

Canadians Need Improved Access to Drugs for Rare Diseases, Not More Denial

LETTER TO THE EDITOR

Dear Editor

Sirrs et al. (2023a) discuss what they consider “explosive growth” (p. 11) in the research and development (R&D) and commercialization of expensive drugs for rare diseases (DRDs). They contend that the “status quo is no longer an option” (Sirrs et al. 2023b: 75), so it is critical to drastically reduce the prices of DRDs and/or ration access.

Canada spends a lot of money on healthcare but less per capita on orphan drugs than four of its Group of Seven peers (France, Germany, Italy and the US) and also spends less than Austria, Belgium, Norway and Switzerland (Lungu 2019). Only 3.2% of public drug expenditure in Canada was spent on DRDs in 2021, and the percentage is forecast to remain small for several years (Lech et al. 2022). Although Canadian governments like to say that they provide first-class healthcare, they have not been investing like other countries in rare diseases.

Expansion in DRDs occurred over the past 40 years following legislation in the US to provide financial and other incentives to stimulate R&D in small-market medicines (Swann 2018). The European Union, Australia, China and Japan have adopted

similar incentivizing programs but Canada has not.

Canada also has no national strategy to treat rare diseases. A pan-Canadian strategy should include early detection of treatable rare diseases and timely diagnosis of all such diseases, equitable and evidence-based care and sustainable access to potentially beneficial treatments uninhibited by restrictive coverage rules (CORD 2015). Canadians with rare disorders have extremely limited resources from which to obtain diagnoses, services and therapies and are often on their own in trying to get healthcare, which can frequently be difficult (Patient Voice 2023). The federal government recently 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” (Government of Canada 2023), but this is only a start on what is needed for a comprehensive strategy.

Drugs are developed for worldwide markets (Hooper and Henderson 2022) and not specifically for the Canadian market, which represents only about 2% of the global market. Nevertheless, some DRDs are

submitted to Health Canada for regulatory approval (Rawson 2023). After approval, developers must steer DRDs through the unaccountable, non-independent and non-transparent health technology assessment (HTA) system that makes recommendations to the same governments that manage and fund the HTA process (Rawson and Adams 2017). This is one of many conflicts of interest and/or duty embedded in healthcare bureaucracies and academia and the interplay of consulting fees in Canada.

After HTA, developers look to be invited into the non-independent and non-transparent collective price negotiation process of all government drug plans (Rawson 2019). Even when developers have successfully passed these hurdles, government drug plans are not required to add medicines to their formularies (Rawson 2022). Due to their siloed accounting practices (Deveau 2013) and their desire to contain drug budget costs, governments are reluctant to cover new expensive DRDs. Too often, they ignore the benefits that effective DRDs can bring not only to the health and well-being of patients and their families but also to other parts of the healthcare system, society and the economy (patients responding to DRDs can be productive and taxpaying contributors to society).

Here are three examples. The list price of Zolgensma, a gene therapy for young children with spinal muscular atrophy (a rare disease that causes muscle weakness throughout the body leading to disability and premature death), is C\$2.8 million, and few government drug plans offer any kind of coverage for it. However, a comprehensive analysis demonstrated that the cost of Zolgensma as a one-time treatment is less than the approximately C\$4 million for 10 years of treatment with alternative therapies with continued doses required for life (Yates and Hinkel 2022).

As another example, Luxturna – a single-dose gene therapy for a specific type of rare inherited retinal disease that causes progressive vision loss leading to blindness – costs over C\$500,000 per eye and is not covered by most government drug plans. Again, an inclusive analysis found bilateral use of Luxturna to be cost effective, given the devastating impact of the disease on sufferers' quality of life (Johnson et al. 2019).

It is not just single-dose DRDs that are cost effective. Trikafta, a therapy for life-threatening cystic fibrosis caused by its most common gene mutation that costs about C\$300,000 per year, has been shown to be cost effective in another comprehensive study (Tice et al. 2020). The full scope and cost of available drugs to treat a disease and other costs and benefits, such as avoiding additional emergency visits and hospital stays or reducing other therapies, should be fully assessed before declaring a DRD “unaffordable.”

While list prices of DRDs – such as those of Zolgensma, Luxturna and Trikafta – appear costly, manufacturers frequently negotiate discounts with large buyers such as governments. The data on DRD prices cited by Sirrs et al. (2023a) do not account for such discounts. Discussion of prices without these discounts overlooks evidence, such as the Ontario Auditor General's report that discounts can be in the range of 36% (CHP 2022).

Developing innovative DRDs is risky for drug developers, scientists and investors, requiring large outlays of time and financial resources on small markets represented by people with rare diseases. In return, developers and their investors expect to recoup their costs and make a good return, resulting in high per-patient prices for DRDs.

Sirrs et al. (2023b) suggest actions that stakeholders (i.e., governments) could take.

While we are unable to address all their proposals on this platform, we consider their most controversial suggestions:

- *Federal regulations related to marketing approval of medicines should be changed so that approval is only given after price negotiations have been completed.*

This would require a major upheaval of the *Food and Drugs Act* (1985). No other country has legislation like this. Waiting for approval and price agreement before being able to access drugs would mean Canadians, even those with private insurance, would have to wait longer for access. France and Germany do the opposite by providing immediate access to many DRDs and by putting patients ahead of HTAs and price negotiations, which follow thereafter (Little 2023; Sieler et al. 2015).

- *Governments should share information on actual prices of drugs with the public.*

What prices should be shared? Discounted prices negotiated in product licensing agreements with manufacturers are confidential. If governments attempted to reveal these prices, they would face legal action – senior courts already ruled this illegal in 2021 (Rawson and Adams 2021a) – and future rebates would be unlikely.

