drugs totaled $348.4 billion in the U.S. during 2020, accounting for eight percent of total U.S. health spending.[II] This spending was used to purchase approximately 6.3 billion prescriptions over the same time frame.[III]

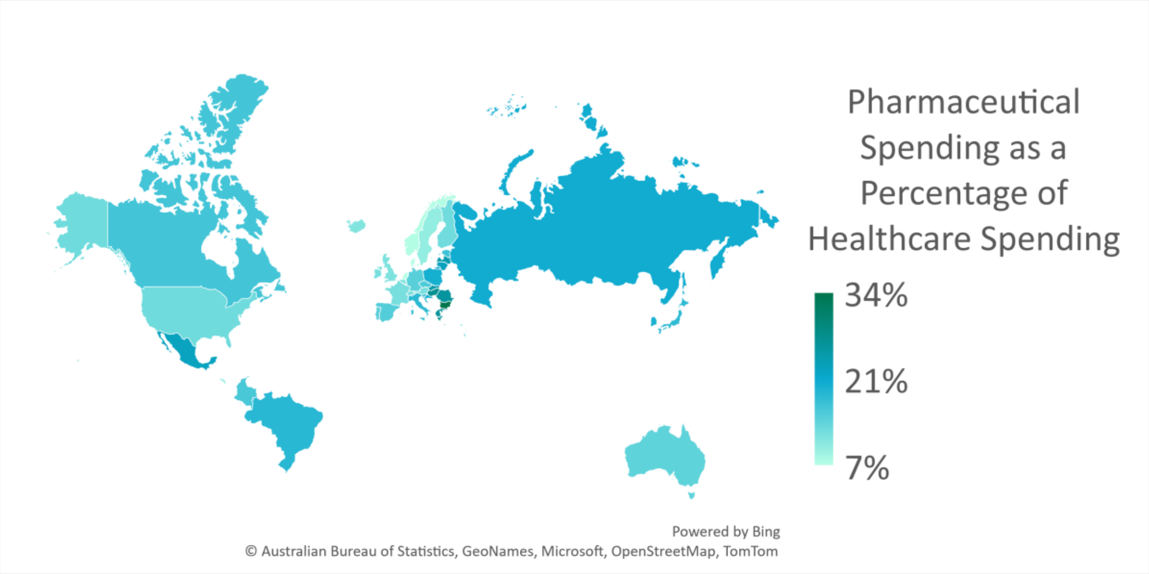
While medications to improve or extend life are certainly of immense value to the modern healthcare system, spending on medications is not equitable across the globe. On a USD per capita basis (using economy-wide purchasing power parity), the U.S. spends more on prescription drugs than comparable countries based on data gathered by the Organization for Economic Co-Operation and Development (OECD) in 2019 (see **Figure 1**).[IV]

Figure 1: USD per capita estimated net drug pricing, OECD countries, 2019



While the per capita basis gives a sense for just how much more expensive medications are on an individual basis in the U.S. in comparison to other countries, it should be noted that the U.S. is not the top country in all OECD measured drug pricing categories. For example, the U.S. is not the top spender on the basis of proportion of GDP represented by pharmaceutical spending or the percentage of healthcare spending associated with pharmaceuticals (both top spots belong to Bulgaria). In fact, with regards to pharmaceuticals as a percentage of healthcare spending, the U.S. is near the bottom of OECD countries (position 28 out of 42, **Figure 2** on the next page).[V]

Figure 2: Pharmaceutical spending as a percentage of total healthcare spending, OECD countries, 2019

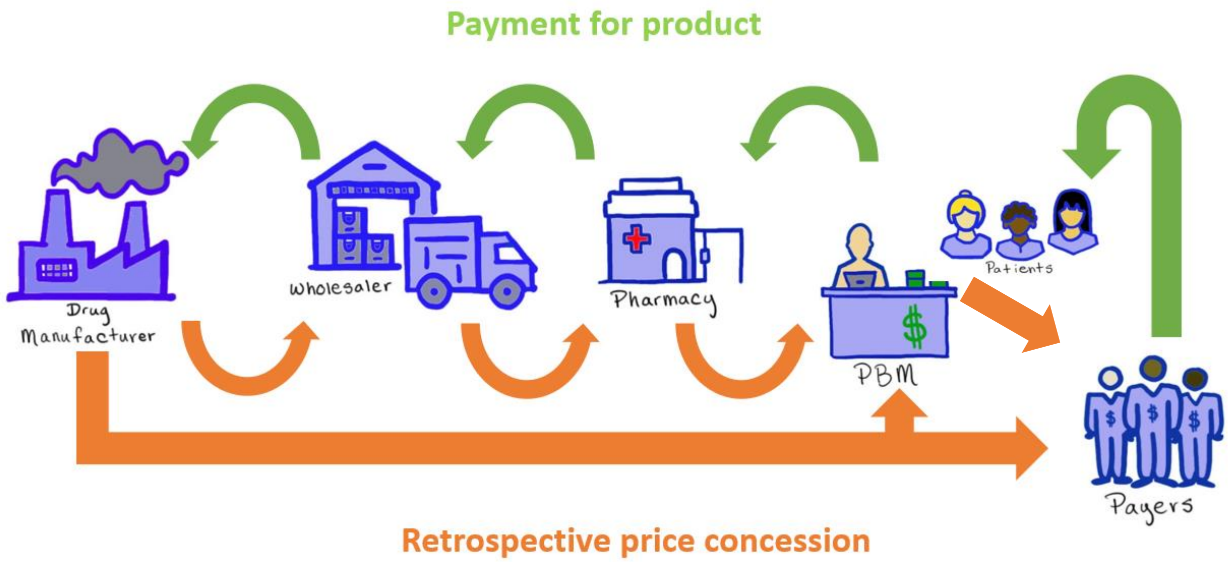


The U.S. position in **Figure 2** may be explained by the fact that the myriad of healthcare services (i.e., doctors' appointments, hospital stays, etc.) in the U.S. have higher costs relative to other countries' comparable healthcare cost.[VI] Alternatively, it could also represent that the U.S. utilizes more healthcare interventions beyond medications to treat medical conditions (and so a lower percentage of healthcare spending in the U.S. is related to drugs relative to these other interventions). On the other hand, it could be that other countries use lower cost options or have a different distribution of healthcare service needs (i.e., less cancer treatments compared to the U.S.). Regardless, it is generally well established that on a drug-to-drug basis, the U.S. spends more on comparable medications compared to other countries.[VII]

While the U.S. undoubtedly spends a significant amount of money on prescription medications, there are a variety of ways to compare prescription drug costs as reflected in the OECD data. Within the U.S., understanding the price of a prescription drug is surprisingly complex. The rationale for the complexity can be attributed to, but not fully explained by, the variety of drug pricing benchmarks available and the variety of ways which people obtain access to prescription drugs, which contributes to segmented, non-standardized prices for U.S. medications.[VIII]

There is no central authority regulating the price of prescription drugs in the U.S.. Rather, the U.S. relies primarily on market forces to control drug prices.[IX] In general, prescription drugs in the U.S. have high list prices set by manufacturers, which are reduced by negotiated retrospective price concessions (i.e., rebates). A variety of parties within the U.S. drug supply chain obtain retrospective price concessions. Manufacturers give price concessions to drug wholesalers, buying groups, pharmacy benefit managers (PBMs), and payers (particularly government programs). Wholesalers provide invoice price concessions to pharmacies as well as retrospective rebates (**Figure 3** on the next page). The secretive and confidential nature of retrospective remuneration from drug manufacturers to PBMs, wholesalers, government programs, or other entities creates a gap when assessing actual net prescription drug prices. High prescription drug prices are routinely cited as a principal healthcare concern by U.S. voters.[X]

Figure 3: High-level overview of retrospective price concessions in U.S. drug supply chain



In comparison to the U.S., many of the other countries of the world do not rely primarily on market dynamics to control prescription drug prices. Rather, the price of pharmaceuticals is set via a variety of pricing regulations. These can include the following, either used individually or in combination[XI]:

- **External Reference Pricing (i.e., International Reference Pricing)** – the process of informing a drug's price in a given country by calculating a benchmark, or reference, price based upon available pricing data from one or more other countries.[XII] The technical aspect of calculating the external reference pricing can vary country-to-country, but the practice is fairly common internationally. For example, the majority of countries in the European Union employed the practice in 2019.[XIII] Furthermore, both Australia and Canada employ drug pricing approaches that contain aspects of external reference pricing.[XIV]
- **Internal Reference Pricing (i.e., Therapeutic Reference Pricing)** – the process of informing a drug's price in a given country by calculating a benchmark price based upon the group of medications used to treat the same, or similar, medical condition(s).[XV] While methodology can differ, the process often involves selecting a product, or products, as a starting point – generally on the basis of them being the lowest or on the lower end of costs. For those products, reimbursement is considered standard with other therapies carrying premium costs, often shifted onto the patients, for product selection that does not conform to the referenced product.[XVI] The use of therapeutic reference pricing may be more common for generic products than all pharmaceutical products based on the methods employed by countries like Australia and Germany.[XVII] Some U.S. insurance groups have attempted to use internal reference pricing to limited success.[XVIII]
- **Therapeutic Valuation** – the process of informing a drug's price in a given country by assigning price markups relative to an existing therapeutic comparator. The concept of therapeutic valuation may overlap with the concepts of value-based pricing.[XIX] In France, for example, therapeutic value assessments consider disease severity, clinical efficacy, effectiveness, safety, and alternative treatments options in determining the government's

reimbursement rate.[XX] In Japan, therapeutic value assessments are then used to assign price markups relative to an existing therapeutic comparator with the most innovative drugs obtaining a markup of up to 120%.[XXI]

- **And Health Technology Assessment (HTA)** – a structured analysis of health technology that is performed for the purpose of providing input to a policy decision.[XXII] The origin of HTA can be traced back to broader technology assessments in the 1960s. The European Network for Health Technology Assessment states the following regarding the approach of conducting HTAs[XXIII]:

  > *Health technology assessment (HTA) is a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value. Despite its policy goals, HTA must always be firmly rooted in research and the scientific method.*

  Ultimately, a HTA attempts to identify whether the technology works, which patients stand to benefit the most, the provided benefit is a meaningful improvement in health status, and whether the therapy is affordable (as measured by both the ability to pay but also the long-term value that the therapy may offer).[XXIV]

There is no central authority regulating the prices of prescription drugs in the U.S.; however, parallels to some of these processes exist in the U.S.. For example, while there is no direct U.S. governmental agency that is equivalent to the European approaches, one of the most recognizable HTA organizations in the U.S. is the Institute for Clinical and Economic Review (ICER), a non-profit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER identifies that because there are limited resources available to invest in medical care, public health, and/or social programs, decisions must be made regarding the prioritization and ultimate payment of healthcare services.[XXV] ICER has identified eight key operating principles that guide their work, identified below[XXVI]:

- Rigorous methodology for literature review and economic evaluation
- Stakeholder inclusiveness in process
- Transparency in process
- Independence in operations
- Impartiality
- Comprehensive review process
- Timeliness of publication of evidence
- Commitment to update reports as new evidence becomes available

As can be seen, there are a variety of ways countries can attempt to determine a drug price. These can range from an overt reliance on competition within the market, as represented by the U.S., to countries with robust government involvement in pricing determination. Germany, for example, uses external reference pricing and added value/innovation in negotiations with brand manufacturers, therapeutic reference pricing for generic medications, and occasionally cost-effectiveness analysis to set a drug's price within their system.[XXVII] Regardless of the system used, there are potential limitations and trade-offs. For example, the U.S. reliance on market forces may fail when the drug supply chain in general promotes higher, not lower, prices.[XXVIII] Many participants of the U.S. drug supply chain, whether manufacturers, wholesalers, pharmacies, or pharmacy benefit managers

(PBMs), stand to profit from higher, not lower prices. As a result, the market forces may not be fully functioning towards lowering "drug costs" in ways that are meaningful to the individuals taking the prescription medication. In contrast, countries employing overt pricing regulations may still struggle to produce a prescription drug market capable of meeting the needs of its citizens. As way of example, the average income in much of the rest of the world is lower than in the U.S. The affordability of drugs may be viewed as less affordable through the lens of cost as a percentage of income (see **Figure 2**) even if the country's drug price is lower than the U.S. Furthermore, access to therapies may be less represented in other countries than the U.S. It is certainly "cheaper" on a direct comparison basis if you compare the expensive cancer therapies available in the U.S., with prices that can exceed $100,000 per treatment, to cancer treatments in other countries that do not even have the same products available in their country. Said differently, cancer costs in comparison can be less on a dollar-per-dollar basis, but the comparison made would not be an apples-to-apples comparison.

