PharmacoEconomics (2022) 40:1131–1142
https://doi.org/10.1007/s40273-022-01195-x

CURRENT OPINION

Getting the Price Right: Lessons for Medicare Price Negotiation from Peer Countries

Leah Z. Rand[1,2,3] · Aaron S. Kesselheim[1,2,3]

Accepted: 11 September 2022 / Published online: 9 November 2022

Abstract

The USA pays more for brand-name prescription drugs than any other country and new legislation from August 2022 gives Medicare the authority to directly negotiate certain drug prices with manufacturers starting in 2026—something the federal insurer had been prohibited from doing for its prior history. As the USA prepares for negotiations, we therefore surveyed how comparable industrialized countries use statutory requirements and procedures to negotiate brand-name drug prices. Guidance documents, regulations, government and academic publications were reviewed to identify the process of negotiating drug prices in peer countries that have been cited as potential examples for US payment reform: Australia, Canada, France, Germany, and the UK. Processes for arriving at a final price for a drug generally fall under three approaches: statutory rebates, setting a maximum price, and arbitration between national (public) insurers and manufacturers. Each approach to price negotiation could be adopted by Medicare and reduce spending even if Medicare does not adopt an exclusionary or closed formulary. Much remains to be determined about how the new price negotiation authority in the USA will be implemented, and policymakers can learn from comparator countries' statutory and regulatory strategies for price negotiation.

Key Points

The Inflation Reduction Act of 2022 authorizes Medicare to directly negotiate prescription drug prices. The statute includes limited guidance on negotiation procedures and does not grant Medicare the ability to exclude drugs from coverage if negotiations fail.

High-income peer countries (Australia, Canada, France, Germany, and the UK) negotiate prices with manufacturers and use different approaches, based around statutory rebates, maximum price setting, and arbitration.

Each identified price negotiation strategy could be used by Medicare to reduce drug spending even without instituting an exclusionary or closed formulary, though the impacts of the approaches may be attenuated.

1 Introduction

Throughout its history, Medicare, the largest federal health insurance program, was prohibited from directly negotiating prescription drug prices with manufacturers [1]. Because the USA devotes about one-in-seven healthcare dollars to prescription drugs and spends more on pharmaceuticals per capita than any other country, there has been increasing political interest in Medicare price negotiation as one strategy to reduce the burden of high drug costs on individual patients and taxpayers, culminating in the passage of the Inflation Reduction Act (IRA) in August 2022 [2, 3]. The IRA authorizes Medicare to negotiate the price of certain drugs.

The Medicare reimbursement system was not originally designed to include federal drug price negotiation. Medicare Part B, established as part of the original Medicare legislation in 1965 to cover physician-administered drugs, reimburses for essentially all US Food and Drug Administration-approved drugs at the drugs' average sales price in the private market, plus an additional administration fee for the provider [4]. The Medicare Modernization Act

✉ Leah Z. Rand
lzrand@bwh.harvard.edu

1 The Program on Regulation, Therapeutics, and Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, 1620 Tremont St., Suite 3030, Boston, MA 02120, USA

2 Harvard Medical School, Boston, MA, USA

3 Harvard Medical School Center for Bioethics, Boston, MA, USA

of 2003 created the Part D outpatient prescription drug benefit, but this benefit was to be administered by private plans and included a noninterference clause that prohibited the Secretary of Health and Human Services (HHS) from interfering in negotiations between manufacturers and plans or formulary design.

The IRA authorized the Centers for Medicare and Medicaid Services (CMS) for the first time to negotiate prices for select drugs and introduced other measures to address high prices [3]. Negotiation is planned for top-selling drugs that are single source with no competitors, beginning with ten drugs in 2026 and expanding to 20 a year by 2029 [3]. To qualify, drugs must have been on the market for 9 years (13 years for biologic drugs) [3]. As envisioned in the statute, the process would entail the manufacturer providing information on development costs and therapeutic alternatives to CMS, which would then offer a price. If the manufacturer makes a higher counter-offer, it must cite relevant justifications [3, 5].

Numerous regulatory details remain to be decided, and a key challenge will be what happens when CMS and the manufacturer cannot come to an agreement on a price [6]. Other highly industrialized countries around the world already negotiate prices for drugs that will be reimbursed through national health insurance or public payers. The processes used by these other countries could inform options for negotiation of Medicare prices. We therefore surveyed how comparable industrialized countries use statutory requirements and procedures to negotiate brand-name drug prices to help determine what mechanism of negotiations could be used and how price disagreements could be resolved in the USA.

2 Methods

We reviewed publicly available guidance, government publications, legislation, peer-reviewed and grey literature on the process of drug price negotiation from US comparator countries—Germany, France, Australia, the UK (England), and Canada—selected because they have been suggested as comparison countries for US drug pricing and have materials available in English on negotiation [7]. These countries engage manufacturers in price negotiation rather than using formulaic price setting [8].

Price negotiation laws and procedures for brand-name prescription drugs were reviewed. Identified documents on the process, disagreement resolution, and regulatory requirements for drug pricing in each country were analyzed for information on how final list prices and net prices are reached (see Electronic Supplementary Material for search details). We excluded descriptions of the health technology assessment (HTA) process that precedes price negotiation, the reasons justifying a certain price (e.g., clinical benefit, manufacturing costs), and other tools for reducing prices, which have been described elsewhere [9–12]. We instead focused on extracting details of the process of arriving at agreement on price between payers and manufacturers. We also included literature identifying the impacts of these pricing processes and policies. To illustrate the processes, we tracked the review and pricing of fingolimod (Gilenya®) in each country, chosen because each reviewed it for its primary clinical indication (Table 2). We use the term national health insurer (NHI) to refer to any national health system or public insurance program that reimburses the cost of drugs. Table 1 includes details for each country.

3 Results

In most countries reviewed, there is a single NHI or governing body that determines the reimbursement status and rate of prescription drugs. The NHI is usually a monopsony or near-monopsony—the largest purchaser of prescription drugs in the country—although for four of the five, a separate HTA body, not the NHI, determines whether a drug will be included in coverage. In only two countries does the NHI negotiate prices (Table 1 and Fig. 1).

3.1 Germany

In Germany, 90% of the population is covered by the NHI—statutory health insurers or "sickness funds". A ceiling price for outpatient drugs is set through the pricing process, while inpatient drugs are covered as part of diagnosis-related bundled payments and subject to the same ceiling prices [13].

