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Waiting for new drugs for rare disorders in Canada

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Overview

Compared with sufferers in the United States and Europe, Canadians living with rare disorders are seriously disadvantaged because fewer new drugs for rare disorders come to Canada. When developers do bring drugs, Canada has barriers that delay or deny access for patients with unmet or poorly met health care needs.

In the first five of a series of eight articles, we discuss how these barriers impact Canadians living with rare disorders. The barriers include health technology assessments that lead to recommendations about which medicines to cover in government drug plans, and the government drug plans' collective price and terms negotiation process. Even when developers successfully pass these barriers, there's no requirement that government drug plans add medicines to their benefit lists. The result is the listing of drugs for rare disorders varies substantially across Canada, which federal Health Minister Jean-Yves Duclos

describes as a "postal code lottery" for patients. The federal government made matters worse over the past six years with a plan to drastically reduce Canadian drug prices, which caused an exceptional degree of uncertainty among patients and drug developers, resulting in further delays.

In the next two articles in the series, we consider whether proposals for national pharmacare and a Canadian Drug Agency are likely to improve access to rare disorder drugs. In the final article, we discuss the need for a comprehensive and actionable pan-Canadian strategy for rare disorders.

Huge unmet needs exist for Canadians with any of 11,000 or so rare disorders. Only 500 of the 11,000 (under five percent) have any treatments other than symptom relief or palliative care. It is high time Canadian governments put the needs of patients with rare disorders before bureaucratic overlapping processes and real or feigned shock at sticker prices.

PART 1: Regulatory approval

Health Canada is ineffective compared with American and European regulators.

Canadians living with rare disorders are seriously disadvantaged compared with sufferers in other countries because, so far, Canada has no national strategy for these disorders. Most developed countries have policies encouraging manufacturers to launch "orphan" drugs for rare disorders. This is the first in a series of articles about obstacles facing patients in Canada to access rare disorder drugs.

In Canada, we make a short-sighted virtue of raising barriers that delay or deny access to important innovative medicines, especially costly ones, for patients with unmet or poorly met health care needs. Canadians with rare disorders are particularly impacted. Patients' experiences manifestly demonstrate evidence of the barriers they confront to gain much-needed access to new medicines.

The primary step in accessing any new medicine is for its developer to submit an application regarding the drug's safety, effectiveness and manufacturing quality for regulatory authorization. Let's look at a new medicine called Roctavian for severe hemophilia A as an example to see differences between review processes of the US Food and Drug Administration (FDA) and Health Canada.

Hemophilia A is a rare genetic bleeding disorder experienced by around one in 10,000 people. Sufferers lack the normal ability for blood to clot after an injury

due to a deficiency of an essential clotting protein called Factor VIII. This inherited deficiency places them at risk for painful, potentially life-threatening bleeds from even modest injuries such as dental work.

The standard of care for severe hemophilia A is infusions of Factor VIII administered intravenously two to three times per week (that's 100 to 150 infusions per year). Sufferers' lives revolve around these infusions. Nevertheless, many continue to experience breakthrough bleeds resulting in progressive and debilitating joint damage.

Few new treatments for hemophilia A have been introduced for decades. However, the new science of human genome sequencing has resulted in novel therapies for many previously untreatable or poorly treated disorders – Roctavian is one. For several years, Roctavian has been undergoing trials in humans that have demonstrated its efficacy, safety and manufacturing quality. A single Roctavian infusion results in low levels of bleeding without need for Factor VIII infusions. That's one infusion versus hundreds.

The FDA has at least four programs to encourage drug developers to bring new therapies to patients who need them and granted Roctavian:

- **Orphan drug status:** this is a program intended to advance the evaluation and development of drugs that demonstrate promise for treatment of rare disorders.
- **Breakthrough therapy designation:** a program to allow Americans early access to important new medicines.
- **Priority review status:** this means the FDA's review performance target is four months shorter than its usual standard, although the review is no less stringent.
- **Regenerative medicine advanced therapy designation:** a recently-introduced program to facilitate the development and review of new treatments for unmet medical needs in patients with serious conditions.

Canada has no program or law to provide incentives for new orphan drugs and Health Canada has no similar programs for breakthrough or advanced regenerative therapies. Health Canada has a priority status review process but can only cope with a limited number of these reviews at a time and the priority reviews we do manage usually duplicate earlier reviews by American or European regulators.