Nevertheless, many studies already exist that have demonstrated that the U.S. pays more for prescription medications than other developed countries.[XXIX] Research conducted by RAND in 2021 conceptualized the price disparity in the following way: a brand-name pill carrying a $10 cost in the United States would cost about $3.50 in Germany and Canada, $3.25 in Japan, $3.00 in the United Kingdom, and $2.75 in Mexico.[XXX] The study more specifically showed that the U.S. prices were 256% of the 32 comparison countries based upon the U.S. generic prices being less (84% of comparable products) while the brand prices were 190% of comparable countries, even after adjusting U.S. prices downward to account for rebates and other discounts.[XXXI]

The high cost of prescription drugs continues to be a top health priority for the U.S. public. In September 2020, the Trump Administration issued a final rule and final Food and Drug Administration (FDA) guidance, creating two new pathways for the safe importation of drugs from Canada and other countries.[XXXII] [XXXIII] In an executive order, the Biden Administration in July 2021 directed the FDA to work with states to import prescription drugs from Canada.[XXXIV] Prior to these initiatives, past discussions of drug pricing at the federal level have included the use of an international reference price for Medicare Part B drugs.[XXXV] Despite the legislative interest and prior study of international pricing, we are not aware of any robust, publicly available comparison between individual U.S. prices and international markets.

Scope of work

As of the publication of this report, no U.S. state has received authorization to import drugs from Canada or other international markets.[a] Given the interest in international pricing (see our prior work on international insulin prices[XXXVI]), and the lack of available comparative references between U.S. drug prices and international markets on a drug-by-drug basis, we undertook a process to collect public information on drug prices in Australia and Canada and translate the public price into a U.S. equivalent price. We then developed a database to publicly report our findings to assist other researchers in understanding the prices of these products.

We accessed the public formulary and pricing information available in Australia via the Pharmaceutical Benefit Scheme (PBS) and the Canadian provinces of British Columbia and Ontario. Australia PBS was selected as it is readily accessible to all Australian citizens.[b] [XXXVII] As a result, the

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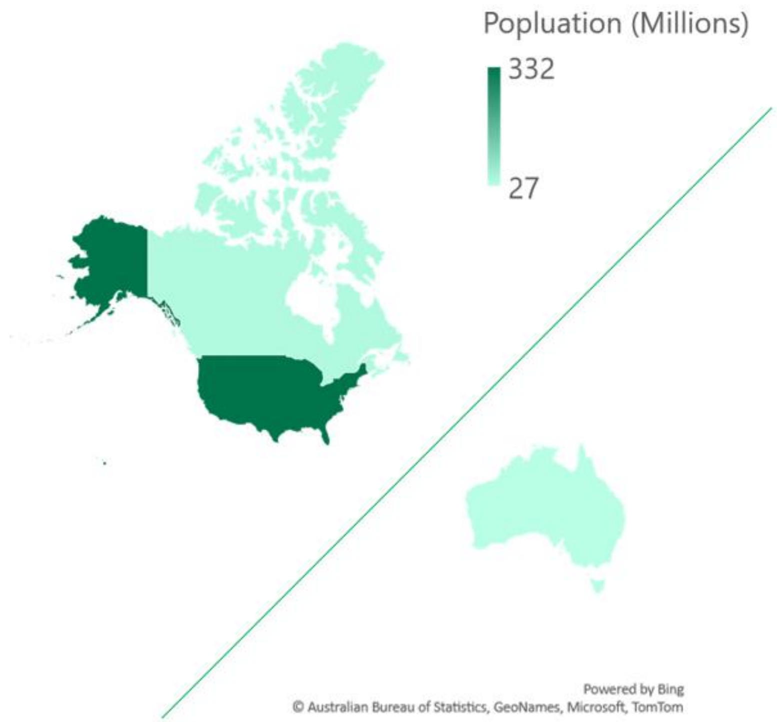
[a] The FDA has exercised its enforcement discretion, on a case-by-case basis, to facilitate the importation of infant baby formula. These actions are not the same as the authorities potentially available. Ben, not sure this last sentence makes sense.

[b] To be eligible for a concessional benefit price on prescription medications, the person must obtain a concession card via the Pensioner Concession Card, the Commonwealth Seniors Health Card, the Health Care Card, or the DVA white, gold or orange card.

Australian program impacts the drug costs of roughly 27 million Australians in 2022.[XXXVIII] For Canada, British Columbia and Ontario were selected, as they are the largest English-speaking provinces, representing approximately 52% of all people in Canada (20 million out of a total Canada population of 38.2 million). The selection of English-speaking provinces was done to ensure language barriers did not contribute to mistakes in identifying drug costs. In comparison to these selected international benchmarks, there are an estimated 332 million people in the U.S. (**Figure 4**).

Figure 4: Comparison of country populations, 2022



While Canada drug prices are often cited as being comparably cheaper than the U.S., unlike Australia, there is not a centralized government program in Canada to provide prescription drug benefits to its citizens. Under the Canada Health Act, medications administered in public hospitals are provided at no cost to patients; however, in the retail setting, many Canadians have some access to insurance coverage for prescription drugs through a combination of public and/or private insurance plans.[XXXIX] More specifically, some Canadian provinces offer income-based universal programs, while others may have public programs for specific populations. The PharmaCare program in British Columbia is available to all British Columbia residents on an income-adjusted basis (the less a family earns, the more help the government provides). In contrast, the Ontario Drug Benefit program is generally available to Ontario residents who turn 65, residents of long-term care facility, those under 24 years of age not covered by a private insurance plan, and residents enrolled in the lower income social support programs of the province. By selecting both British Columbia and Ontario we also get an approximation for the variance in drug benefit design across Canada (i.e., universal vs. restricted).

Ultimately, we are focusing our analysis in this report on the top 200 brand medications dispensed in Medicare in the U.S. We do this in part due to narrative and length restrictions (we cannot reasonably write a report on thousands of drugs). Therefore, we feel comparisons to the selected public programs in Canada are appropriate. We will also be benchmarking prices in relation to National Average Drug Acquisition (NADAC) prices in the U.S. and the Federal Supply Schedule to get a sense of individual price points in a more complete sense of the U.S. drug supply chain.

Methodology

We accessed the public pricing files (text, XML) from the government websites of Australia and the Canadian provinces of British Columbia and Ontario. Within each data file we identified the field of drug name sufficient to identify the label name, the active pharmaceutical ingredient(s), the dosage form, and the strength of the medication. In some files, this was one field, and in others, this was multiple fields. We then identified and correlated these fields into U.S. equivalent values based upon matching, via text algorithms, the degree to which the listed label name correlated to a U.S. labeled name, a strength matched a strength, and so on. We assigned a score based upon matches such that other researchers could access the data and perform comparative analysis without relying upon our methods for when a match is sufficient to be appropriately correlated. Once products were identified, we made comparisons between prices based on unit prices converted to USD.

We ultimately compared prices based on drugs having a matching co-efficient of greater than 70. For greater details on our methods and approach to scoring, see our **Detailed Methodology** section later.

On an ongoing, quarterly basis, 3 Axis Advisors, LLC is making available on its website at 3AxisAdvisors.com a file with USD pricing for the international products with equivalent NDCs based on our methods for other researchers to support comparator price studies between the U.S. and these international markets.

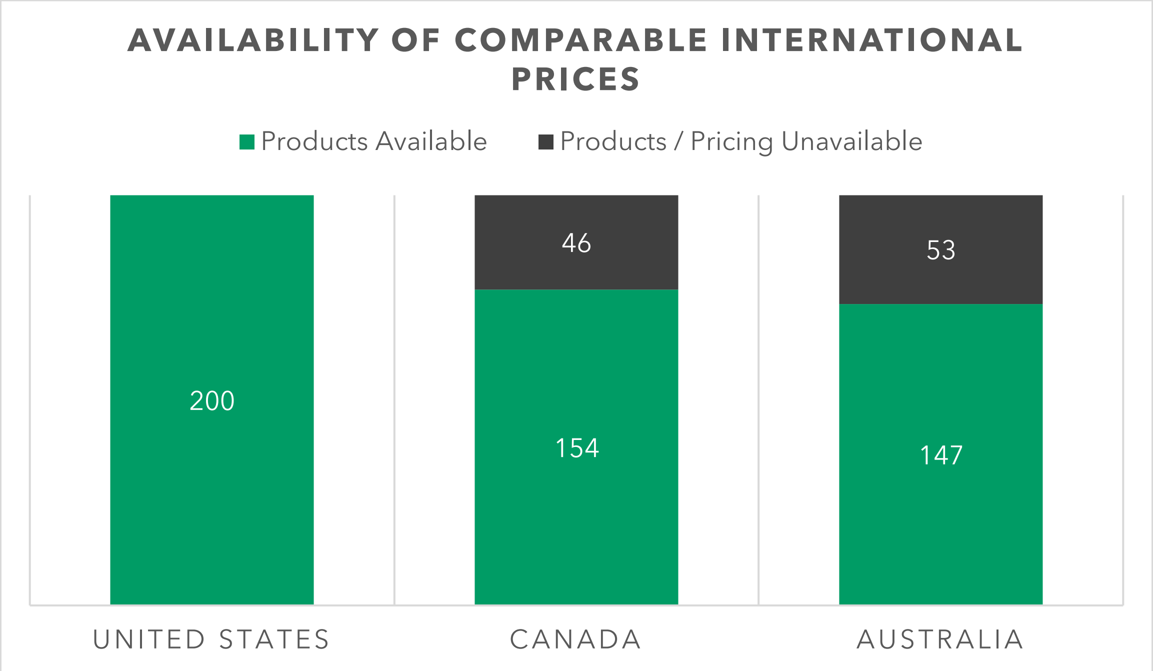
Results

All of our pricing analyses are predicated off the Top 200 medications by spend in Medicare in 2020. Please note that more price comparisons exist within the data file but are not included in our analyses (see **Tool Availability**).