Two statutory tools limit prices. First, drugs that, according to HTA, offer no additional benefit over comparators are reference priced such that the reimbursement price cannot exceed the cost of the comparator. If the manufacturer sells the drug at a higher price than the reference, then patients must pay the out-of-pocket the difference between the two [13]. Second, drugs that do not have a reference product group face a mandatory 7% discount off list prices [13].

For drugs the HTA judges to offer an additional benefit over available alternatives, the GKV-Spitzenverband, an association of the statutory health insurers, negotiates with manufacturers. During the 6–12 months after market authorization, the GKV-Spitzenverband and manufacturer negotiate a new, lower price [14]. Table 2 illustrates how a finding of additional benefit led to price negotiations for fingolimod to treat multiple sclerosis, ultimately resulting in a rebated price. If agreement cannot be reached, either party can initiate arbitration proceedings [16]. The arbitration

Table 1 Negotiating entities, payers, and system features for branded prescription drug coverage

	Australia	Canada	France	Germany	UK (England)	Medicare
NHI responsible for prescription drug coverage	Medicare (health insurance); PBS (prescription drugs)	Province-based public insurance plans	Statutory health insurers (over 40 insurers)	Statutory health insurers (over 100 insurers)	National Health Service England (NHS England)	Medicare Parts B and D
HTA body	Pharmaceutical Benefits Advisory Committee (PBAC)	Canadian Agency for Drugs and Technologies in Health (CADTH)	National Health Authority (HAS)	Institute for Quality and Efficiency in Health Care (IQWiG); recommendation made by the Federal Joint Committee (G-BA)	National Institute for Health and Care Excellence (NICE)	None
HTA type of organization	Independent, appointed by the government	Independent, publicly funded	Independent, publicly funded	Independent, publicly funded	Independent. publicly funded but statutory role and regulations	Not applicable
Body responsible for determining reimbursement status	HTA body	Individual insurance plans	HTA body	NHI coalition, GKV-Spitzenverband, a self-governing coalition of statutory insurers created through legislation	HTA body	MEDPAC for Part B; Medicare Advantage Part D plans; statutory reimbursement requirements
Negotiation-eligible drugs	All brand-name, on-patent prescription drugs	All brand-name, on-patent prescription drugs	All brand-name, on-patent prescription drugs	All brand-name, on-patent and outpatient prescription drugs	All brand-name, on-patent prescription drugs	Up to 20 single source, brand-name drugs (starting in 2026)
Body responsible for negotiating price	Pricing Section of the PBS, and the Ministry of Health	Public plan coalition (private plans are independent)	Economic Committee on Pharmaceuticals, (CEPS), which sits under the Department of Health	NHI coalition, GKV-Spitzenverband	Department of Health and Social Care	Parts B & D: HHS Secretary for up to 20 drugs a year
Party agreeing to final price	Minister of Health (via PBS/NHI recommendation)	Public plan coalition	Department of Health	NHI coalition or arbitration board	HTA body or Department of Health and Social Care	Part B: as set by CMS Part D: Plan or PBM Negotiated drugs: HHS Secretary
Other types of drug price negotiation		Private plans conduct their own price negotiations	Insurers, hospitals, and wholesale purchasers of drugs may negotiate additional discounts	NHI insurers and other purchasers may negotiate additional discounts	Purchasers (local NHI groups) may negotiate lower prices	Part D: Medicare Advantage plans and PBMs negotiate plan prices and coverage
Type of insurance	Public: national health insurance	Public and private mix	Public: national health insurance	Public and private mix	Public: national health insurance	Public with additional private plans (Medicare Advantage)
NHI Payer(s) ("Government" indicates financing through taxation)	Government	Government or provincial public plan	Government; supplemental private plans	Government or private insurance plans	Government	Federal government, and/or private insurance plans
Population covered by NHI	All	Low-income, armed forces for outpatient drugs; all for inpatient drugs	All	Available to all	All	Age 65+ years and individuals with certain disabilities

Table 1 (continued)

	Australia	Canada	France	Germany	UK (England)	Medicare
Supplementary insurance for drugs offered?	Yes, private insurance available but does not cover PBS-listed drugs	Population not covered by NHI, has private insurance or none	Yes, private insurance for when NHI does not reimburse full price	No	Yes, private insurance for drugs not covered by the NHI	Yes, Medicare Advantage, Part D prescription plans
Patient out-of-pocket costs for prescription drugs on public plan (low-income groups exempt)	Yes, fixed rate for all drugs; plus brand-name premium when generics available	Yes, variable rate	Yes, portion not covered by NHI	Yes, variable rate; plus difference between list and reference price	Yes, fixed rate for all drugs	Yes, variable premiums, co-pays and cost sharing
Type of formulary						
Positive: only drugs that have been included are covered	Positive list	Positive list	Positive list	Negative list	Negative list (but if HTA body recommends it then drug must be covered)	Negative list generally: plans make their own formularies
Negative: only drugs that have been excluded are not covered						

Terms for government bodies and agencies, e.g., "department of health", are generic and not specific to the particular name of the entity in the relevant country

CMS Centers for Medicare and Medicaid Services, *HHS* US Department of Health and Human Services, *HTA* health technology assessment, *NHI* national health insurer, *PBM* Pharmacy Benefits Manager, *PBS* Pharmaceutical Benefits Scheme

board comprises a chair, two impartial members, and two representatives from each party. The proceedings begin by identifying the cause of the failed negotiation, followed by each side explaining the reasons for its preferred price. The members of the arbitration board try to propose a solution that is mutually agreeable, but if that does not happen, then the board decides the price by considering the facts of each case and the condition being treated [17]. The board makes its own price decision, which is usually between the GKV-Spitzenverband and manufacturer's proposed prices. The decision is binding for 1 year, after which it may be re-negotiated using the same procedures [17, 18].

Once a net price is determined for a drug, through either the reference pricing or negotiation, the manufacturer can no longer raise prices. Manufacturers may request a new price based on the generation of new evidence about the drug's clinical benefits, in which case the assessment and price negotiation processes restart [19].

The GKV-Spitzenverband price sets the maximum that will be reimbursed by the NHI, but additional rebates may be negotiated through insurer tendering, especially when comparator products are available [20]. If there is not enough evidence to determine whether the drug offers additional benefit, a price below a reference comparator price is advised. This rule was enacted in 2017 out of concern that manufacturers were withholding information that would risk demonstrating a lack of additional benefit [13]. Manufacturers are therefore incentivized to share relevant evidence on the new drug during the pricing process.