Health Canada talks about being a world-class regulator. However, the lack of incentive programs and the limit on priority reviews tell a different story. Instead, Health Canada merely repeats the work of world-class American and European regulators.

The FDA approved Roctavian in June 2023. The European Union also gave Roctavian orphan drug status and conditionally authorized the medicine in June 2022. No submission for regulatory approval for Roctavian has been made to Health Canada so far. This could be due to the lack of a rare disorder strategy or other incentives, combined with the last six years of uncertainty around Ottawa's plan to reduce the cost of new expensive therapies to a level that would be unsustainable for their developers. It could also be due to the multiple barriers erected by payers in Canada over the last 20 years that manufacturers must overcome to get new medicines to patients who need them, which we discuss in the next four articles in this series.

Canada's place in global launches of new drugs is slipping. We have fallen out of the top tier. Wait times for patients to access new medicines are growing. Canadians with rare disorders desperately need incentives to encourage developers to launch their drugs here. Health Canada should work collaboratively with drug developers to rapidly move new medicines through its regulatory process – as the FDA does – or mutually recognize medicines approved in the United States or the European Union as being marketable in Canada.

PART 2: Health technology assessment

Canada needs a new approach to assess the cost-effectiveness of new drugs for rare disorders.

The first article in our series focussed on the lack of incentives to encourage developers to seek marketing approval for drugs for rare disorders in Canada. We now consider the second step in the process of getting a new drug to Canadians. This is health technology assessment (HTA) performed by the *Institut national d'excellence en santé et en services sociaux* (INESSS) for Quebec and the Canadian Institute for Drugs and Technologies in Health (CADTH) for the rest of Canada.

HTAs try to evaluate the cost-effectiveness of new medicines – a noble concept in principle. They generally involve measuring a new drug's cost and its health

effect. Health effect is commonly estimated using something called quality-adjusted life-year (QALY), which is intended to measure the effect of the treatment on a patient's health and wellbeing.

The metric used to assess whether a medicine is cost-effective is called the incremental cost-effectiveness ratio (ICER). ICER is the excess cost of a new drug over the cost of any existing treatment divided by the increase in QALYs achieved with the new drug over QALYs attained with existing treatment. The result is compared with a notional threshold dollar value to decide whether the medicine is cost-effective.

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QALY is a generic measure of a patient's health and wellbeing, which attempts to include both quality and quantity of life lived into a single value on a linear scale between 0 meaning death and 1 meaning full health. Several limitations exist when using QALYs and ICERs in HTAs. Three critical issues are:

- QALY is a simplistic and inadequate measure of health whereas, in reality, health is a complex, multi-faceted physical, psychological and social state. QALYs don't capture the social value of a medicine, such as reduced caregiving needs or benefits to individuals and society in productivity from reduced absenteeism from work or school and inability to perform when at work or school.
- QALYs don't account for severity of the disorder being treated. Sicker individuals frequently place more value on gains in health than less sick people. The value of health improvement for a person with a severe rare disorder causing much suffering and potentially premature death is particularly high.
- The threshold against which an ICER is assessed should be high for rare disorders. However, in Canada, a threshold of $50,000 per QALY is regularly applied by CADTH, regardless of whether a medicine is for a

common or rare disorder. Organizations in other countries use multiple and higher thresholds. CADTH's threshold has been in use for decades and never been adjusted for inflation, rarity or severity.

Other concerns exist about how HTAs are performed in Canada. First, they take time to complete, which delays access. CADTH's website shows HTAs of 62 drugs for rare disorders given regulatory approval in Canada between 2015 and 2022 took an average of almost 8.5 months. For 6.5 percent of the drugs, the time required was a year or more.

Second, HTAs are commonly performed shortly after regulatory authorization when the only information usually available on a new drug's benefits and safety comes from clinical trials. These trials are performed under carefully monitored conditions in which participants are selected because they have a narrowly-defined diagnosis and they take the medicine as prescribed, often under supervision. In real life, patients may not have precisely the same diagnosis and don't have the same level of supervision, so they often fail to take the medicine exactly as prescribed. HTAs are, therefore, typically trying to predict what a new drug's cost-effectiveness will be in everyday clinical practice based on highly-controlled environment of randomized trials.