Product availability

The first analysis we conducted was to determine how many products within the Top 200 medications in Medicare had comparative prices within our Canada and Australia datasets. We identify available Canadian price comparisons in 154 out of 200 instances (77%) and comparative Australian price comparisons in 147 out of 200 instances (74%) (**Figure 5**).

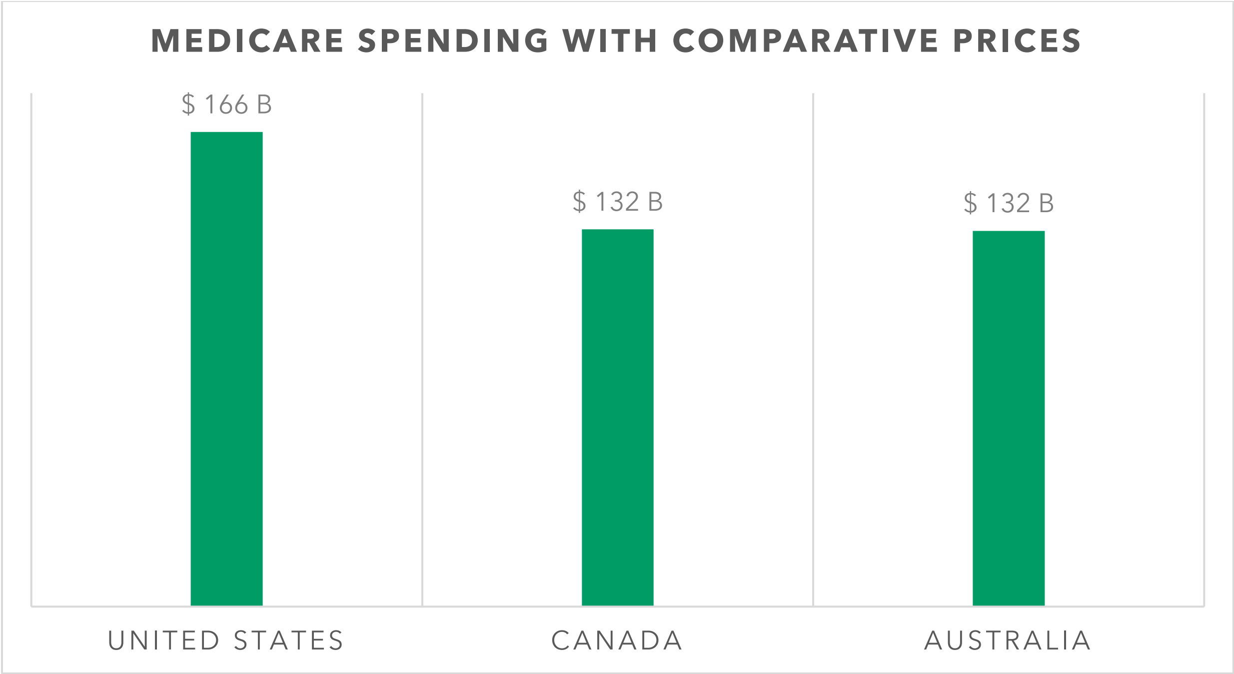
Figure 5: Availability of international price comparisons

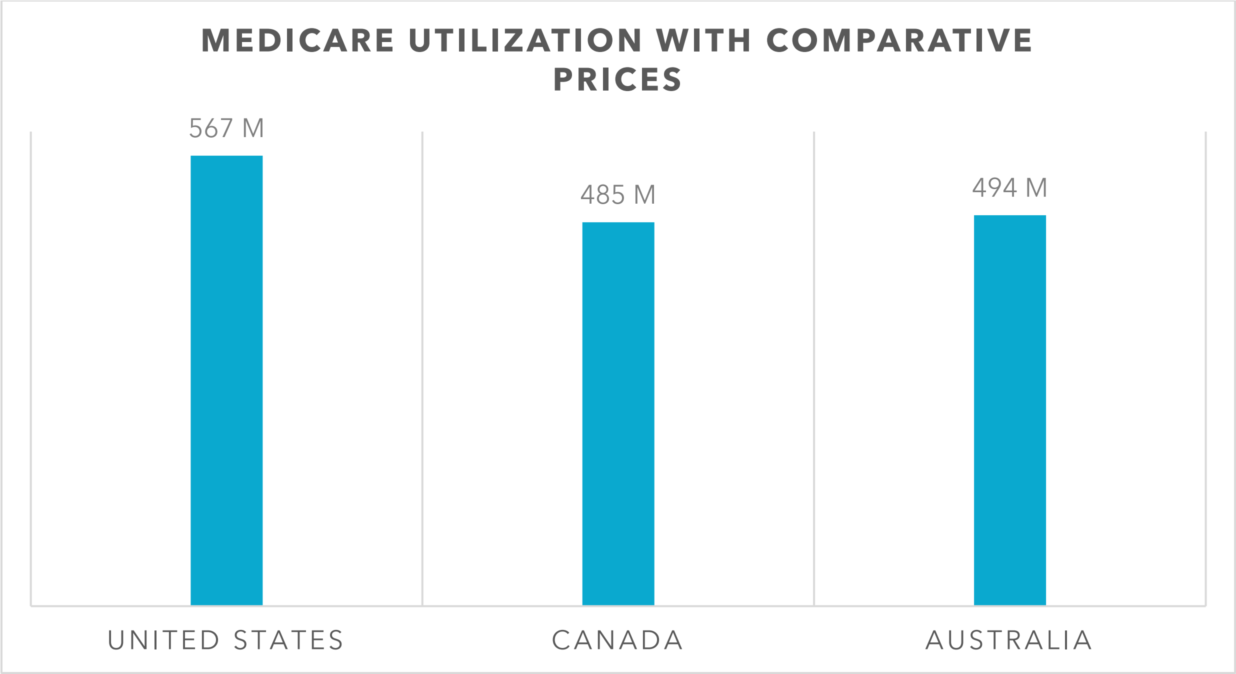


Note that some of the unavailable products are listed within the drug files of these countries; however, government prices for those products are not listed (and so comparisons cannot be made). For example, Victoza (liraglutide) is a product approved for use in Canada, but for which a Canadian price from one of the provinces could not be found (as a result, it appears as an unavailable comparative product for our purposes though Canadian prices certainly exist). This is due to the formulary restrictions of the provincial programs. Not all products are going to be available and so Canadian residents accept some product restrictions on access in order to achieve their savings. This is no different from formulary restrictions in the U.S., except perhaps that the scale of the formularies is more "normalized". What we mean is that everyone in British Columbia has the same access to the same set of drugs whereas in the U.S. where one resident in Ohio may have a plan that prefers Victoza whereas another resident has a plan that does not.

The products available for price comparisons represent approximately 79% of drug spending and 85% of all prescriptions dispensed within the Medicare Top 200 drug list (**Figure 6** on the next page).

Figure 6: Comparison of Medicare Top 200 expenditures and utilization with comparative international prices





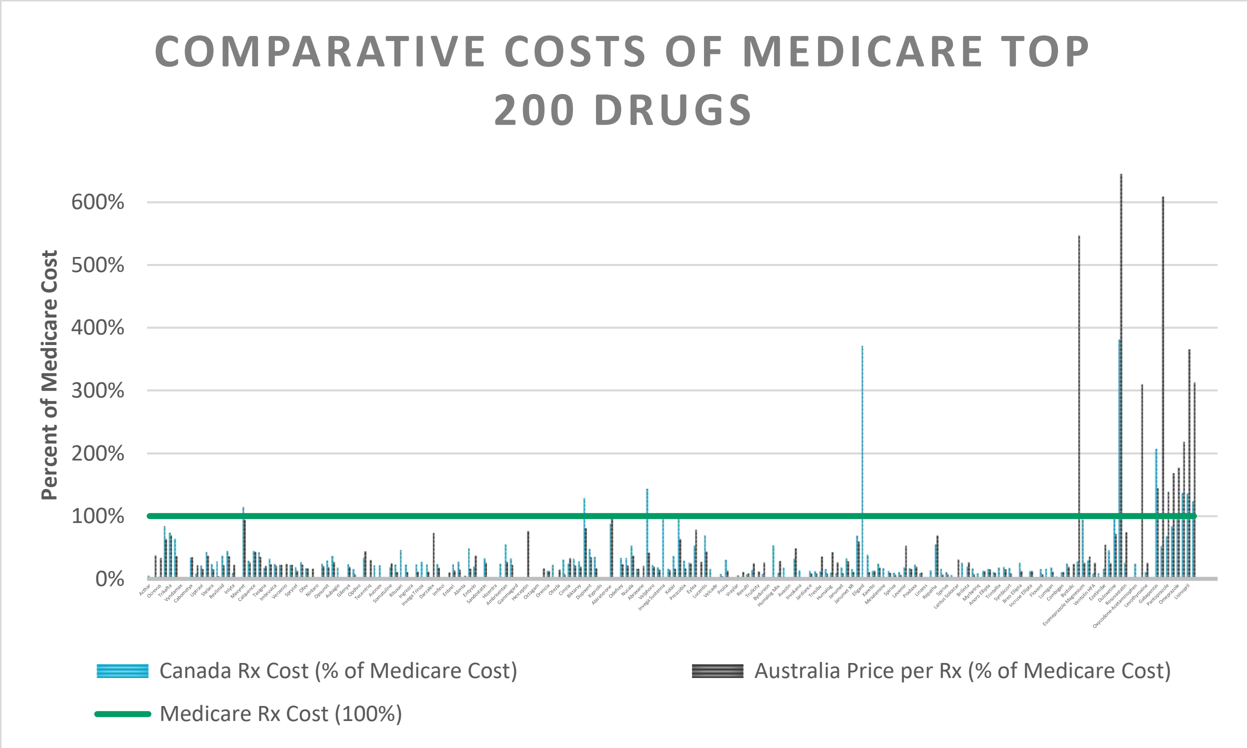
Price differences

Per prescription, per product basis

Having gathered pricing for the majority of the Medicare Top 200 drugs, we proceeded to compare the list prices between the United States and these international markets. Initial price comparisons were made on a per prescription, per product basis. The U.S. price was arrived at based on the average gross cost per prescription identified in the Medicare program in 2020. The international prices were arrived at using the average number of units per prescription according to the Medicare program and multiplying that value by the unit price in Canada or Australia (converted to USD equivalent).

All 200 products were compared in **Figure 7** (below). A comparison was made on the basis of the international price as a percentage of Medicare gross costs. For example, if the Medicare program spent $100, but Canada spent $70, then the product would appear at 70% in **Figure 7**. This was done, as the range of observed differences in Medicare gross costs to international prices for the Top 200 drugs was large; almost 9,000x (minimum $7.09 per claim to maximum $63,090.61 per claim). Displaying the results proportionally limits the range to 0 to 6.5 (as opposed to $5 to $64,000) to make graphing the results easier to interpret. Note, products without comparative pricing to the U.S. were left blank.