While the decisions of the arbitration board in Germany often align with the NHI's proposed price [17], the arbitration-determined prices tend to be higher than if the arbitration procedure had not been pursued [21]. In the first 5 years (2011–16) of this process, 106 non-rare disease oncology or infectious disease drugs were reviewed, of which the price was negotiated for and 24 went to arbitration [22]. Dissatisfaction over price has led some manufacturers to withdraw their drugs from the German market, but previous studies have shown that all the withdrawn drugs had no additional clinical value as rated by a German HTA or not enough evidence to claim an additional value compared to existing therapies [13, 23, 24].

3.2 France

The NHI in France is made up of statutory health insurers that form the public insurance system, which covers all residents [25]. Following the market authorization of a new drug, the National Health Authority (HAS) reviews the absolute and additional therapeutic benefits of the drug. Drugs with no additional benefit are reference priced, such that the NHI will reimburse them only to save money. Drugs with certain levels of additional benefit will

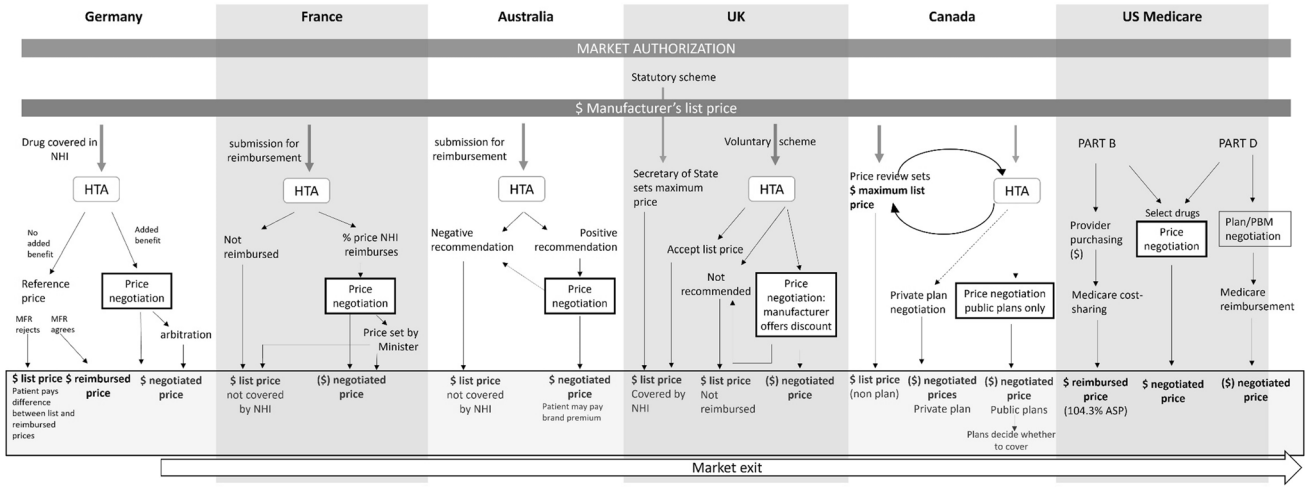

Fig. 1 Comparative flowchart of pricing process in Germany, France, Australia, the UK, Canada, and Medicare. *ASP* average sales price, *HTA* health technology assessment, *MFR* manufacturer, *NHI* national health insurer, *PBM* pharmaceutical benefits manager, $ public price, ($) confidential price—negotiated price not publicly available

be guaranteed a list price that is neither the highest nor the lowest of four other countries (Germany, Italy, Spain, the UK) [26–28]. If the NHI does not reimburse the drug, then the manufacturer can set its own price that patients will pay out-of-pocket.

The French health system sets an annual spending target and prices are negotiated with a budget impact in mind. The Economic Committee on Pharmaceuticals (CEPS) is a government committee that brings together representatives of several ministerial offices and insurers to negotiate drug prices. The negotiation procedure is outlined in an agreement between CEPS and the pharmaceutical trade association. The most recent agreement protects negotiated prices from reductions for 3–5 years. The agreement also introduced a new procedure for disagreements: after ten rounds of negotiation, the manufacturer has 2 weeks to propose a new price that CEPS will either accept or decline; CEPS may make one counter-offer that the manufacturer can either accept or decline. If the offer is not accepted, then the negotiations are put on hold for 4 months [29, 30]. This new procedure was coupled with a promise to speed up pricing (15 days from market authorization) for drugs with good additional value that HAS deems cost effective [30, 31].

Other statutory requirements minimize increases in drug spending over time. An annual spending rate cap is set, and manufacturers must return a portion of revenues exceeding the cap. These price clawbacks can be tied to daily treatment costs, volume of sales, or spending by drug class [28]. Price increases are statutorily prohibited without further regulatory review [27]. In addition to the price negotiated by CEPS, hospitals and other purchasers may negotiate discounts with manufacturers through purchase agreements.

The French approach to drug pricing and negotiation has kept launch prices lower than US launch prices and prevented year-on-year price increases. For six drugs with the highest Medicare expenditures in 2017, Medicare would have saved $5.1 billion in 2018 if it had paid French prices [27].

3.3 Australia

The Australian HTA agency, the Pharmaceutical Benefits Advisory Committee (PBAC), reviews drugs with market authorization and makes recommendations whether the drug should be reimbursed through the Pharmaceutical Benefits Scheme, the prescription drug benefit of Medicare, the NHI, which automatically covers all Australians. A positive recommendation from the PBAC is necessary for reimbursement; though the PBAC is not directly involved in negotiations, it influences price. Frequently, a manufacturer's submissions to the PBAC to include a drug for Pharmaceutical Benefits Scheme coverage go through multiple rounds of review if the PBAC decides that the drug is not sufficiently cost effective at the proposed price, as was the case for fingolimod, which was only approved following a price reduction (Table 2).