Third, Canada's HTA agencies rarely follow-up their first evaluation after a medicine has been used in medical practice for an extensive period when both clinical and real-world evidence of its use could be assessed. Canada has no process for conditional recommendations from HTA agencies for the use of new medicines while longer-term evidence of their benefits, risks and costs are collected. Some countries, like the United Kingdom, have this type of system for selected medicines, such as cancer drugs.

Last but definitely not least, INESSS and CADTH are managed and funded by the federal, provincial and territorial governments to which they report. Input from real patients is limited. Despite claims of independence, the truth is they are not independent of their funders and governors, leading to real or perceived conflicts of duties or interests.

Canada needs a new approach to the assessment of the cost-effectiveness of new drugs for rare disorders. One that allows real evaluations of benefits, risks and costs by a truly independent agency, not ones with conflicts of duty or interest providing long-lasting recommendations based on limited initial information on health benefits.

Part 3: Price negotiation

Price negotiation bureaucracy further delays innovative drugs from reaching patients.

In the previous article in our series, we discussed concerns related to the way health technology assessments (HTAs) of drugs for rare disorders are performed in Canada. We now examine issues related to the manner in which price negotiations for these medicines for government drug plans take place in Canada.

The price negotiation process is the second of the multiple barriers erected in this country over the last 20 years that developers must overcome to get new medicines to patients who need them.

Following positive regulatory and HTA recommendations, drug developers usually look to be invited into a collective bargaining process with all government drug plans, known as the pan-Canadian Pharmaceutical Alliance (pCPA). The pCPA is an alliance of provincial, territorial and federal governments collaborating on public drug plan initiatives "to increase and manage access to clinically effective and affordable drug treatments."

The pCPA commenced business in 2010. Its objectives are to increase access to clinically relevant and cost-effective treatments; achieve consistent and lower drug costs; improve consistency in government funding decisions; and reduce duplication and optimize resource utilization.

Using recommendations from Canada's HTA agencies – the *Institut national d'excellence en santé et en services sociaux* for Quebec and the Canadian Institute for Drugs and Technologies in Health (CADTH) for the rest of Canada – the pCPA determines whether it will start a negotiation for a drug.

HTAs from CADTH now regularly include a recommendation for a specific percentage price reduction to achieve a notional cost-effectiveness threshold of $50,000 per quality-adjusted life-year (we discussed the significant limitations of this measure in our previous article). The recommended price cuts for drugs for rare disorders are frequently over 50 percent – some as high as 90 percent or more. These recommendations set the stage for price negotiation with pCPA.

If a price agreement is reached with the pCPA, the result is a letter of intent that implies the drug will be listed in any subsequent agreement with government

drug plans with an established price and listing criteria. Using the letter of intent's terms, manufacturers negotiate individual product listing agreements with each participating government plan. Government plans can choose whether to participate in a negotiation and which ones do is confidential. All plans usually participate in a pCPA negotiation for new innovative medicines.

In Australia, when a medicine has a positive HTA recommendation and a price has been negotiated, it is reimbursed in all states and territories. This is not the case in Canada. Government drug plans are not mandated to reimburse a medicine that has been successfully negotiated with their own pCPA. Years can elapse before they decide to cover a drug.

> *Since all negotiations with the pCPA are confidential, we don't know what pricing concessions drug developers make.*

Since all negotiations with the pCPA are confidential, we don't know what pricing concessions drug developers make. Limited information available for the Ontario drug plan from an independent review by the Ontario Auditor General indicates that manufacturer rebates reduce prices by 35 percent or less.

Data from the pCPA's website shows that completed price negotiations for 41 rare disorder drugs given marketing approval in Canada between 2015 and 2022 took an average of more than seven months. For 10 percent of the drugs, the time required was a year or more. The average time between Health Canada's regulatory approval and completion of the pCPA negotiation for these drugs was 20 months and, for over a third, the delay was more than two years. These steps add an extensive and potentially harmful wait time for patients.

CADTH and the pCPA have been aligning their processes for several years so that they are now closely interconnected. The result has been that medicines receiving a negative HTA recommendation rarely have a price negotiation and are not listed in government drug plans, while medicines receiving a positive HTA recommendation generally have a successful price negotiation and many are listed, but certainly not all. Canadians relying on government drug plans must wait yet again as these plans decide whether to list the medicines.