Figure 7: Comparative cost of Medicare Top 200 drugs



While individual drug results are impossible to observe in **Figure 7**, we should appreciate that there is a great deal of disparity in prices for drugs in the United States to these international markets. The majority of the time, list prices for products are cheaper internationally. Specifically, 145 out of 154 (94%) products with Canadian prices available, and 135 out of 147 products (92%) with Australian prices available have lower prices in their respective international markets then the U.S. Take for example Eliquis, the drug associated with the highest aggregate expenditures in Medicare in 2020. This product has an average gross cost per prescription of approximately $700 in Medicare, and yet is approximately $100 per prescription (14% of the cost) in either Australia or Canada. If Medicare were to recognize savings on this one medication to the degree recognized in these countries (rebates and retrospective price concessions that Medicare may currently be getting notwithstanding), the program would save approximately $8.4 billion on this single therapy alone.

However, that does mean there are exceptions (6 to 8% of Top 200 medicines) where the U.S. is paying less. The exceptions – that is products **with prices higher internationally** than the United States – are overwhelmingly multisource generic products (as opposed to brand name products). For example, consider atorvastatin. Atorvastatin is the most utilized therapy in Medicare, and despite being a relatively low-cost generic option, the volume of atorvastatin used in Medicare is sufficient for it to show up in the Top 200 drugs in regard to Medicare expenditures. In 2020, the medication had an average gross cost of $14.55 per prescription (average quantity per prescription of 70 pills). That same prescription (70 pills) would carry a $23.65 cost in Australia (163% greater than the U.S. Medicare price) and up to a $138.74 cost at the highest level for some of the Canadian provinces (954% greater than the U.S. Medicare price). There were 58.3 million prescriptions for atorvastatin in Medicare in 2020. Even slight changes in cost to these therapies can be associated with significant added costs to the programs (given the volume of prescriptions at issue). As way of perspective, if Medicare's cost for atorvastatin were to increase to the high end of Canada's costs, the program would add approximately $7.2 billion (nearly equivalent added costs to the earlier identified savings with Eliquis that identified above).

Interestingly, challenges related to the affordability of generic products in the Medicare program is a topic that has previously been researched.[XL] The appearance of cheaper Medicare generic prices relative to international prices is therefore slightly unexpected. Said differently, how is Medicare overpaying for these generic products that on an international basis (at least within Canada and Australia) carry higher costs than existing Medicare prices? This may be an area of future research, given:

(1) some of the recent challenges related to international sourcing of drugs in countries employing pricing caps on therapies; and[XLI]
(2) the fact that the majority of prescription drug utilization (80%+) currently is in generic drugs within programs like Medicare. [XLII]

To the extent that drug policy looks towards international models for payment reform, particularly on expensive brand name medications, we should appreciate that not all products are cheaper internationally – including some of the most utilized agents.

Table 1 (on the next page) describes the average, median, minimum, and maximum discounts of either the Canada or Australia programs to that of Medicare. The cheapest drugs were a fraction of their cost in the United States (2%), whereas there were some that were more expensive than U.S. prices (maximum was six-times the U.S.). The averages and median discounts to the U.S. were comparable.

Table 1: Comparison of discounts to U.S. prices produced with international prices

Description	Canada	Australia
Average Discount (to U.S. Medicare Cost)	23% (77% cheaper than U.S.)	21.4% (78.6% cheaper than U.S.)
Median Discount (to U.S. Medicare Cost)	38%	48.1%
Minimum Discount (to U.S. Medicare Cost)	3.8x more expensive than U.S.	6.5x more expensive than U.S.
Maximum Discount (to U.S. Medicare Cost)	2% (98% cheaper than U.S.)	1.4% (98.6% cheaper than U.S.)
Number of Products Whose Price is Cheaper	145	135
Number of Products Whose Price is More Expensive	9	12

We can see from **Table 1** that based on average gross prices, the U.S. is consistently more expensive to fairly significant degrees (20%+ on average) on the vast majority of Medicare's Top 200 most expensive therapies. However, we can also observe that the variance between Canada and Australia is not as extreme as that of the U.S. Both countries are producing similar average and median discounts to the U.S. despite materially different approaches to government price controls (Australia centralizing price negotiations across the country within the Pharmaceutical Benefits Scheme whereas Canada's provinces are responsible for managing their own formularies and prices).

U.S. House Oversight Committee investigations on drug prices

Beginning in January 2019 and concluding in December 2021, the U.S. House Oversight and Reform Committee investigated ten U.S. drug companies and their pricing practices related to twelve of the most expensive drugs under the Medicare program. Each of those reports looked at the business practices of the companies and the pricing strategies employed for their respective medications. These investigations focused primarily on the list price and net price (price after rebate) in the U.S. over time with analyses on how those practices impacted revenues overtime. However, several of their reports compared the U.S. price of the company's medication(s) to the international prices for the same product (note that Canada was often included in these analyses, but Australia never was). **Table 2** (one the next page) details the available price comparisons from the U.S. House Oversight and Reform Committee.

Table 2: Identified international Canadian price from the U.S. House Oversight and Reform Committee

Drug	Year	U.S. House Committee on Oversight and Reform			3 Axis Advisors
		U.S. Price (WAC)	Canada Price	Canada to U.S. Price Ratio	Identified Canada to U.S. Price Ratio
Gleevec[c] (month supply)	2016	Not stated	Not stated	39%	
Enbrel (month supply)	2017	$4,442	$1,299	29%	23% to 27% (depending upon vial vs. syringe)
Sensipar (30 tablets)	2020	$806	$447.99	56%	
Copaxone 20mg/mL (net price per day)[d]	2015	$97	$33	34%	
Humira[e] (40-milligram Syringe)	2015	$1,727	$661	38%	23%

Some of the products that the U.S. House investigated are no longer brand-name only products (meaning they have substitutable, often generic, alternatives). Brand-name medication pricing availability within Canada and Australia is more challenging when a generic is available. The programs within those countries do not appear to prefer brand-over-generic options.[f] Our tool approximates some of the product prices identified in U.S. House Committee reports. Though temporally different (current price dynamics relative to those from five to seven years ago), our tool identifies similar pricing for both Enbrel and Humira. The differences between our tool and the U.S. House Committee reports are likely due to the fact that our analysis is focusing on the price of medication in Medicare specifically. The U.S. House Committee investigations were often presenting data on the U.S. market at large. The other drugs do not have available Canadian price comparisons (though Australia ones exist, there is no comparator to Australia prices within the U.S. House investigations).

Medicare Savings with International Prices

Utilizing the average cost per prescription derived above, we then compared the aggregate differences in Medicare spending for these Top 200 products based on the average prescription cost of each multiplied by the total number of prescriptions actually dispensed for the products in 2020. For products without a comparative price, we left Medicare spending unchanged (i.e., carried the

[c] Staff Report - Committee on Oversight and Reform U.S. House of Representatives, October 2020; Available at: https://oversightdemocrats.house.gov/sites/democrats.oversight.house.gov/files/Novartis%20Staff%20Report%2010-1-2020.pdf#page=40 ; WAC estimate derived by 3 Axis Advisors, LLC

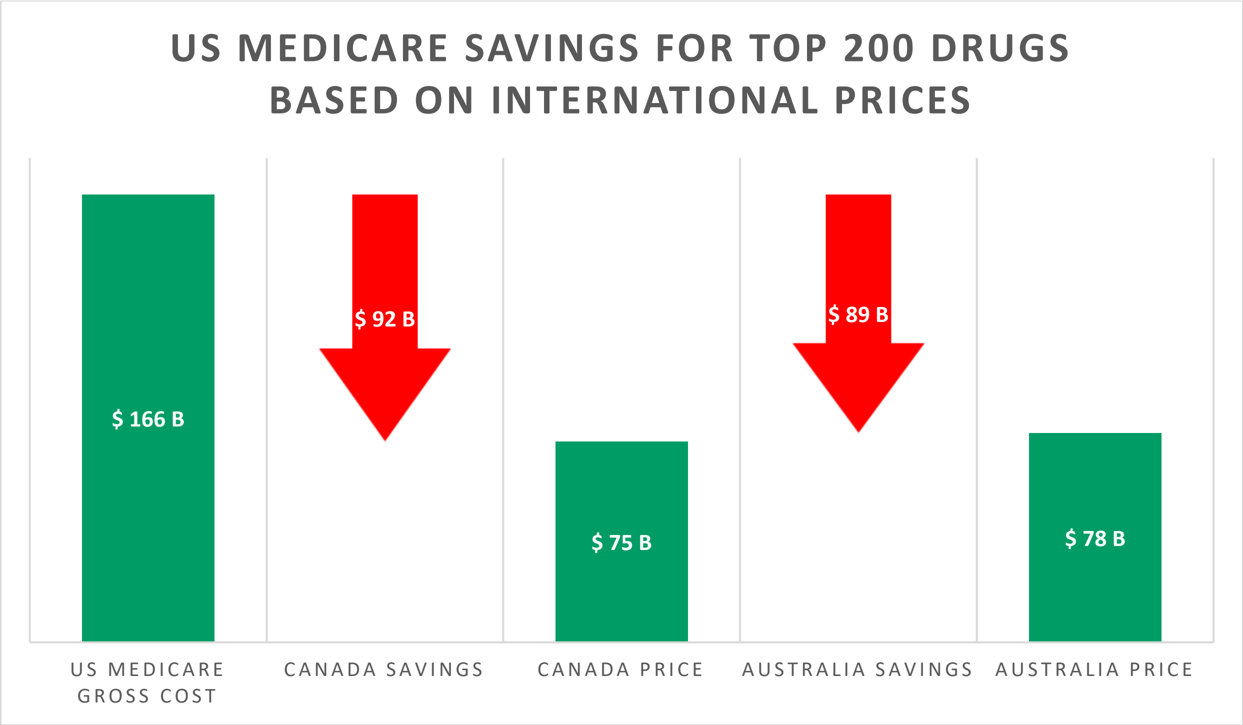
[d] Staff Report - Committee on Oversight and Reform U.S. House of Representatives, September 2020; Available at: https://oversightdemocrats.house.gov/sites/democrats.oversight.house.gov/files/Teva%20Staff%20Report%2009-30-2020.pdf

[e] Staff Report - Committee on Oversight and Reform U.S. House of Representatives, May 2021; Available at: https://oversightdemocrats.house.gov/sites/democrats.oversight.house.gov/files/COR-AbbVie-Selected-Investigation-Documents.pdf#page=133; WAC estimate derived by 3 Axis Advisors, LLC

[f] In Australia, brand prices can approximate the generic when a substitutable option enters the market. This is the opposite effect to the U.S., where brand products often continue to increase in list price even after a generic is launched.

price through). **Figure 8** identifies the aggregate savings possible with the use of these international prices.

Figure 8: US Medicare savings for Top 200 drugs by spend based on international prices



As can be seen in **Figure 8**, the use of an international reference price to the Top 200 drugs in Medicare result in approximately 53% to 55% savings relative to current Medicare spending. Both Canada and Australia produce similar savings even though the number of comparable products is different (as are the individual prices within their programs). It should be noted that the savings produced with these international price comparisons are greater than the known price concessions from manufacturers at the time. In 2020, according to data from the Medicare Payment Advisory Commission (MedPAC), the value of drug manufacturer rebates (and other manufacturer price concessions) was $43.9 billion.[XLIII] This is roughly half the savings identified with applying either Canadian or Australian prices to the Medicare program.