- *Drug developers should provide actual R&D costs in HTA submissions to allow return on investments to be considered in reimbursement recommendations.*

A requirement to reveal such confidential business information would be a deterrent to developers bringing new innovative

medicines to the Canadian market because it would have the potential to negatively impact their business globally. Attempting to institute this proposal would lead to further contentious litigation based on appeal court rulings in the recent Patented Medicine Prices Review Board (PMPRB) debacle (Rawson and Adams 2021a).

- *Provinces and territories should collaborate in managed access agreements that allow medicines to be conditionally covered while further evidence of the benefits and costs is collected.*

Experience in other countries shows that a robust digital infrastructure is needed to support managed access agreements (MAAs) (Grubert 2023). In Canada, this would require collaboration on standardized pan-Canadian data collection and analysis, something long overdue but missing as seen in the COVID-19 pandemic (The Canadian Press 2022). The development of a pan-Canadian system would not be straightforward, given the disparities in how different government systems work and what they record. Provincial and territorial governments are reluctant to change their processes.

Key elements of MAAs are making promising innovative medicines available to patients with unmet needs and limiting risks to the healthcare system by gathering additional evidence to overcome uncertainty about the medicines' benefits and/or risks. MAAs should not be used as another tool to contain spending and restrict patient access.

- *Rationing DRDs.*

Government drug plans already ration access to medicines, especially DRDs, which results in variation between provinces, leading to unfair and discriminatory access. Existing restrictive access criteria can be excessive (Rawson 2022). Some criteria are not clinically sensible when, for example, they deny access to patients who are in the first stages of a disease and might benefit the most but provide access to patients who are at a later stage in disease progression, are sicker and may not benefit as much.

Ill-conceived access criteria can also lead to patients taking harmful actions to maximize their opportunity of accessing a DRD. For example, four new DRDs that treat cystic fibrosis caused by specific gene mutations have been launched over the past decade. The first was Kalydeco, and the most recent and more effective one is Trikafta. Clinical criteria for accessing Trikafta require baseline measurements of untreated lung function. This ignores the fact that many cystic fibrosis sufferers are taking Kalydeco and have no untreated measurements for years. Consequently, patients taking Kalydeco and wanting to change to Trikafta face a choice: continue on Kalydeco and risk having lung function measurements that fail to comply with Trikafta's 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 criteria for Trikafta (Begovic 2022).

Neither of the articles by Sirrs et al. (2023a, 2023b) includes a patient perspective. The authors do not acknowledge that patients suffering and dying from over 10,000 known

rare diseases (Haendal et al. 2020; Lamoreaux et al. 2022) have a right to healthcare and have huge unmet needs for new therapies. Treatments exist for only 500 of the 10,000+ disorders – less than 5% (Lamoreaux et al. 2022).

The proposals of Sirrs et al. (2023b) are impractical within the Canadian pharmaceutical environment and, if implemented, would restrict or deny Canadians' access to innovative scientific advances in rare diseases even more than it already is. Biopharmaceutical companies would not launch innovative medicines, including DRDs, in Canada due to the threat to prices and sales in other larger markets with less punitive policies.

This is not a theoretical prediction. The threat over the past six years of drastic price reductions from proposed changes to the PMPRB's regulations and guidelines led to a significant reduction in the number of DRDs submitted to Health Canada. Almost 80% of DRDs submitted to the US Food and Drug Administration and/or the European Medicines Agency between 2006 and 2014 were also submitted to Health Canada. However, the percentage fell to only 39% between 2015 and 2020 (Rawson 2023).

Canadians' access to innovative DRDs is at risk as long as governments and their advisers perceive the value of DRDs only through the lens of high prices, instead of a collaborative approach to comprehensively accounting for the benefits they can bring to patients' lives, scientific innovation, healthcare and the economy (Rawson and Adams 2021b). If Canadians with rare diseases are to benefit from advances created from human genome sequencing, they need their governments to provide incentives for developers to perform innovative trials and launch DRDs in Canada, not deter them by adding to existing impediments (Abunassar et al. 2022).

Implementing the proposals of Sirrs et al. (2023b) would reduce the cost of DRDs in

Canada because fewer DRDs would be available here. Patients living with rare diseases and unable to access DRDs that extend their lives or improve their health and well-being would suffer more than necessary. Patients need more DRDs and better access to them, not less.

Conflict of Interest

During the past three years, Nigel Rawson has received research and consultation fees from the Canadian Health Policy Institute, the Fraser Institute, the Macdonald-Laurier Institute, the Canadian Cancer Survivor Network, 3Sixty Public Affairs and AbbVie Canada. John Adams has received research and consulting fees from the Alliance for Safe Online Pharmacies, Aptatek BioSciences, Canadian PKU and Allied Disorders and the Macdonald-Laurier Institute.

Both authors certify that they or their immediate family have had no affiliations with or involvement in any organization with any financial interest, such as employment, stock ownership, honoraria, royalties or paid expert testimony, for the past three years in the subject matter or materials discussed in this letter.

Disclosure

The views expressed are the authors' own and do not necessarily represent those of organizations with which they have collaborated.

Thank you,

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An advertisement for jobs.Longwoods.com. The background is a close-up photograph of several lit green candles with yellow flames, arranged in a row on a reflective surface. The text is overlaid on the image. At the top, the text reads "Avoid burnout" in a large, white, serif font. Below that, in a smaller white serif font, is "Healthcare Jobs: Better Careers | Better Candidates". At the bottom, centered in a white rectangular box, is the website address "jobs.Longwoods.com" in a black serif font.

Avoid burnout

Healthcare Jobs: Better Careers | Better Candidates

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