The Pricing Section of the Pharmaceutical Benefits Scheme leads negotiations with the manufacturer and follows a set of guidelines for a reasonable price offer, taking into account expected use, PBAC advice on cost effectiveness, manufacturing costs, and overseas prices, and other relevant factors raised by the manufacturer [33]. The

Table 2 HTA findings and prices for fingolimod (Gilenya®, Novartis) 0.5 mg for severe relapsing-remitting multiple sclerosis in each of the reviewed countries

	Germany	France	Australia	UK	Canada	USA
HTA finding(s)	1. "Added benefit not proven." for patients with previous IFN-beta "Indication of considerable added benefit" for patients with no previous IFN-beta and for female sex 2. "Indication of minor added benefit" for male sex [57]	1. "substantial" clinical benefit 2. "minor" clinical added benefit 3. Concerns that the trials did not enroll groups who are covered by the indication [58]	1. Superior comparative effectiveness to comparator 2. Base-case ICER $45,000–$75,000 per QALY 3. Given the uncertainties, "the base case ICER was unacceptably high to recommend listing ... could be managed with a lower price offer ...would need to be in the range of $15,000-$45,000 per QALY" [59]	1. Most likely ICER range of £25,000 to £35,000 per QALY gained 2. Lack of evidence for some groups included on marketing authorization indication [60]	1. Cost per QALY estimates ranged from $48,698 to $337,381 2. Recommends listing for patients who meet certain criteria (more restrictive than indication) 3. A reduced price similar to comparator would increase the likelihood of a less restrictive recommendation [61]	not appplicable
HTA impact on price negotiation	Original HTA assessment found "Added benefit not proven" but a subsequent reanalysis of data by the manufacturer demonstrated benefit in 2/3 of the patient population. Proof of benefit allows for a negotiation of a price that exceeds the reference group price [62]	Finding of substantial clinical benefit (absolute clinical value) results in agreement that the NHI will reimburse 65% of the costs for patients [63]. Patients pay the remainder out of pocket or with supplemental insurance However, because there is only a "minor" additional clinical benefit, the price of the drug should not be higher than its comparators by more than a small amount	HTA organization, PBAC, recommended that fingolimod be prescribed to a restricted patient population than the label covers Given the high ICER range (cost per QALY), PBAC deferred its decision. The manufacturer then negotiated a further price reduction with the Ministry of Health and NHI. PBAC approval is required for NHI coverage. Following the agreement on a price reduction, PBAC recommended Gilenya® for coverage by the NHI	HTA finding led the Department of Health to negotiate a patient access scheme, i.e., a simple discount off the list price. HTA recommended the drug for coverage by the NHI under the condition that the manufacturer offer the discount [60]	The pCPA, engaged the manufacturer in price negotiations in 2012 and concluded them with a letter of intent in 2013, indicating that an agreement on a discount that would be offered to the public plans was reached [64] The Patented Medicines Prices Review Board found fingolimod not to be excessively priced, thus did not impose a maximum price [65]	not applicable
Manufacturer list price per person/year (year listed) calculated from 28-day supply price	€24,116 (2011) [66]	€22,700 (2011) [67]	Approximately AUD 40,000 (2011) [68]	£19,169 (2012) [60]	CAD 30,992 (2011) CAD 40,450 (2022, online pharmacy) [61, 69]	$66,616 (2015) [70] increased to $116,193 (2022)[b] [70, 71]
Manufacturer list price per person/year 2022-adjusted USD[a]	$43,450	$40,899	$55,069	$39,120	$41,796 (2011 price) $31,449 (2022, online pharmacy)	$84,461 (2015 price) $116,193

Table 2 (continued)

	Germany	France	Australia	UK	Canada	USA
Negotiated price per person/year (year listed)	€18,980 (2022) [66]	Confidential Possibly no discount [67]	AUD 28,934 (2022) [72]	Confidential	Confidential Listed in formulary: CAD 31,738 (2021)[d] [73]	$92,954 (2022)[c]
Negotiated price per person/year, 2022-adjusted USD	$34,195	not available	$20,030	not available	$28,258	$92,954

HTA health technology assessment, *ICER* incremental cost-effectiveness ratio (difference in cost divided by difference in effect), *IFN* interferon, *NHI* national health insurer, a generic term used for a country's public insurance plan and payer, *PBAC* Pharmaceutical Benefits Advisory Committee, *QALY* quality-adjusted life-year, pCPA pan-Canadian Pharmaceutical Alliance

[a]Conversion to dollars using Xe historic rates for January of (year), and then inflation adjusted to June 2022 using the Bureau of Labor Statistics CPI Inflation Calculator and rounded to the nearest whole number

[b]Wholesale acquisition cost. Prices calculated from a 30-day supply. The wholesale acquisition cost nearly doubled from 2015 to 2022

[c]Estimated Medicare rebated price using SSR Q1 2022 rebate of 20%. Annual spending using Medicare average spend per unit (weighted) for 2020 would be $108,434 (unit price × 365); Medicare average spend per beneficiary in 2020 of $87,660. Note that average spend per unit increased 33% from 2016 to 2020 [74]

[d]Listed in the Ontario Drug Benefit formulary. Confidential discounts to formulary prices in Ontario average 30%, which if applied here would make the net price CAD 20,947 or $18,650 in 2022 USD [75]

negotiation concludes with an agreement on the price, expected use (budget impact), any special pricing procedures (e.g., risk-sharing agreements), and any proposed restrictions that would limit reimbursable indications. At any point, either the manufacturer or Pricing Section can choose to stop the negotiation, in which case the drug will not be covered [34, 35].

Drugs similar to comparators in terms of safety and efficacy are reference priced, and patients may be required to pay the difference between the manufacturer's price and the reference price in addition to a co-pay [33, 36]. For drugs that provide additional benefit to patients and are the first in their therapeutic group (i.e., no benchmark), a cost-plus method may be used, which pegs price to manufacturing costs plus a margin around 30%, accounting for prescription volume. Manufacturing costs for the Australian market do not include research and development or market authorization costs [33].

A recent analysis found that 2018 US prices were 300% of Australian prices and up to 432% for the top 60 drugs by US sales [37]. Manufacturers have expressed concern that the Australian process is too heavy handed because it lacks an effective appeal mechanism [38].

3.4 UK: England

The pricing of drugs is regulated by an agreement, the Voluntary Scheme, between the national payer, NHS England, and the pharmaceutical trade association. All newly authorized drugs, including line extensions launched within 3 years of the originator, are reviewed by the National Institute for Health and Care Excellence (NICE), an independent, publicly funded HTA organization with a statutory role in determining NHI coverage. NICE uses an explicit cost-effectiveness threshold range (£20,000–30,000 per quality-adjusted life-year gained) to inform its recommendation; if a manufacturer is unable to set a cost-effective price, then it is expected to offer a confidential discount to the NHI to reach this threshold [39]. NICE therefore claims not to negotiate prices, but for a drug to be covered, it must be priced in accordance with the cost-effectiveness threshold. To achieve this, NICE can recommend coverage for a restricted subset of approved indications or populations. When there is uncertainty about evidence, a discount may also be recommended, as happened with fingolimod (Table 2). These agreements are made between NICE, the Department of Health and Social Care, and the manufacturer.