The savings we identify in this report are in line with other estimated savings from international reference pricing for prescription drugs. In a 2021 research letter, Drs. Mulcahy, Schwam, and Rao identified 52.3% savings available to 2020 Medicare spending with international prices.[g] The CBO estimated $456 billion in savings over 10 years with international reference pricing.[XLIV] However, unlike prior aggregate analysis, our estimate is the first to our knowledge to be accompanied with a tool to individually research specific drug price comparisons to the international market.

We hope that the added transparency of international prices will enable future research efforts into drug pricing policy in the U.S. and abroad.

[g] https://jamanetwork.com/journals/jama/fullarticle/2784289

Adjusting price comparison based upon median income

While the prior analysis gives ample takeaways, we wanted to try to adjust savings based upon a measure of affordability within each country. While it appears to be confirmed, from this study and studies prior, that the United States has higher drug costs relative to the rest of the world, we also are one of the wealthiest. It seems unreasonable to compare prices country-to-country without recognizing that the economic differences between the countries are of consequence. As we explored previously in our 2021 study of insulin prices, some of the "cheapest" insulin prices across the globe can actually be the most unaffordable to citizens of that country.[XLV] To help put this into context, while it may be true that eggs at the grocery store the same price for each customer (coupons, store discounts not withstanding), if one customer's income is 10-times than a different customer, then **the affordability** of those eggs between the two purchasers is magnitudes of difference. Said differently, in such a scenario, more of a poor customer's income will be consumed buying eggs than a wealthier customer given the differences in their incomes. It is this concept that our next set of analyses seeks to overcome.

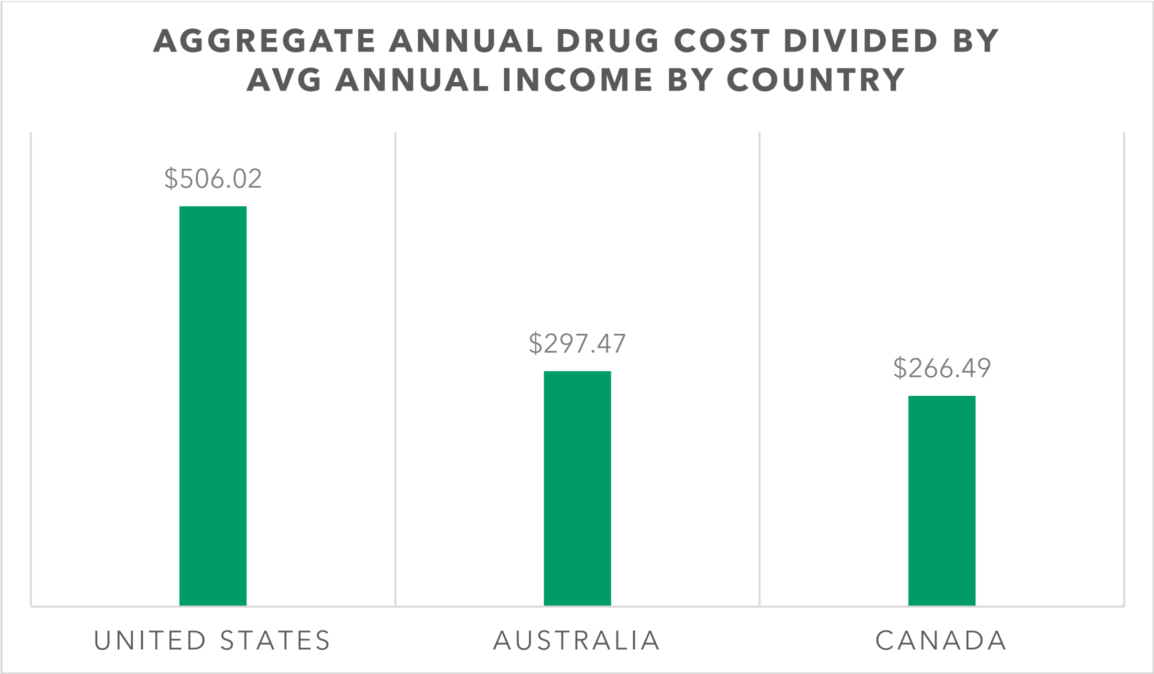
To that end, we performed an analysis to adjust pricing as displayed in **Figure 8** by average and median income as well as GDP per capita (PPP) in each country. **Table 3** details these values for each country based upon our sources[XLVI]:

Table 3: Average, median and GDP per capita (PPP) for each country

Country	Average Income ($USD)	Median Income ($USD)	GDP per Capita (PPP) [$USD]
Australia	$21,329	$17,076	$53,381
Canada	$22,042	$18,652	$51,668
United States	$25,332	$19,306	$65,297

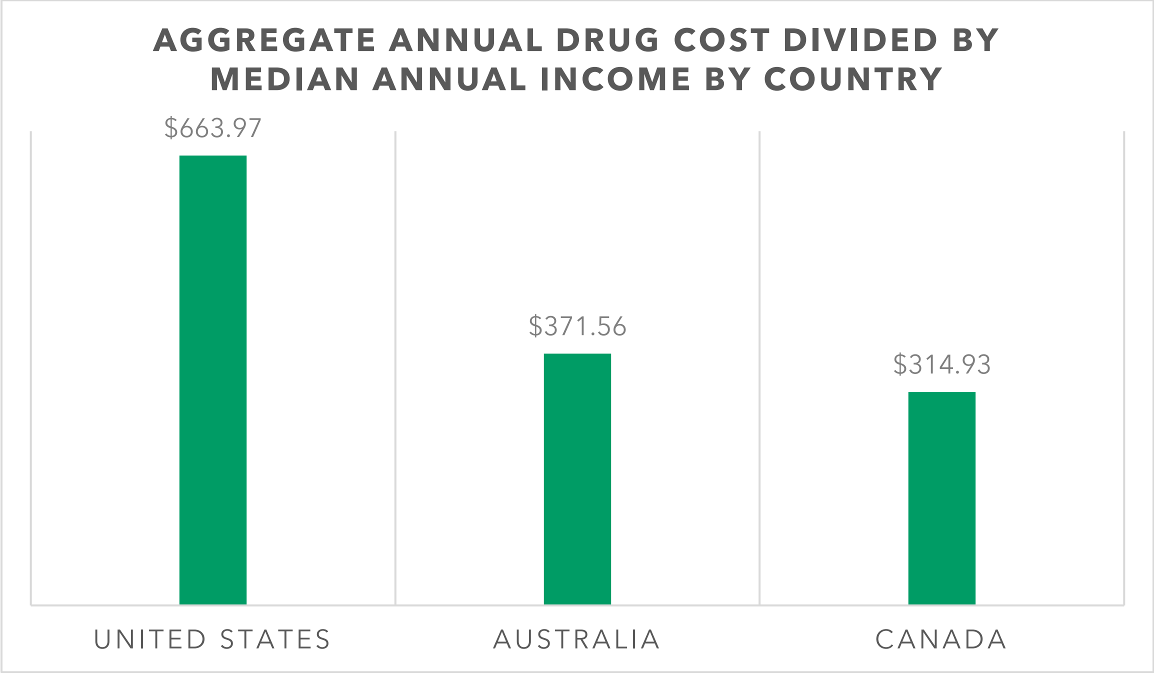
Our first attempt to measure affordability is presented as a comparison of the aggregate annualized payment rate for each of Medicare's Top 200 drugs relative to the average annual income of each country. To do this, each per prescription price in each country was multiplied by 12 (to approximate an annual cost of the therapy) and then divided by the average income of the country. The value for each annual medication cost after being divided by the median income was then summed across all prescriptions. In this way, the data presented in **Figure 9** (on the next page) represents the cost for a basket of goods of the Top 200 products in Medicare.

Figure 9: Medicare Cost Comparisons based upon Avg Annual Income of Country



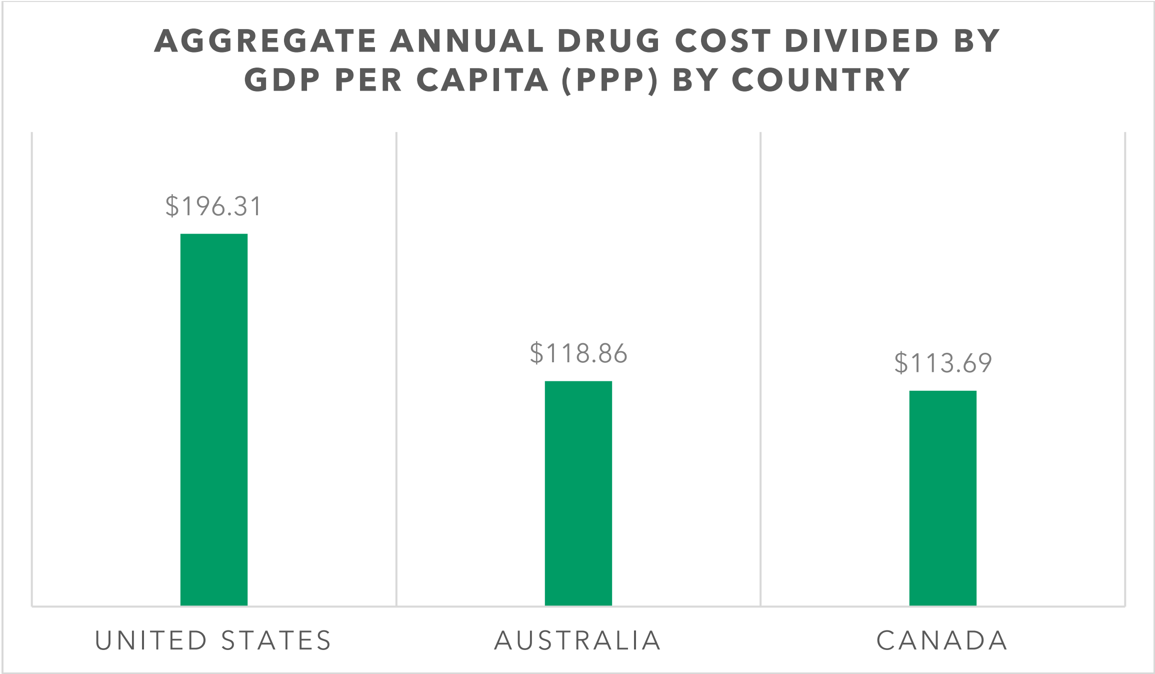
In **Figure 10**, we do the same math as before, except we substitute median income for average income in our calculations.

Figure 10: Medicare Cost Comparisons based upon Median Annual Income of Country



In **Figure 11** (on the next page), we do the same math, but again we're substituting GDP per capita (PPP) for the income measurement.