Governments that run the public drug plans are in favour of this approach to drug access. That is, only drugs considered to have "value" by certain narrow definitions are recommended for reimbursement and listed as long as the developer is willing to negotiate an acceptable price.

Anti-pharmaceutical industry activists want significant reductions in prices of drugs for rare disorders and/or an expansion of already-existing rationing of these drugs. This would lead to drug developers deciding not launch innovative rare disorder drugs in Canada due to the threat to prices and sales in other larger markets with less punitive policies. Access to innovative medicines is at risk as long as policy-makers and their advisers see them primarily through the lens of high prices, instead of the benefits they can bring to patients, scientific innovation, the health care system and the economy.

PART 4: Government drug plan listing

The time taken by government drug plan officials to decide whether to list a new rare disorder drug further extends the wait for patients trying to get access to it.

So far in our article series, we have explained that medicines are submitted to Health Canada for regulatory approval later than in the United States and Europe and that access delays are caused by health technology assessment (HTA) and collective price negotiation instituted by government drug plans.

The time taken by drug plan officials to decide whether to list a new rare disorder drug further extends the wait for patients trying to get access to it. Listing means physicians can write prescriptions and eligible patients get them filled and paid for.

Government drug plans are not mandated to list medicines that successfully pass through government-funded and managed HTA and price negotiation steps. They can negotiate further price concessions with the developer before deciding whether or not to list a drug.

Other than recognizing a need for a medicine among their covered population, drug plan officials have no motivation to list when their government employers want to contain drug costs in their siloed accounting systems (they rarely evaluate benefits of medicines to the health system as a whole or the economy). The result is the listing of drugs for rare disorders varies substantially across Canada.

Of 43 rare disorder drugs given regulatory approval in Canada between 2015 and 2022 with completed HTAs and price negotiations, seven provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick and Nova Scotia) list 65 percent or more. The percentage is considerably lower in the other provinces, especially Prince Edward Island (33 percent) and Newfoundland and Labrador (15 percent).

Although 65 percent in a majority of provinces may appear reasonable, just 22 (42 percent) of the 52 rare disorder drugs approved by Health Canada between 2015 and 2020 have been listed in seven or more government plans, despite an average of four years elapsing since regulatory approval.

Listing of drugs for rare disorders in government plans is closely aligned with outcomes of the HTA and price negotiation processes. Medicines with an unsuccessful price negotiation typically have a negative HTA and usually are not listed. However, not all drugs with a successful price negotiation are listed. In other words, a negative HTA generally means "no" listing, while a positive HTA means only "maybe."

> *Listing does not necessarily mean all patients can access a rare disorder drug.*

Furthermore, listing does not necessarily mean all patients can access a rare disorder drug. In most government plans, they are only available through special access programs subject to patients satisfying defined criteria, usually copied from clinical trials. Patient experiences indicate that drugs for rare disorders are often only accessible through government plans on a case-by-case basis, but this is not widely known until patients actually try to access them.

Access criteria recommended by HTA agencies and implemented by government drug plans have become more detailed and more stringent in recent years. Some criteria limit access to children, literally cutting off their access after a certain age. Other criteria deny access to patients in the first stages of a disorder who might benefit most, but provide access to patients at a much later stage in disease progression when patients are much sicker and may not benefit as much.

Access criteria can lead to patients taking perilous action to maximize their opportunity of meeting the requirements. For example, four drugs that treat life-threatening cystic fibrosis caused by specific rare gene mutations have been launched over the past decade – the first was Kalydeco and the most recent and more effective is Trikafta. HTA-defined clinical criteria for accessing Trikafta require untreated lung function measurements to be below a certain level, but this ignores the fact that many cystic fibrosis sufferers are taking Kalydeco and don't have "untreated" measurements. Kalydeco patients wanting to change to Trikafta face a choice: continue on Kalydeco and risk having lung function measurements that don't comply with Trikafta access criteria, or cease Kalydeco for a washout period and suffer a decline in health and lung capacity to ensure their lung function level fulfills the Trikafta criteria. This is unnecessary suffering simply to satisfy poorly-devised bureaucratic requirements copied from clinical trial criteria.