In addition to negotiations, the Voluntary Scheme includes an explicit profit control and affordability measure that sets an allowable drug spending growth rate. Manufacturers exceeding it must make rebate payments back to the NHI [39]. When there is disagreement over rebates, either party can trigger dispute resolution in which a three-person

panel (a chair agreed to by both sides and one member each appointed by the NHI and manufacturers' trade association) receives reasons for their position on pricing and information from each party. The panel makes a decision that is binding on both parties, but at any point during the process, either may withdraw and concede the dispute [40].

Manufacturers that do not participate in the Voluntary Scheme or drugs that do not qualify, such as drugs with no new active substances or line extensions introduced 3 years or more after the originator, are priced through the Statutory Scheme. Unlike the Voluntary Scheme, which allows the manufacturer to set its list price, the Statutory Scheme gives the Department of Health and Social Care greater leeway to specify a maximum price. Considerations for the decision include reference pricing to comparators, cost-basis pricing, the manufacturers' profit level, clinical need, and prices in other comparable markets [39]. The Statutory Scheme includes a fixed rate of discount that must be paid back to the Department of Health and Social Care [41].

Under both Schemes, prices may not be increased without NHI approval [39]. The negotiated price is the maximum NHI reimbursement, but hospitals and purchasing consortia may negotiate additional discounts with manufacturers and wholesalers [42].

One study of cost trends found that although overall expenditure on high cost drugs grew during the study period (2008–17), this was driven by increased use, while the cost index decreased [43]. One concern about the use of an explicit cost-effectiveness threshold is that manufacturers target prices at the higher end [44].

3.5 Canada

The national Patented Medicines Prices Review Board is a government agency responsible for determining maximum prices allowable in Canada for brand-name, on-patent drugs and whether prices are excessive [45]. A primary mechanism for determining "excessive" prices is the reference to international prices, and new guidelines that took effect in 2022 expanded possible comparator countries while also removing high-price countries, including the USA, from the list. The Board also considers prices of drugs in the same therapeutic class, price increases above inflation, pricing trends for the drug in Canada, and manufacturing costs. The Board may convene hearings and apply retroactive price maximums if it finds a drug price excessive [46].

Apart from the price maximum, Canadian insurance plans are responsible for negotiating prices for their enrollees. In 2010, the provincial public health plans formed a coalition, the pan-Canadian Pharmaceutical Alliance, to negotiate prices [47]. Manufacturers submit offers to the pan-Canadian Pharmaceutical Alliance, which then negotiates the terms for provincial procurement of drugs for public plans. The negotiations are not transparent, and there is no clear basis for the agreed prices [48, 49]. The public plans only account for 40% of the market, and the prices the pan-Canadian Pharmaceutical Alliance negotiates do not apply to private plans or people without insurance [49]. Another negotiation challenge is that each provincial public plan makes a decision whether to include the drug at the negotiated price in its formulary; some provinces conduct further reviews to decide on coverage [50, 51]. Given this patchwork of coverage, the government announced in 2019 that it will create the Canadian Drug Agency, which by 2024 will assess effectiveness and negotiate prices on behalf of all Canadian plans [52].

The creation of a new agency to negotiate drug prices stems from government concerns about Canada's relatively high spending on pharmaceuticals—third among OECD countries, following the USA and Switzerland—and formulary variation among plans, both public and private [49]. However, efforts to introduce more robust national price regulation have faced setbacks: planned regulations to expand the Board's purview to include cost-effectiveness assessments and require reporting of confidential-rebate prices were struck down in court [53]. Legislation implementing national prescription drug insurance was voted down in 2021 over disagreements about costs and federal versus provincial funding of the program, but there remains a strong movement to adopt a national policy [54, 55].

4 Discussion

Negotiation of Medicare prescription drug prices is just beginning in the USA. Peer countries that negotiate prices demonstrate several approaches to negotiation—examples that offer models of how a process of price negotiation in the IRA could be implemented. Three key features provide important lessons for US implementation of drug price negotiation: NHI maximum price setting, negotiation procedures that include arbitration, and statutory requirements for pricing.

Whereas the countries reviewed, except Canada, negotiate drug prices starting with market authorization, the IRA negotiation provisions take effect only after a drug has been marketed for a minimum of 9 years. Other than Germany, where the NHI reimburses drugs for up to a year while negotiations proceed, agreement on a price between the NHI and manufacturer is usually a precondition for reimbursement. Both the manufacturer and the NHI want to ensure patient access to drugs, but each has divergent goals and leverage in the negotiation process. The NHI aim is to provide clinical

benefits at a reasonable cost because it is responsible for the health of its whole population. If the price of a prescription drug is higher than the NHI is willing to pay, it has two options: (1) not list or reimburse the drug, but patients will struggle to access it or (2) pay a higher price than it considers appropriate. This will have a negative impact on the budget and opportunity costs in the health system. By contrast, manufacturers of brand-name, patent-protected drugs hold a monopoly. If the price that is negotiated is too low for the manufacturer, it can: (1) exit the market and stop selling the drug in that country or (2) offer the drug only at the list price and not reimbursed through the NHI, but then the market in that country will be much smaller. Negotiations that delay NHI coverage of drugs run counter to the access goals of both the NHI and the manufacturer, though give the NHI an opportunity to agree to a reasonable price for the drug.

Unlike the NHIs in the countries reviewed, not only does CMS not negotiate during the period of initial coverage, but it also cannot exclude a drug from Medicare formularies or require Medicare Advantage plans to do so based on cost alone. (Mechanisms like tiered formularies can decrease utilization by shifting costs to patients.) Therefore, implementation of negotiation for Medicare prices must include leverage and resolution options—other than formulary exclusion—when there is disagreement between the parties. A well-designed negotiation procedure should address NHI/Medicare and manufacturer interests while ensuring fair patient access and affordability.

Under the IRA, once a drug is selected for negotiation, a ceiling price based on historic price levels is set. Canada and France use ceiling prices, setting upper limits based on prices in comparator countries. A key difference between the IRA approach and Canada's is that the IRA sets the ceiling at the weighted average of prices across Medicare Advantage plans (Part D) or the average sales price (Part B and biologics) from prior years, reflecting US market conditions and private plan rebates. It is uncertain whether this approach, which relies on domestic market competition, will lead to lower prices compared to an approach that relies on international pricing.