Figure 11: Medicare Cost Comparisons based upon GDP per Capita of Country



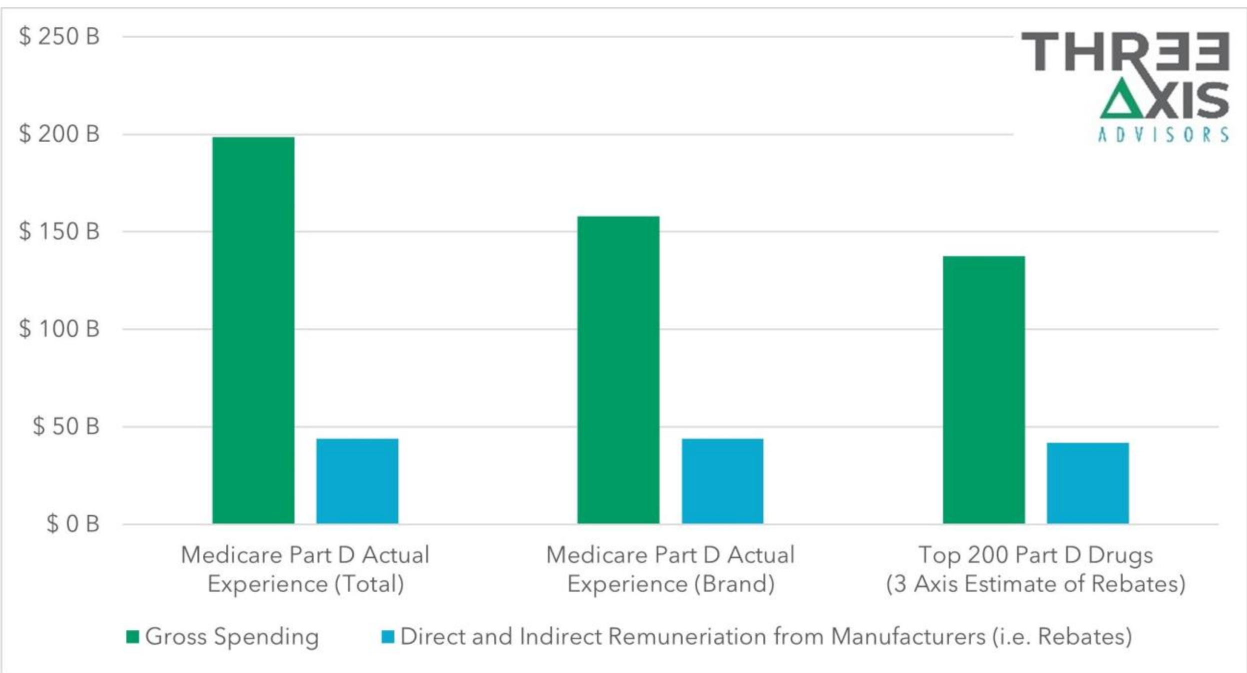
What we can see from **Figures 9, 10 & 11** is that the savings are playing out regardless of whether we try to account for the differences in economic status between the countries. This is due, in no small part, to the fact that the economic statuses of these countries according to our measures are not that different. The differences in average, median and GDP per capita (PPP) are within approximately +/- 15% to 20% at the extreme ends. As a result, international prices still appear over 50% more affordable even when we attempt to account for income.

Discussion

Our report adds to the existing body of research that documents that U.S. drug prices are higher than international prices for the same medication. While we do recognize that the United States has retrospective price concessions not being accounted for within our measures, MedPAC estimates manufacturer price concessions to equate to 22% of aggregate drug spend for the program. Other programs are able to obtain even greater price concessions. According to the Medicaid and CHIP Payment and Access Commission (MACPAC), the Medicaid program receives 54% aggregate rebates on its drug expenditures. According to our aggregate analysis of international prices, savings for drugs in Australia and Canada are more closely related to net Medicaid expenditures than net Medicare expenditures, at least based on the aggregate discounts being produced.

On an individual product basis, we see there are products that are significantly cheaper internationally as well as significantly more expensive. Cheaper products are largely brands, which have hidden retrospective price concessions that we cannot take into account due to our study's granular focus. For example, Eliquis, the drug associated with the highest aggregate expenditures in Medicare in 2020. This product has an average gross cost per prescription of approximately $669 in Medicare, and yet is approximately $100 per prescription (a seventh of the U.S. price) in either Australia or Canada. Note that the international prices for this medication are in line with our prior work from February 2023 studying prices within the federal supply schedule (FSS).[XLVII] (**Figure 12**)

Figure 12: Federal Supply Schedule (FSS) Savings to Medicare, 3 Axis Advisors Study



At the time of the issuance of this report, the FSS price for Eliquis is approximately $100, suggesting that at least some U.S. payers can access net prices akin to international markets. On the other hand, recall from our earlier discussion that atorvastatin is the most utilized therapy in Medicare, and despite being a relatively low-cost generic option, the volume of atorvastatin used in Medicare is sufficient for it to show up in the Top 200 drugs in regard to Medicare expenditures. In 2020, the medication had an average cost of $14.55 per prescription (average quantity per prescription of 70 pills). That same prescription (70 pills) would carry a $23.65 cost in Australia (163% greater than the U.S. Medicare price) and up to a $138.74 cost at the highest level for some Canadian provinces (954% greater than the U.S. Medicare price). The primary point being that while much research has been done to demonstrate that U.S. prices are higher then international prices in the aggregate, we are not aware of any research that highlights that the aggregate experience may mask higher international prices for select medications (and hence our desire to provide a tool to perform individual product price comparisons).

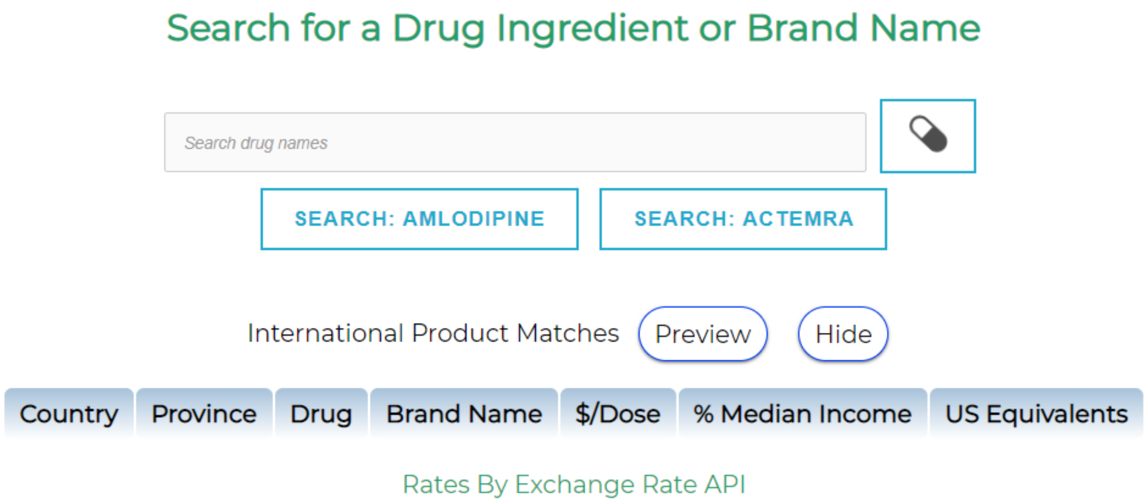
Note that one of the primary differences between international price comparisons to the United States is the uniformity around price that exists within these international programs in comparison to the U.S. While we are using an aggregate Medicare pricing figures to discuss prices, the truth is that there are thousands of Medicare plans, each with potentially different prices for Eliquis. That does not exist within the Australian PBS system or the individual provincial programs in Canada. The normalization of price allows these programs to focus on other drivers of prescription drug spending beyond getting the drug's price accurate. For example, when drug costs are known, quantified, and transparent, the other drivers of healthcare spending can be targeted to savings. For example, limiting dispensing fees of pharmacy providers. The Canadian province of Ontario limits dispensing fees, which range from $9.93 CAD to $13.25 CAD (based on the presence of other pharmacies in the area),[h] to two per 28 days, five dispensing fees per 365-day period for chronic medications.[XLVIII] This enables them to produce significant savings. Let us revisit the atorvastatin example. We identified that the average Medicare payment for this medication is approximately $15. We can break this down, based upon National Average Drug Acquisition Cost (NADAC), to assume that the ingredient cost is approximately $3 (based upon the average atorvastatin NADAC for 70 pills) and the dispensing fee value is approximately $12 for this drug. Annualizing this current cost to Medicare, we get $180 in annual costs ($15 per month * 12 months). However, if we were instead to limit dispensing fees to no more than five per year, the new total cost of therapy would be $96 ($3 ingredient cost per month * 12 months plus $12 dispensing fee * five events). This is a theoretical 53% savings on the most utilized therapy in Medicare.

This example is intended to only be demonstrative of the matter at hand. At 70 pills per prescription, some 90-day supply prescriptions of atorvastatin are clearly being filled within Medicare today. However, mail order prescriptions represent just 10% of Medicare prescription volume.[XLIX] There have been historical challenges with mail order or extended day supply adaptation in the U.S. drug supply chain. We assume this has to do with poor incentives in the current design. When drug pricing is disparate, opaque and non-transparent, providers may see value in maximizing their spins of the proverbial roulette wheel of reimbursement. Like the gambler who is too long at the table, providers may value continued participation in an effort to make up for 'near-misses' in regards to reimbursement (i.e., reimbursement that was close, but just below their expectations). Such incentives discourage consolidated filling, and promote shorter day supply to get more chances at higher reimbursements. Ultimately, providers lack incentives within the current system to minimize operational expenses through consolidated fills.

Until normalization of prices occurs more broadly across U.S. programs, it seems highly likely that disparities in price will continue to result in drug pricing "haves" and "have nots" from a payer's perspective.

[h] Approximately $7.50 USD to $10.41 USD

Tool Availability



Detailed Methodology

The purpose of this section is to discuss the technical methodology used to gather, analyze, and compare international drug pricing data to U.S. prices. This has been accomplished through the use of an automated process developed by 3 Axis Advisors that scans publicly available web-based files. Before we dive into the details, here is a brief summary of the process:

- Find international drug pricing data
- Develop methods to acquire and understand international data in an automated fashion
- Match drug ingredient information to U.S. registered drugs
- Match discovered drugs with pricing information
- Analyze results

The tools used to develop this process were a combination of Microsoft products (Excel, VS Code) and NodeJS, an open source software development library.

Data Sources

Canadian Data Locations (actual data locations differ from main website):

- British Columbia: https://www.health.gov.bc.ca/pharmacare/outgoing/pddf.zip
- Ontario: https://www.health.gov.on.ca/en/pro/programs/drugs/formulary43/summary_pricechanges_edition43_20220513.xlsx
- Fredericton: https://www2.gnb.ca/content/dam/gnb/Departments/h-s/misc/MLPList.xlsx
- Central Canada: https://www.canada.ca/en/health-canada/

National Institutes of Health (NIH) Website:

https://druginfo.nlm.nih.gov/drugportal/jsp/drugportal/DrugNameGenericStems.jsp

Executive Office of Health and Human Services (EoHHS) Website:

https://eohhs.ri.gov/

https://eohhs.ri.gov/sites/g/files/xkgbur226/files/Portals/0/Uploads/Documents/Pharmacy/dose_form_ref_guide.pdf

Medi-Span Database:

https://go.wolterskluwer.com/why-medispan-b-c.html

VA Formulary Prices:

https://www.va.gov/opal/nac/fss/pharmPrices.asp

Finding International Data

Numerous countries and provinces around the world publish a spectrum of pharmaceutical data ranging from what was actually used by citizens, to the amount a central insurance scheme is willing to pay per drug. For instance, several Canadian provinces publish data sets containing their approved formulary, the prices they will reimburse a provider/patient, and/or the maximum price a drug will be covered at. The more populous provinces have the most readily available data:

- British Columbia: https://www.health.gov.bc.ca
- Ontario: https://www.health.gov.on.ca
- Fredericton: https://www2.gnb.ca/

Additionally, the central Canadian government lists data sets of drug information:

- Canada: https://www.canada.ca/en/health-canada/

Developing Methods for Acquiring International Data

Finding Data

Once actual data files were located, the details of where and how each data file is stored were cultivated into a flexible web scanner that can run automatically at pre-defined schedules. Public drug data files are largely meant to be accessed one at a time, by individuals, and updated regularly. As such, they tend to be named and stored according to calendar data.