Canadians with rare disorders can wait years for a medicine to be listed in government plans and still may not be able to access it due to restrictive access criteria. In contrast, Germany has a regime for rare disorder drugs in which patients get a drug as soon as the country's regulator approves it. Once HTAs and price negotiations are complete, the outcome is made retroactive to the date of first regulatory approval as long as the budget impact of the drug across all German payers does not exceed 50 million euros. This puts patient needs ahead of HTAs and price negotiations.

It is high time Canadian governments put the needs of patients with rare disorders before bureaucratic overlapping processes and real or feigned shock at sticker prices.

PART 5: Patented Medicine Prices Review Board

The PMPRB has outlived its usefulness. In fact, the PMPRB is now a problem.

Earlier articles in our series have considered steps that are generally completed in sequence. In this article, we discuss the quasi-judicial tribunal known as the Patented Medicine Prices Review Board (PMPRB). The PMPRB's role is not to set drug prices nor to decide whether prices are reasonable or appropriate, but to prevent time-limited, patent monopolies granted for new medicines from being abused by excessive prices.

The PMPRB's jurisdiction officially begins after a new patented medicine is sold for the first time in Canada. So, its work can start soon after regulatory approval from Health Canada or much later after health technology assessment and price negotiation processes have been completed and patients can receive benefit.

Before first sale, most drug developers have a target Canadian list price in mind based on factors including investments in research and development and costs of regulatory compliance, manufacturing, distributing, sales promotion, and any patient support program. Developers assess whether their list price will be PMPRB-compliant and, if not, must decide whether to decrease the price to achieve compliance, keep the price and risk PMPRB action against the company, let its patent lapse to avoid PMPRB jurisdiction, delay launching in Canada, or not launch here. Delaying launching means a further wait for patients; not launching denies access entirely.

The PMPRB has performed its role since 1987 using a test in which a company's intended Canadian list price for a new patented medicine is compared with list prices (not actual prices paid by government and private insurers after negotiated rebates) in seven countries: France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States. Using advice from a clinical advisory committee, new medicines are categorized into breakthrough, or substantial, moderate or slight/no improvement over existing therapies. The ceiling list price for breakthrough medicines is the median of list prices in the comparator countries; progressively lower ceiling prices are set for less innovative medicines.

However, the PMPRB has been trying to expand its powers to severely reduce list prices of new drugs in Canada, especially costly rare disorder drugs. The original plan included replacing higher price countries (United States and Switzerland) in the international comparison test with six lower price countries; implementing new untested pharmacoeconomic tests to determine prices; and requiring drug developers to report details of confidential rebates negotiated with public and private insurers.

Case studies demonstrated the change in countries would likely lead to a reduction in list prices of about 20 percent. The novel pharmacoeconomic tests could reduce them by another 25 to 55 percent. The PMPRB would have been converted from a patent abuse watchdog into a price setter, and prices of new medicines in Canada could have been drastically reduced to levels potentially unsustainable for drug developers.

The PMPRB's plan met much opposition from patients, drug developers and others. Challenges in federal and Quebec courts led to rulings against using pharmacoeconomic tests and reporting confidential discounts as unconstitutional and violating trade secrets. The courts found that the PMPRB is "not empowered to control or lower prices" without evidence of excessive pricing. The change in countries in the price comparison test is all that remains. Despite claims that the withdrawal of the other proposed changes was due to the federal Minister of Health capitulating to the biopharmaceutical industry, they were withdrawn because courts and the rule of law prevailed over an out-of-control PMPRB bureaucracy aided and abetted by certain academic, journalist and partisan spins.

Regulations forcing drastic price reductions lead to delayed drug access. Extensive published work has repeatedly demonstrated this relationship. Just the threat of the PMPRB changes significantly reduced the number of new drugs submitted to Health Canada in recent years. Since rare disorder drugs would likely be particularly impacted, the proposed changes caused much concern among Canadians with unmet rare disorder health needs.

> *The PMPRB is now a problem for Canadians needed to access new medicines.*

When the PMPRB was established, Canadians had no other protection against excessive drug prices. Now we have agencies to evaluate the cost-effectiveness of new medicines and the collective bargaining tool of all federal, provincial and territorial drug plans to negotiate prices, the PMPRB is no longer as relevant. It has outlived its usefulness. In fact, the PMPRB is now a problem for Canadians needed to access new medicines.