The countries reviewed use the threat of non-reimbursement to move drug price negotiations forward. For example, in the French process, if there is protracted disagreement, then negotiations are put on hold for several months, thus manufacturers lose market time, though patients also lose coverage. Because Medicare already reimburses for the drugs that will have negotiated prices, and the IRA does not authorize exclusionary formularies, instead civil monetary penalties are introduced to encourage engagement in the negotiations. Manufacturers that fail to provide the requested information for negotiation will be subject to a penalty of $1 million per day. This is a substantial penalty even if some of the highest-spend drugs have daily Medicare revenues exceeding this amount [56]. The IRA also enforces negotiations through a penalty of up to $100 million for each item of false information manufacturers supply during the negotiation process. Lacking the ability to exclude drugs from coverage, the IRA instead authorizes Medicare negotiators to assess financial penalties for failure to participate in the negotiation process.

The IRA provides no dispute resolution mechanism in the legislation. This is a feature that will have to be developed through agency regulation and guidance and thus can be guided by the experience in other countries. According to the IRA, the HHS Secretary makes a price offer, and the manufacturer has 30 days to make a counter-offer. The two parties have 4 months (July–November) to conclude the negotiation, though no process is specified [3]. The ceiling price provides a backstop, but the arbitration approach adopted by Germany could be a strategy for resolving disagreements when the HHS offer is below the ceiling. Two important features of the German approach are that it uses conventional arbitration (the arbitration board decides on a reasonable outcome between the two proposed prices), and it is binding on both parties. The IRA requires both parties, manufacturer and HHS Secretary, to justify their proposed maximum fair price (counter-)offer, based on factors such as the extent of public funding for drug development, sales volumes and revenues, and comparative effectiveness, which the arbitration board would consider. The creation of an arbitration board could be realized through agency regulation and guidance: a legal precedent for contract arbitration with federal agencies exists and was clarified in the Administrative Dispute Resolution Act of 1996, which permits arbitration of health insurance disputes [57].

Compared with the countries reviewed, which have NHI price reviews for all brand-name drugs, the IRA authorizes limited price negotiations for Medicare only. Another key difference between the IRA approach to drug price negotiation and that of the reviewed countries is that even with the IRA, the USA still relies on market competitiveness to reduce prices over time, while the other countries regulate more directly. Countries such as the UK, Australia, and France designed their pricing approach to balance between the quick uptake and coverage of new drugs and regulating public spending, rather than relying on market competition for brand-name drugs. Statutory requirements linked to pricing offer a direct means for a government to limit price increases and reduce prices. For example, in addition to limits on price increases over time, France and Australia require rebates when manufacturers exceed predicted sales volumes. These types of rebate agreements tie pricing and profits to the available evidence and expected utilization, incentivizing manufacturers to share their sales expectations during the negotiation. In France, negotiations on new drug prices have made innovative medicines available

soon after approval, while clawbacks and price decreases on older medicines keep spending growth in check [32]. All the countries surveyed prohibit price increases without first submitting evidence and reasons for the increase. The IRA will require rebates to Medicare for increases greater than inflation, though it does not prevent drug list price increases [3]. As Medicare price negotiations gain a foothold and develop, future legislation could consider adopting similar statutory price requirements and rebates like those already in place abroad.

5 Conclusions

As US policymakers authorize CMS to begin Medicare drug price negotiation, key implementation questions remain unresolved [6]. While the IRA offers an overview of negotiation procedures, it provides no mechanism for resolving a disagreement except reverting to the maximum fair price ceiling. A major barrier for CMS negotiation is that Medicare does not have a closed formulary such that it can exclude certain drugs from coverage for price reasons.

Surveying other health systems' approaches to negotiating drug prices highlights several ways to construct a process that can accommodate an open formulary and both the manufacturer's and the government's interests. In addition to the maximum fair price ceiling, dispute resolution through arbitration would consider the claims of both the manufacturer and CMS. Finally, a suite of statutory pricing requirements can reduce prices even when negotiations have a limited impact. An important part of any US policy will be the details of the negotiation process, and other countries provide sound models for procedures that can bring the USA closer to fair prices.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40273-022-01195-x.

Acknowledgments The authors thank Huseyin Naci, Veronique Raimond, Edward R. Cliff, Kerstin N. Vokinger, and Matthew Herder for feedback on the article.

Declarations

Funding Arnold Ventures provided funding for the preparation of this article.

Conflicts of interest/Competing interests Leah Z. Rand and Aaron S. Kesselheim have no conflicts of interest that are directly relevant to the content of this article.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and material Not applicable.

Code availability Not applicable.

Authors' contributions Both authors contributed to the study conception and design. Data collection and analysis were performed by LZR. The first draft of the manuscript was written by LZR, ASK commented on and revised the manuscript. Both authors read and approved the final manuscript.

References

1. Medicare Prescription Drug, Improvement, and Modernization Act of 2003. 108th Congress ed 2003.
2. LaRosa J, Slifer E. Key provisions of drug pricing proposals. Commonwealth Fund, New York, NY. https://www.commonwealthfund.org/publications/2021/apr/key-provisions-drugpricing-proposals. Accessed 26 May 2021
3. Inflation Reduction Act of 2022. 117th Congress ed 2022.
4. Werble C. Medicare Part B. Health Affairs Blog: Project Hope; 2017. https://www.healthaffairs.org/do/10.1377/hpb20171008.000171/full. Accessed 22 September 2021
5. Sachs R. Understanding the Democrats drug pricing package. Health Affairs Forefront: Project Hope; 2022.
6. Kelly C, Karlin-Smith S. Medicare price 'negotiation' process gets broad brush treatment in new law. Scrip. 16 Aug 2022.
7. H.R.3 - Elijah E. Cummings lower drug costs now act. 116th Congress ed: Congress.gov; 2019.
8. Rand LZ, Kesselheim AS. International reference pricing for prescription drugs: a landscape analysis. J Manage Care Spec Pharm. 2021;27(9):1309–13.
9. Emanuel EJ, Zhang C, Glickman A, Gudbranson E, DiMagno SSP, Urwin JW. Drug reimbursement regulation in 6 peer countries. JAMA Intern Med. 2020;180(11):1510–7. https://doi.org/10.1001/jamainternmed.2020.4793
10. Kristensen FB. Mapping of HTA methodologies in EU and Norway. Corporate author: European Commission, Directorate-General for Health and Food Safety, Publications Office, Brussels; 2017. https://op.europa.eu/en/publication-detail/-/publication/4d364ea4-113a-11e8-9253-01aa75ed71a1
11. Rand LZ, Kesselheim AS. An international review of health technology assessment approaches to prescription drugs and their ethical principles. J Law Med Ethics. 2020;48(3):583–94.
12. Rodwin MA. Common pharmaceutical price and cost controls in the United Kingdom, France, and Germany: lessons for the United States. Int J Health Serv. 2021;51(3):379–91.
13. Wenzl M, Paris V. Pharmaceutical Reimbursement and Pricing in Germany. OECD. Paris. June 2018. https://www.oecd.org/health/health-systems/Pharmaceutical-Reimbursement-and-Pricing-in-Germany.pdf. Accessed 6 May 2021
14. The benefit assessment of medicinal products in accordance with the German Social Code, Book Five (SGB V), section 35a. https://www.g-ba.de/english/benefitassessment/. Accessed 21 Oct 2019.
15. GKV-Spitzenverband. Digitalisation in the healthcare system: annual report 2019. GKV-Spitzenverband, Berlin; 2020. https://www.gkv-spitzenverband.de/media/dokumente/service_1/publikationen/geschaeftsberichte/GKV_GB2019_englisch_Barrierefrei.pdf. Accessed 2 Aug 2022.
16. Ludwig S, Dintsios CM. Arbitration board setting reimbursement amounts for pharmaceutical innovations in Germany when price negations between payers and manufacturers fail:

an empirical analysis of 5 years' experience. Value Health. 2016;19(8):1016–25.
17. Rother J. Is arbitration an answer for high drug prices? To the Point: Commonwealth Fund; GKV-Spitzenverband. https://www.gkvspitzenverband.de/media/dokumente/service_1/publikationen/geschaeftsberichte/GKV_GB2019_englisch_Barrierefrei.pdf 2019.
18. Robinson JC. Lower prices and greater patient access: lessons from Germany's drug-purchasing structure. N Engl J Med. 2020;382(23):2177–9.
19. Moorkens E, Barcina Lacosta T, Vulto AG, Schulz M, Gradl G, Enners S, et al. Learnings from regional market dynamics of originator and biosimilar infliximab and etanercept in Germany. Pharmaceuticals (Basel). 2020;13(10):324.
20. Lauenroth VD, Stargardt T. Pharmaceutical pricing in Germany: how is value determined within the scope of AMNOG? Value Health. 2017;20(7):927–35.
21. Gandjour A, Schussler S, Hammerschmidt T, Dintsios CM. Predictors of negotiated prices for new drugs in Germany. Eur J Health Econ. 2020;21(7):1049–57.
22. Jantschak F. Pricing and reimbursement decisions in Germany. Access to innovative oncology drugs in Europe. Berlin, Madrid; 2017.
23. Staab TR, Walter M, Mariotti Nesurini S, Dintsios CM, Graf von der Schulenburg JM, Amelung VE, et al. "Market withdrawals" of medicines in Germany after AMNOG: a comparison of HTA ratings and clinical guideline recommendations. Health Econ Rev. 2018;8(1):23.
24. Isabelle DZ. International Health Care System Profiles: France. The Commonwealth Fund. New York, NY. 2020. https://www.commonwealthfund.org/international-health-policy-center/countries/france. Accessed 25 August 2021.
25. Haute Autorité de Santé. Pricing & reimbursement of drugs and HTA policies in France. 2015. https://www.has-sante.fr/jcms/c_1729421/en/transparency-committee. Accessed 17 Mar 2021.
26. Raimond V, Feldman WB, Rome BN, Kesselheim AS. Why France spends less than the United States on drugs: a comparative study of drug pricing and pricing regulation. Milbank Q. 2021;99(1):240–72.
27. Nouguez Et, Benoît C. Governing (through) prices: the State and pharmaceutical pricing in France. Rev Fr Sociol. 2017;58(3):399–424.
28. Comité économique des produits de santé and LEEM. Accord-cadre du 05/03/2021 entre le Comité économique des produits de santé et les entreprises du médicament (Leem). Ministère des solidarités et de la santé. 5 March 2021. https://solidarites-sante.gouv.fr/IMG/pdf/accord_cadre_21-24_signe.pdf. Accessed 17 May 2021
29. Dumitrescu R, Cahuzac C. New "Accord Cadre" finally released by the CEPS in France. 13 July 2021. https://www.simon-kucher.com/en-us/blog/new-accord-cadre-finally-released-ceps-france. Accessed 26 Aug 2021.
30. Comité économique des produits de santé and LEEM. Accord-cadre du 05/03/2021 entre le Comité économique des produits de santé et les entreprises du médicament (Leem). Ministère des solidarités et de la santé. 5 March 2021.https://solidarites-sante.gouv.fr/IMG/pdf/accord_cadre_21-24_signe.pdf. Accessed 17 May 2021
31. Leem. Economic regulation of medicines: Leem and CEPS (the French Economic Committee for Health Prodcuts) sign a new threeyear framework agreement (2021-2024). Les Entreprises du Médicament; Paris, 2021. https://www.leem.org/sites/default/files/2021-03/Communiqué%20de%20presse%20version%20anglaise%20accord-cadre.pdf. Accessed 17 May 2021
32. Rodwin MA. Pharmaceutical price and spending controls in France: lessons for the United States. Int J Health Serv. 2020;50(2):156–65.
33. Pharmaceutical Benefits Scheme. Fact sheet: setting an approved ex-manufacturer price for new or extended listings. 25 July 2017. Paris. Online press release https://www.leem.org/sites/default/files/2021-03/Communiqu%C3%A9%20de%20presse%20version%20anglaise%20accord-cadre.pdf. Accessed 17 May 2021
34. PBS. Procedure guidance for listing medicines on the Pharmaceutical Benefits Scheme. ed. 2.0. updated 11 May 2022 Australian Government, Department of Health. https://www.pbs.gov.au/pbs/industry/listing/listing-steps. Accessed 3 August 2022
35. Services Australia. PBS for pharmacists. 1 July 2022. https://www.servicesaustralia.gov.au/about-pbs-for-pharmacists?context=22861/. Accessed 3 Aug 2022.
36. Mulcahy AW, Whaley C, Tebeka MG, Schwam D, Edenfield N, Becerra-Ornelas AU. International prescription drug price comparisons. RAND Corporation, Santa Monica, CA; 2021. https://www.rand.org/pubs/research_reports/RR2956.html. Accessed 16 December 2021
37. Williams G, Rose A. Reimbursement of medicines in Australia: maximising opportunities in an increasingly challenging environment. Practical law. Thomson Reuters; 2016.
38. Department of Health and Social Care, ABPI. The 2019 voluntary scheme for branded medicines pricing and access: chapters and glossary. In: Care HaS, editor. gov.uk: Department of Health and Social Care; Crown; RAND Corporation, Santa Monica, CA https://www.rand.org/pubs/research_reports/RR2956.html 2019.
39. Community Care/Medicines and Pharmacy/Medicines Pricing and Supply/Cost Centre No. 17080. The 2019 voluntary scheme for branded medicines pricing and access - Annexes 2018. Eagan, MN. Online resource on law. https://content.next.westlaw.com/4-627-2988?__lrTS=20200901092320075&transitionType=Default&contextData=(sc.Default)&firstPage=true. Accessed 16 December 2021
40. Department of Health and Social Care. Statutory scheme to control costs of branded health service medicines. 2020. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/859212/statutory-scheme-to-control-costs-of-branded-medicines-impact-assessment.pdf. Accessed 15 April 2021
41. Rodwin MA. How the United Kingdom controls pharmaceutical prices and spending: learning from its experience. Int J Health Serv. 2021;51(2):229–37.
42. Rodriguez Santana I, Aragon MJ, Rice N, Mason AR. Trends in and drivers of healthcare expenditure in the English NHS: a retrospective analysis. Health Econ Rev. 2020;10(1):20. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/859212/statutory-10.1007/s40273-022-01195-xscheme-to-control-costs-of-branded-medicines-impact-assessment.pdf. Accessed 15 April 2021.
43. Wang S, Gum D, Merlin T. Comparing the ICERs in medicine reimbursement submissions to NICE and PBAC: does the presence of an explicit threshold affect the ICER proposed? Value Health. 2018;21(8):938–43.
44. MacPhail E, Shea B. An inside look at the early history of the CADTH common drug review in Canada. 2017.
45. PMPRB draft guidelines. 2020.
46. pCPA. About pCPA. 2021. https://www.pcpacanada.ca/about. Accessed 7 Apr 2021.
47. pCPA. The negotiation process. 2021. https://www.pcpacanada.ca/negotiation-process. Accessed 7 Apr 2021.
48. Standing Committee on Health, Casey (chair) B. Pharmacare now: prescription medicine coverage for all Canadians. 42nd Parliament, 1st Session 2018.