For example, you can access data files at the following locations:

- https://www.health.gov.bc.ca/pharmacare/outgoing/pddf.zip
- https://www.health.gov.on.ca/en/pro/programs/drugs/formulary43/summary_pricechanges_edition43_20220422.xlsx
- https://www.health.gov.on.ca/en/pro/programs/drugs/formulary43/summary_pricechanges_edition43_20220513.xlsx
- https://www2.gnb.ca/content/dam/gnb/Departments/h-s/misc/MLPList.xls
- https://www.pbs.gov.au/downloads/2021/01/2021-01-01-v3extracts.zip
- https://www.pbs.gov.au/downloads/2021/03/2021-03-01-v3extracts.zip

This is easy enough to understand and to utilize manually, however, downloading the files this way takes considerable time. In order to automate the process, a pattern recognition process was utilized to predict, test, and record various mutating file paths. Thus, to the software developed:

> .../summary_pricechanges_edition43_20220513.xlsx
> becomes:
> .../summary_pricechanges_edition43_<<yyyymmdd>>.xlsx

In this manner, all possible, reasonable combinations of year, month, and day are accounted for and tested. The results of the test are stored in success and fail files respectively. If the test results in a success, a quick glance at the program's file system determines if the file needs to be downloaded based on file ages and other parameters. If the test results in a failure, the file path is saved in order to make sure it can be tested again in the future, so as to accommodate for files being retroactively published.

The patterns of file name and location can become quite complicated, but the flexibility of the system ensured a smooth data gathering process.

Translating Files

Public drug data is often formatted in such a way to provide an individual user with an easily understandable file. This unfortunately means formatting Excel files, zip files, and variable column names must all be considered. While data may not truly have to be translated from one language into another, it does have to be managed in order to be useful.

An example file for each country/province was opened and studied to determine what was required to get flexible, stable data. Excel files must be transformed into comma-delimited files. Zip files must be opened to locate a specific set of files inside. Text files must be tested to determine how data columns are delineated within. Lastly, column names must be identified and normalized.

This process yields a set of instructions for how to find a file, where and when to store it, what– if anything – must be done to read it, and a dictionary of column names so that the data may be transported to a single database for ease of analysis. An example of this set of instructions looks like the following:

```
{
  "table_name": "Canada_Ontario_Drug_Prices"
  ,"host":"https://www.health.gov.on.ca/en/pro/programs/drugs/formulary43/"
  , "url_like":"summary_pricechanges_edition43_<<yyyymmdd>>.xlsx"
  , "min_year":2022
  , "db":"international_pricing"
  , "post_process":"./lib/internationalHelper.js"
  , "column_map":{
    "DBP":"international_price",
    "Product Name":"product_name",
    "Generic Name":"drug_definition",
    "Dosage Form":"unit_of_measure",
    "Strength":"strength",
    "date_updated":"price_effective_date",
    "DIN_PIN":"international_drug_id"
  },
  "xlsx_header_row":2
},
```

That small bit of code tells the program where to find files, what they may look like, how to process the file, where its data must be stored, and how to convert it to a standardized international database. This process was undertaken for each international data source, country, and province. Now, when the data gathering program runs, it can detect, download, and convert any file it has the correct parameters for.

As of the publishing of this paper, this data gathering process is undertaken automatically twice per month on the 7th and the 18th. This process may be triggered manually at any time as well.

Example of the International Database:

source	drug_name	drug_definition	international_price
Canada_Ontario_Drug_Prices	NULL	Alendronate	1.7804
Canada_Ontario_Drug_Prices	NULL	Alendronate	1.7804
Canada_Ontario_Drug_Prices	NULL	Alendronate	1.7804
Canada_BC_Drug_Prices	NULL	ERYTHROMYCIN LACTOBIONATE 500 MG IF	15.0336
Canada_BC_Drug_Prices	NULL	ERYTHROMYCIN LACTOBIONATE 500 MG IF	15.0336
Canada_BC_Drug_Prices	NULL	ERYTHROMYCIN LACTOBIONATE 500 MG IF	15.0336
Australian_Drug_Prices	rifaximin	rifaximin 550 mg tablet 56	475.46
Australian_Drug_Prices	olmesartan + amlodipine + hydrochlorothiazide	olmesartan medoxomil 20 mg + amlodipine 5 mg...	18.07
Australian_Drug_Prices	olmesartan + amlodipine + hydrochlorothiazide	olmesartan medoxomil 20 mg + amlodipine 5 mg...	18.07

Matching International Drug Data to U.S. Registered Drugs

Retrieving data from the international pharmacy community was just the first hurdle to being able to reliably analyze the data. International boundaries create a volatile situation for pharmaceutical information. Companies can operate under different names, utilize different branding, or different packaging to meet demand in foreign markets. Additionally, there is not a global standard for how to identify a particular drug. Each country, province, or region may use a different pattern of letters and numbers to codify their drug formulary. In the United States alone, there are several categorization schemes used to identify drugs. When drugs do have the same branding, dosage form, and packaging across international borders, they may still be described in inconsistent ways across different governing bodies and different data files.

Luckily, drug ingredients, though formatted to fit the needs of the various file originators, tend to have specific patterns that are more consistent. The global medical and pharmaceutical industry has, more or less, decided to use a naming convention for drug compounds that tends to differentiate them from mundane words. These names are relatively consistent across borders, with the greatest exception being spelling alterations arising from language differences. However, language differences are easier to recognize and account for in a programmatic way.

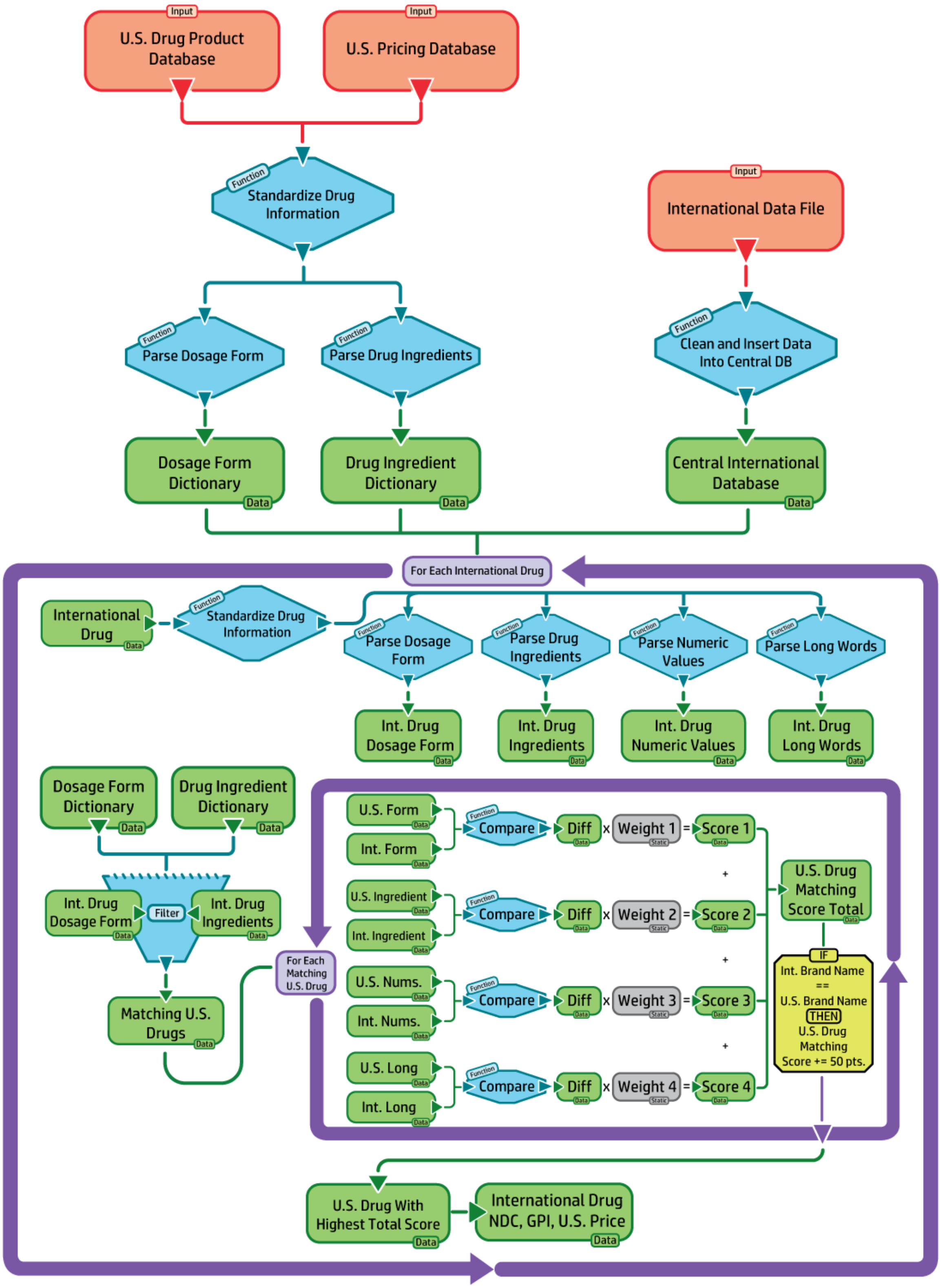
source	drug_name	drug_definition
Australian_Drug_Prices	buprenorphine	buprenorphine 40 microgram/hour patch 2
Australian_Drug_Prices	buprenorphine	buprenorphine 40 microgram/hour patch 2
Australian_Drug_Prices	buprenorphine	buprenorphine 40 microgram/hour patch 2
Canada_BC_Drug_Prices	NULL	BUPRENORPHINE HCL 400 MCG TU
Canada_BC_Drug_Prices	NULL	BUPRENORPHINE HCL 400 MCG TU
Canada_BC_Drug_Prices	NULL	BUPRENORPHINE HCL 2 MG TU
Canada_Fredericton_Drug_Prices	NULL	Buprenorphine / Buprnorphine
Canada_Fredericton_Drug_Prices	NULL	Buprenorphine / Buprnorphine

Matching International Drug Names and Definitions with U.S. Equivalents

In the U.S., all pharmaceuticals have a National Drug Code (NDC) and most have a Generic Product Identifier (GPI) that is unique. We have developed a methodology to find a best fit match between international drugs and U.S. equivalents. This way, we can assign international drugs a U.S. NDC, and GPI where available, that allows us to determine a realistic cost comparison between any successfully identified drug product. To do this, we use information from a combination of proprietary databases from Medi-Span, and publicly available drug information from the U.S. Department of Veteran Affairs.