Other countries have better access for patients and lower net prices as a result of negotiations. It is time to admit that Canada's unique approach to drug price regulation has failed and become mostly irrelevant.

Instead of trying to drive prices down by arbitrary means leading to further delays for Canadians with rare disorders, the federal government should be working positively with all provinces and territories and the biopharmaceutical industry to accelerate access to medicines for those who need them.

PART 6: National pharmacare

A government-monopoly national pharmacare would be unrealistically expensive and unlikely to succeed. Better options are available.

In previous articles in our series, we have demonstrated the various, often lengthy, delays in getting drugs for rare disorders reimbursed by government drug plans due to the many steps in the overall process and a lack of commitment to put patients first. In this article, we consider what many Canadians think will offer a solution to the variability in access across Canada – this is national pharmacare.

Opinion polls regularly show that most Canadians are supportive of the idea of national pharmacare. Key questions, however, are what does "national pharmacare" mean to Canadians, how many drugs would be covered, how would a pan-Canadian system be implemented, and how much would it cost?

Some assume national pharmacare implies access to all medicines approved by Health Canada for all Canadians who need them at modest or no direct cost to individual patients, so that there is no need for private drug insurance. The replacement of employment-based health benefits for drugs seems to be fantasyland. The health system could never afford it and the two-thirds of Canadians with these plans are unlikely to stand for it.

Approaches to national pharmacare have been studied and costs estimated by the Parliamentary Budget Officer, the Canadian Health Policy Institute, the federal government's Advisory Council on the Implementation of National Pharmacare, and the tax consulting company RSM Canada for the Canadian Taxpayers Federation. Cost estimates range from $19 to $52 billion. Political parties have offered lower amounts that would be totally inadequate. Without sufficient funding, national pharmacare would turn into just another way to ration and delay access to new drugs.

A comprehensive nationwide scheme would also be unlikely to work because it would mean all government drug plans changing their data systems and payment structures to a pan-Canadian program. Obtaining agreement for this would be extremely difficult, if not impossible, as the COVID-19 pandemic demonstrated.

Another interpretation of national pharmacare is coverage for those Canadians not presently covered by government or private drug plans. The majority of this

small and shrinking number of Canadians live in Ontario and Newfoundland and Labrador and are generally lower-income working individuals. Some academics envisage a plan that would cover only what are labelled essential drugs, with "essential" having various interpretations but frequently meaning older and cheaper medicines for common illnesses. Facilitating access to necessary medicines for lower-income working Canadians is a worthy objective, but achieving it doesn't require a government national pharmacare. The goal could be achieved more effectively and affordably using a targeted approach, such as exempting lower-income patients from copayments and deductibles in existing government drug plans.

> *"Innovative medicines that significantly improve the lives of people suffering once untreatable life-threatening disorders should also be considered essential.*

Innovative medicines that significantly improve the lives of people suffering once untreatable life-threatening disorders should also be considered essential. If the quality or existence of your life is at risk, you may be forgiven for thinking that the medicine you need is essential. Which drugs are deemed essential should not be decided behind closed doors by government officials.

Calls for national pharmacare from certain academics, journalists and politicians don't mention rare disorder drugs, which few Canadians can afford no matter what their income is. In the 2019 federal budget, the Liberals said they would introduce a rare disorder strategy and, in their 2021 election platform, promised $500 million per year to fund drugs for rare disorders. A rare disorder strategy will be discussed in a later article.

Some politicians, academics, labour unions and others have advocated for regulating drastically lower prices for new medicines to allow for the cost of national pharmacare. As we described in the previous article, forcing major price cuts by heavy-handed government rules would result in developers launching their new drugs in other countries before Canada or not bringing them to Canada at all.

Even the threat of such price cuts has led to fewer drugs being submitted to Health Canada. Between 2006 and 2014, 79 percent of new drugs for rare disorders submitted for regulatory approval in the United States or the European Union were also submitted for approval in Canada but, by 2020, the rate fell to just 39 percent. In other words, less than 40 percent of new rare disorder drugs are coming to Canadians.