49. The drug review process in B.C. Detailed. 2020. https://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/drugrevproc.pdf. Accessed 8 Apr 2021.
50. pan-Canadian Pharmaceutical Alliance. pCPA Brand Process Guidelines. rev. April 2019. pCPA Office, Toronto.https://www.pcpacanada.ca/sites/default/files/aoda/pCPA_Brand_Process_Guidelines_EN_FINAL-s.pdf. Accessed 7 April 2021
51. Morgan, S. We need innovation in our drug price regulations. 30 May 2019. In Policy Options. IRPP, Montreal.https://policyoptions.irpp.org/magazines/may-2019/we-need-innovation-in-our-drug-price-regulations/. Accessed 19 May 2021
52. Regulations amending the regulations amending the Patented Medicines Regulations (additional factors and information reporting requirements), No. 5: SOR/2022-162. Canada Gazette. 24 Jun 2022.
53. An Act to enact the Canada Pharmacare Act. 43rd Parliament, 2nd Session ed. 2021.
54. Lexchin J. After more than 50 years, Pharmacare (and Dental Care) are coming to Canada. Int J Health Serv. 2022;52(3):341–6.
55. Committee on Oversight and Reform. Drug pricing investigation: AbbVie: Humira and Imbruvica. Staff report. Washington DC; 2021.
56. Administrative Dispute Resolution Act of 1996. 104th Congress ed.
57. IQWiG. Fingolimod:benefit assessment according to §35a Social Code Book V. Cologne. 29 Jun 2015.
58. HAS. Gilenya (fingolimod). 18 May 2018.
59. PBAC. Public summary document: fingolimod, capsule, 0.5 mg (as hydrochloride), Gilenya®, 1 Jul 2011.
60. NICE. Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis. 25 Apr 2012.
61. Canadian Drug Expert Committee. CDEC final recommendation: fingolimod. 16 Nov 2011.
62. Virji S. New analyses convince IQWiG that Novartis's MS drug is better than previously thought. Scrip. 7 Jul 2015.
63. Transparence Cdl. Avis: Gilenya 2011; 20 Jul.
64. pCPA. Gilenya (fingolimod). https://www.pcpacanada.ca/negotiation/20787. Accessed 3 Aug 2022.
65. Patented medicines for human use reported to the PMPRB in 2020*. 31 March 2022. https://www.canada.ca/en/patented-medicine-prices-review/services/annual-reports/patented-medicines-reported-2020.html#listn. Accessed 2 Aug 2022.
66. Lauer-Taxe. CGM Lauer; 2022.
67. Bruce F. Intermune's 'minor improvement' ges $25k-a-year price in France. Scrip. 12 Sep 2012.
68. Hussein S. 'My' MS, a magic pill, and what the PBS fight means to me. Crikey. 29 Apr 2011.
69. Gilenya (Fingolimod). 2022. https://www.canadapharmacyonline.com/DrugInfo.aspx?name=Gilenya6772. Accessed 2 Aug 2022.
70. First Databank. AnalySource; 2022.
71. Red Book. IBM Micromedex; 2022.
72. PBS. Fingolimod, general schedule. 2022. https://www.pbs.gov.au/medicine/item/5262Y. Accessed 19 May 2021.
73. Ontario Drug Benefit Formulary/Comparative Drug Index: Gilenya. 17 December 2021; version 2.12. Available from: https://www.formulary.health.gov.on.ca/formulary/results.xhtml?q=gilenya&type=2. Accessed 2 Aug 2022.
74. Centers for Medicare and Medicaid Services. Medicare Part D spending by drug. 2020. Available from: https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-d-spending-by-drug. Accessed 3 Aug 2022
75. Office of the Auditor General of Ontario. Annual Report 2017. vol 1. 2017. Queen's Printer for Ontario, Ontario. https://www.auditor.on.ca/en/content/annualreports/arreports/en17/2017AR_v1_en_web.pdf. Accessed 4 August 2022