This was accomplished with an algorithm that accepts a few simple parameters and changes a database table that relates international drugs to U.S. drugs and attempts to find a best fit U.S. price to match it. Here is a brief summary of how this is accomplished with an accompanying simplified process flow chart for the matching algorithm:

1. Gather information from U.S. Drug Definition and Pricing Databases
    a. Standardize all information
    b. Parse out dosage form
    c. Parse out drug ingredients
2. Develop a Drug Ingredient Dictionary and a Dosage Form Dictionary
3. Gather information from International Data File/Database
    a. Clean and insert international drug information into centralized database
4. Iterate through each international drug
    a. Standardize all information
    b. Parse out dosage form
    c. Parse out drug ingredients
    d. Parse out drug strength and all numbers in drug definition and brand name
    e. Create filtered list of U.S. drugs based on matching dosage forms and ingredients
    f. Compare all U.S. drugs from the filtered list and find a best fit match based on a weighted score calculated from percent matches of words relating to dosage form and drug ingredients, numbers, and all other words with more than three letters.
        i. If the international drug matches a U.S. drug's brand name, adjust the weighted score to indicate that this drug should be chosen
    g. If the best matching U.S. drug from this process meets or exceeds a pre-set scoring threshold, save its NDC and GPI information to the international drug being examined
    h. Save all updated information into the centralized international drugs database


Input
U.S. Drug Product Database
Input
U.S. Pricing Database
Function
Standardize Drug Information
Input
International Data File
Function
Parse Dosage Form
Function
Parse Drug Ingredients
Function
Clean and Insert Data Into Central DB
Dosage Form Dictionary
Data
Drug Ingredient Dictionary
Data
Central International Database
Data
For Each International Drug
International Drug
Data
Function
Standardize Drug Information
Function
Parse Dosage Form
Function
Parse Drug Ingredients
Function
Parse Numeric Values
Function
Parse Long Words
Int. Drug Dosage Form
Int. Drug Ingredients
Int. Drug Numeric Values
Int. Drug Long Words
Dosage Form Dictionary
Drug Ingredient Dictionary
Int. Drug Dosage Form
Filter
Int. Drug Ingredients
Matching U.S. Drugs
For Each Matching U.S. Drug
U.S. Form
Int. Form
Compare
Diff
x
Weight 1
=
Score 1
U.S. Ingredient
Int. Ingredient
Compare
Diff
x
Weight 2
=
Score 2
U.S. Nums.
Int. Nums.
Compare
Diff
x
Weight 3
=
Score 3
U.S. Long
Int. Long
Compare
Diff
x
Weight 4
=
Score 4
Static
+
U.S. Drug Matching Score Total
IF
Int. Brand Name
==
U.S. Brand Name
THEN
U.S. Drug Matching Score += 50 pts.
U.S. Drug With Highest Total Score
Data
International Drug NDC, GPI, U.S. Price
Data

The most important functions in the drug matching process are the following:

- Standardization of drug information
- Finding dosage form information
- Finding drug ingredients in drug information
- Weighted scoring

Standardizing Drug Information:

Pharmaceutical information found within U.S. and international data sources has a wide range of formatting standards. Data sources can list some combination of dosage form (injection, tablet, etc.), strength, and unit of measurement (mg, mcg, ml, etc.) in with the drug generic name, drug definition, and/or drug brand name. Some data sources keep this information separated into different columns. Other sources list dosage forms with drug strength with or without a unit of measurement. Thus, we have built a function to standardize all likely possibilities into a single, reliable format. This was achieved by concatenating all brand name, drug information, generic name, drug strength, dosage form, and unit of measurement information into a single set of words. From there, the standardized definition has all duplicate groupings of words removed, and it also removes all pre-determined irrelevant words (this, the, for, of, in, etc.).

Next, the standard definition undergoes a series of word-for-word replacements. During our research, it was found that different basic pharmaceutical phrases and chemical names can appear as chemical variations or non-uniform abbreviations. For example:

- Hydrochlorothiazide may appear as "HTCZ"
- Paracetamol may appear as "acetaminophen" or "APAP"
- Acetic acid may appear as "acet"

There is also uncertainty in the way drug strengths appear between data sets. They may appear as different ratios or different units in different databases. This is due to the databases listing drug strengths as they relate to the package type or dosage form they come in, where in others, they are listed at their base value. Additionally, drug strengths were found to have equating formats (e.g. 1000 mg instead of 1 g). Thus, all numeric ratios in the standard definition are reduced to a denominator of 1, and all drug strengths are factored down to their milligram equivalents where possible.

This results in a uniform standard of drug definition across international boundaries that enhances computational matching.

Finding Dosage Information

Dosage information is often plainly listed in U.S. and international data sources. It is also often stuffed into drug ingredient columns, brand name columns, or mixed and matched with drug strength information.

To combat these irregularities and to ease the creation of a dosage form dictionary, where a dosage form can be looked up and all relating drugs can be found, we developed a list of dosage form categories with as many likely matching words or word groupings as we could determine.

For example, a drug may be listed as coming in the form of "IV", "Intravenous", "piggy", or "piggyback".

We built a library of dosage forms that can be reasonably lumped together and then use this library to build a dictionary where the algorithm can ask for all drugs that match anything in a particular group and return a list of U.S. drugs that may come in that dosage form.

In some cases, no English words are used to describe dosage form. In this case, we found that the U.S. and some other Canadian and Australian data sources list dosage forms in two-letter abbreviations that match a list of approved dosage form codes published by the Executive Office of Health and Human Services (EOHHS). Such matches only occur when no other dosage form words are found, but a grouping of two letters is found.

- AA = Aerosol in milliliters
- AU = Non-aerosol spray
- DL = 24-hour biphasic extended release capsule.

This abbreviation data can be found on the EOHHS website.

https://eohhs.ri.gov/sites/g/files/xkgbur226/files/Portals/0/Uploads/Documents/Pharmacy/dose_form_ref_guide.pdf

This then necessitates a direct substitution of the two-letter code with the long form description of what the code means. That set of words can be parsed for common dosage forms so that the drugs may be categorized into the existing system.

If a dosage form is found that simply doesn't fit into the existing dosage form library, it is added to the library so that other drugs with the same dosage format may be successfully matched.

Finding Drug Ingredients

Drug name etymology has a consistent ethos that is well documented by the National Institutes of Health (NIH). Their website lists likely suffixes, prefixes, and other lexical patterns of common drug names.

Stem	Definition	Examples
-abine	(see -arabine, -citabine)	deci***tabine***
-ac	Anti-inflammatory agents (acetic acid derivatives)	bromfen***ac***; dexpemedol***ac***
-acetam	See -racetam	
-actide	Synthetic corticotropins	ser***actide***
-adol, -aldol-	Analgesics (mixed opiate receptor agonists/ antagonists)	taz***adol***ene; spir***adol***ene; levonantr***adol***
-adox	Antibacterials (quinoline dioxide derivatives)	carb***adox***
-afenone	Antiarrhythmics (propafenone derivatives)	alpr***afenone***; dipr***afenone***
-afil	PDE5 inhibitors	tadal***afil***
-aj-	Antiarrhythmics (ajmaline derivatives)	lor***aj***mine

https://druginfo.nlm.nih.gov/m.drugportal/jsp/drugportal/m.DrugNameGenericStems.jsp

The NIH data was used as a starting point to develop a list of more than 400 drug ingredient identifying patterns.

While this worked well for many drugs, it proved to be both inefficient in terms of computational energy, and ineffective at recognizing too many drug ingredients. We went back to the very beginning and scanned hundreds of different drug ingredients and drug brand names. This is when it came to our realization that many drug names phonetically sound and feel similar:

- Furosemide
- Famciclovir
- Bexarotene
- Naproxen

Most drugs follow a certain lexical pattern that makes them stand out from other words in most languages. This pattern was distilled down to the following pattern searching algorithm:

- Any series of letters, a consonant, 1-2 vowels including y, 1-3 consonants, and ending with 0-2 vowels.
- Which translates to machine code as:
    - [a-z]{1-999} [bcdfghjklmnpqrstvwxyz] [aeiouy]{1-2} [bcdfghjklmnpqrstvwxyz]{1-3} [aeiou]{0-2}

This obviously matches more than pertinent drugs (e.g. diagnostic, ampule, benefit). However, it turned out to be easier to create a list of words to ignore than it did to continually update a list of over 400 drug name endings.

This ingredient matching algorithm is used to both create a dictionary of U.S. drugs that contain each specific drug, and to filter the U.S. drug ingredient dictionary when iterating through international drugs.

Weighted Scoring

After standardization, each international drug description is compared to a filtered list of U.S. drug information that contains only U.S. drugs with matching dosage forms and drug ingredients. Each potential match is assigned a weighted score and ranked according to how strongly the standardized definitions match.

The strongest weighting is given to the highest number of matching drug ingredients and the highest number of matching dosage form words. The next highest weighting is given to how many numerical matches there are between standardized definitions. Just to cover any remaining important words that were not parsed by the algorithm before iteration, the percent match of words with at least three characters is given a low weight. Lastly, if a U.S. drug in question has a matching brand name, it is given a bonus weight equal to half of the total possible score.

For human readability, the natural maximum, before brand name matching bonuses, is 100 points. The matches with the highest total scores are assumed to be the best matches.

The algorithm then filters all matches based on strength into buckets of likely very good matches, suspect matches, and poor and unmatched drug definitions. This allows for human review and fine-tuning of the matching algorithm. This iterative process was undertaken many times to obtain a reliable and stable running algorithm and will be continually revisited to constantly improve this process.

As a final note, it should be stated that some programming decisions were made to balance the load of computer resources during the algorithm's execution. Memory usage had to be balanced with CPU load to allow the program to be run automatically from a cloud-based server so these discoveries can be made public as efficiently as possible.

Match International Drug Prices to U.S. Prices

With sufficient confidence in the matching algorithm comparing price differentials between international and U.S. drugs is straightforward. International drug data will now have a U.S. NDC equivalent that can be matched to National Average Drug Acquisition Cost (NADAC), Average Wholesale Price (AWP), and Wholesale Acquisition Costs (WAC) prices using a mixture of public and proprietary data.

To accommodate for fluctuating currency valuations, all conversions will be calculated live on the 3 Axis Advisors website. This is accomplished by querying free, publicly available data from ExchangeratesAPI.io. For analysis in this report, the currency conversions will be accurate up to the date this study is submitted.

About 3 Axis Advisors LLC

3 Axis Advisors is an elite, highly specialized consultancy that partners with private and government sector organizations to solve complex, systemic problems and propel industry reform through data driven advocacy. With a primary focus on identifying and analyzing U.S. drug supply chain inefficiencies and cost drivers, 3 Axis Advisors offers unparalleled expertise in project design, data aggregation and analysis, investigative research, and public education. 3 Axis Advisors arms clients with independent data analysis needed to spur change and innovation within their respective industries. 3 Axis Advisors co-founders were instrumental in exposing the drug pricing distortions and supply chain inefficiencies embedded in Ohio's Medicaid managed care program that ultimately uncovered more than $244 million in secret prescription drug mark-ups and inspired a national reckoning on hidden cost drivers within the prescription drug supply chain. They are also the co-founders of 46brooklyn Research, a nonprofit organization dedicated to improving the transparency and accessibility of drug pricing data for the American public. To learn more about 3 Axis Advisors, visit www.3axisadvisors.com.

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