Any national pharmacare program must not only ensure that lower-income Canadians can afford the medicines they need for common illnesses but must also ensure that all Canadians who need costly rare disorder drugs can obtain access to them without unnecessary cost or restrictive access criteria. This should be the goal of national pharmacare. No patient should be left behind.

Nevertheless, a fully comprehensive pharmacare program seems improbable in today's Canada given the politics of federal-provincial relations. A fill-the-gaps approach for both the working poor and those suffering from treatable rare disorders could offer a better alternative for Canadians. Patients will continue to suffer and die if the status quo continues.

PART 7: Canadian Drug Agency

Canadians need a transparent and accountable drug agency, not another overlapping bureaucracy.

In earlier articles in our series, we considered issues that can lead to delays in patients accessing drugs for rare disorders, and discussed national pharmacare which many Canadians think will offer a solution to the delays and the variability in access across Canada. In this article, we examine a development that some believe will also improve access to medicines – this is the establishment of a Canadian Drug Agency (CDA).

Over the past 20 years, a private member's motion in Parliament and other calls have proposed an independent agency that would evaluate and warn about potential drug safety issues. However, nothing came of them. The idea of the CDA was introduced by the Liberals in their 2019 election platform for an agency that would both assess the effectiveness of new prescription drugs and negotiate drug prices on behalf of some or all of Canada's government drug plans.

This objective implies that the CDA would incorporate the present health technology assessment agencies and the federal, provincial and territorial collective drug price bargaining organization and perhaps some regulatory roles.

The federal government's 2019 budget provided $35 million over four years to establish the Canadian Drug Agency Transition Office (CDATO). The CDATO began in the spring of 2021 and is responsible for developing options for a vision, mandate and plan to create the CDA.

The CDATO's initial activities include:

- Consulting with provinces, territories and a wide range of stakeholders to ensure many points of view are included in developing and implementing the CDA.
- Working with partners to determine how the CDA can support government drug plans and helping to standardize and improve access to drug and health data and analysis.
- Partnering to build a CDA well-positioned to adapt and evolve to address the pharmaceutical landscape.
- Collaborating with leaders in the appropriate use of medicines to improve health outcomes and ensure patients are prescribed the safest and most effective treatments for their conditions.

This is the typical Canadian bureaucratic approach of consulting stakeholders, although it doesn't always impact the direction in which government wants to go.

The partners are provincial and territorial governments, the Canadian Institute for Drugs and Technologies in Health (CADTH), the Canadian Institute for Health Information, Canada Health Infoway, health care professionals and other stakeholders in the health sector and academia, patients and their families and advocates, and the biopharmaceutical industry. Some partners seem to be more senior than others. Over 300 meetings have taken place between the CDATO and its partners that emphasized the need for improving the pharmaceutical landscape for the benefit of all Canadians.

A cornerstone of the plans for the CDA and national pharmacare is the development of a national formulary (list) of prescription medicines. To recommend principles and a framework for developing a national formulary of medicines that government drug plans would be willing to insure – one

that could eventually replace the list each government plan already has – the government established the pan-Canadian Advisory Panel on a Framework for a Prescription Drug List.

The reason for developing a national list is to try to introduce consistency and conformity in access across Canada. This sounds reasonable. However, we don't know whether the intention is to develop a bare-bones list of so-called essential medicines for a small number of common diseases, or a comprehensive list of medicines in line with the best provincial formularies or, even better, like the benefit lists of private insurance companies.

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Fundamental elements of how the cost of implementing a national formulary would be paid for and what patients' out-of-pocket costs would be were deemed out of scope for the advisory panel. This is ducking key questions and nonsensical for patients because being able to access a covered medicine is not simply a matter of whether it's on the list. Access also depends on whether patients can afford any required copayments and satisfy the often highly restrictive patient access criteria.

Moreover, the advisory panel intends to begin with cardiovascular, diabetes and psychiatric drugs for which the consistency of coverage by existing government formularies is already comparatively good. Instead of addressing medicines, such as rare disorder drugs, where inconsistency exists among government plans, the panel is starting with those that need the least attention.

CDATO actions so far point to the CDA being developed just as CADTH and the pCPA have – as non-transparent and unaccountable to patients and health care providers and far removed from parliamentary scrutiny. Patient engagement within CADTH is largely tokenism and not genuine participation. Real discussions take place behind closed doors, unlike other countries. Canadians need legislation that the CDA will guarantee transparency and accountability to them, not just to federal, provincial and territorial governments as CADTH and the pCPA are.

PART 8: Need for a national strategy

Unlike almost all other developed countries, Canada doesn't have a rare disorder strategy that includes incentivizing research, development and commercialization of new medicines.

In the previous two articles in our series, we discussed proposals for national pharmacare and a Canadian Drug Agency. Neither appear to include plans for accelerating access to drugs for rare disorders for Canadians who need them. Huge unmet needs exist for Canadians afflicted with any of the 11,000 or so rare disorders. Only 500 of those 11,000 rare disorders (less than five percent) have any treatments, other than symptom relief and palliative care.

Unlike almost all other developed countries, Canada doesn't have a rare disorder strategy that includes incentivizing research, development and commercialization of medicines in this country. A strategy must be more comprehensive than a focus just on medicines. It should comprise early detection and prevention and the provision of timely, equitable, evidence-based and coordinated care, in addition to sustainable access to potentially beneficial treatments.

Early detection should include fair and comprehensive screening of newborns for rare disorders. Canada currently has no national standards or guidelines or federal leadership for newborn screening, resulting in screening being inadequate and inconsistent across the country.

Diagnosing rare disorders can take months, even years, with patients being referred from specialist to specialist, often with misdiagnoses, in the hope that one will identify their condition and be able to help them. During this diagnostic odyssey, patients frequently receive treatments that may or may not be beneficial but can waste the health care system a lot of time and money. Procedures must be implemented to shorten the diagnostic process in Canada.

Many patients with rare disorders require services and treatments that are commonly not recognized as essential in Canada. Because such specialized services are lacking in much of the country, repeated travel from home to a distant centre of highly specialized care, which may be out of province or even out of country, is often necessary. This places a heavy burden on individual patients and their families.

A rare disorder strategy must include affordable access to drugs for these disorders uninhibited by burdensome and restrictive coverage rules. The creation

of new genetic and cell therapies following increased understanding of the human genome has led to treatments for diseases that 20 years ago were untreatable. However, their development is a time-consuming and costly enterprise with the potential for limited sales if the medicine is one of the few that makes it through all the testing to being accessible by patients. Consequently, drugs are priced to provide returns justifying the pre-marketing investment and inevitable failures, as well as produce a profit once successfully launched.

All these components – early detection and diagnosing, coordinated and evidence-based care, and sustainable access to potentially beneficial treatments – were elaborated in the Canadian Rare Disease Strategy managed and launched by Canadian Organization for Rare Disorders in 2015 and revived in 2022. The federal government should have used this strategy as a starting point to improve the lives of Canadians with rare disorders.

Instead, in their 2019 federal budget, the Liberals said they would introduce their own strategy and, in their 2021 election platform promised $500 million per year starting in 2022-23 to help fund drugs for rare disorders. A comprehensive strategy for rare disorders is significantly different from a plan focused only on limiting the cost of these medicines. Nevertheless, in March 2023, the federal government re-committed $1.5 billion over three years to "increase access to, and affordability of, effective drugs for rare diseases to improve the health of patients across Canada," with over 93 percent earmarked for bilateral agreements to be negotiated between Health Canada and provinces and territories.

> *People living with rare disorders are like other Canadians – they want affordable access to medicines for their unmet health needs.*

People living with rare disorders are like other Canadians – they want affordable access to medicines for their unmet health needs. No one with a rare disorder should go broke paying for their treatment and no one should be left behind. But Canadians with rare disorders don't want access denied by the federal government's plans to force down drug prices to levels that are unsustainable for developers, who could easily decide the Canadian market isn't worth entering.

Canadians living with rare disorders need many things: a comprehensive and actionable policy that includes incentives (such as time-limited market exclusivity provisions and support for data protection of new uses for old medicines) and funding to encourage developers to launch drugs in Canada; a mandatory requirement that all government drug plans list all rare disorder drugs with a successful price negotiation within a short period of time; and less restrictive and burdensome criteria that patients must satisfy before being able to obtain coverage. Without these actions, Canadians with rare disorders will not have timely access to the many innovative treatments on the research horizon that can reduce suffering, improve and even save lives. **MLI**

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