

***SUBMITTED VIA EMAIL***

Advisory Council on the Implementation  
of National Pharmacare Secretariat  
Brooke Claxton Building  
70 Colombine Driveway  
Ottawa, ON K1A 0K9

**RE: Ensuring national pharmacare works for patients living with rare diseases**

Honourable Councillors,

On behalf of a group of rare disease treatment innovators in Canada, we welcome the opportunity to contribute to the national dialogue on implementing affordable national pharmacare for Canadians and their families, employers and governments.

Our group develops and commercializes treatments for rare disorders, and consists of the following companies: Alexion Pharma Canada Corp., Biogen Canada Inc., Biomarin Pharmaceutical Inc., Horizon Therapeutics Canada, Ipsen Biopharmaceuticals Canada Inc., Shire Pharma Canada ULC, Sobi Canada Inc., and Vertex Pharmaceuticals (Canada) Inc.

For the sake of rare disease patients in Canada, we strongly encourage the Advisory Council on the Implementation of National Pharmacare to fully consider the specific issues of rare diseases in its study of pharmacare options. **We recommend that the federal government create the first truly national pharmacare program for patients living with rare disease.**

The momentum behind national pharmacare is based on the desire to ensure that no Canadian is left without adequate coverage for medications. Based on recent evidence, fewer than 5% of Canadians have no access to public pharmaceutical coverage.<sup>1</sup> However, many lack adequate coverage to pay for needed medications or to continue prescriptions. As well, coverage varies widely depending on geography and condition. Across Canada, access is slow relative to other countries with similar health care systems and time to access varies dramatically between provinces from several months to years. More than 79% of Canadians believe there should be equal access to rare disease therapies across the country.<sup>2</sup>

The rare disease innovators group therefore understands and fully supports efforts to give all Canadians equitable access to the medications they need. We would like to work with you to improve patient access to rare disease therapies

However, our concern is that without measures to recognize and address the specific challenges of rare diseases, any system of national pharmacare, regardless of which model the government eventually implements, will not adequately address the needs of patients living with rare disease.

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<sup>1</sup> Innovative Medicines Canada, Understanding the Gap: An Analysis of Prescription Drug Insurance Coverage, December 8, 2017 – <http://innovativemedicines.ca/understanding-the-gap-a-pan-canadian-analysis-of-prescription-drug-insurance-coverage/>.

<sup>2</sup> Polisen J et al, Engaging the Canadian public on reimbursement decision-making for drugs for rare diseases: a national online survey, *BMC Health Services Research*, May 26, 2017 - <https://doi.org/10.1186/s12913-017-2310-4>.

A national pharmacare model that only extends *existing coverage to more people* will not increase access to rare disease treatments or alleviate the suffering of patients living with rare disease. The current system of health technology assessment (HTA) and other related medication review and funding approval processes set hurdles that are too high for most rare disease treatments to overcome. Unlike common diseases, rare disease trials lack large scale data sets to demonstrate treatment value and because the patient numbers are small in these trials, results are more difficult to interpret. As well, public reimbursement systems have grown more complex and restrictive, further limiting the likelihood that a rare disease treatment will be publicly covered. Only 60% of rare disease treatments make it to the Canadian market. Those that are approved arrive much later (up to six years) than in the United States and Europe<sup>3</sup>. Therefore, simply expanding the system already in place will have no positive impact on access to rare disease treatments.

In this submission, we would like to draw attention to two critical issues:

1. First, we ask for caution in designing any new system. Whatever form it takes, the system should not undermine the already precarious access that rare disease patients have to new treatments.
2. Second, rare disease treatments require a distinct process, separate from that for more common medications, for regulatory approval, health technology assessment, pricing, negotiation and funding decisions.

We will address each of these issues in turn below.

Finally, we also draw attention to how proposed changes to the Patented Medicine Prices Review Board (PMPRB) regulations and guidelines will affect patients' access to rare disease treatments – and render moot any discussion of national pharmacare as it relates to these treatments. Put simply, if implemented, the regulatory changes will make Canada a less attractive place to launch all new medications – but especially rare disease treatments, most of which will no longer be economically viable if marketed in Canada.

Even if national pharmacare includes a separate pathway for rare disease treatments, as we hope, it will make little difference if none of these treatments are available in Canada due to a prohibitive pricing review regime.

## **1) The Specific Challenges for Rare Disease Treatments & Patients**

Due to the nature of rare diseases, bringing treatments for these conditions to market in Canada is more difficult than for more common conditions. The delays in reimbursement period can seriously affect patients living with rare disease. These are chronic conditions, mostly affecting children younger than six years-old, since more than 80% of rare diseases have a genetic component. Challenges start with research and development, where there is more uncertainty and longer timelines than for common conditions. Linked to this, once developed and submitted for approval, rare disease treatments struggle to overcome barriers within the review and reimbursement processes.

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<sup>3</sup> Canadian Organization for Rare Disorders, *Our Work*. Retrieved from <https://www.raredisorders.ca/our-work/>.

The end result is that public plans cover relatively fewer rare disease treatments, leaving rare disease patients in Canada with limited access to viable options.

## **Challenges in Developing DRDs**

There are a number of issues that make developing rare disease treatments more challenging compared to common medicines.

### **Low Prevalence of Rare Diseases**

Clinical trial sizes are small due to the limited number of patients suffering from these conditions. This makes it extremely difficult to find enough patients for research and development within a localized region, hence the need to recruit patients globally via numerous clinical trial sites. It's also challenging to find clinicians to administer trials. Randomized, double-blind studies are often simply not feasible or ethical, forcing innovators to rely on alternative research methodologies such as adaptive clinical trials, that are not favoured by HTA reviewers.

### **Uncertainty of Evidence and Limited Expertise**

There is more uncertainty, and thus risk, in creating these treatments. This is due to a nascent scientific understanding or consensus about clinical endpoints for rare diseases, and relatively few clinical experts or reference centres. As a result, most development of rare disease treatments ends in failure.

### **Early Exploration of Epidemiology and Pathology**

When development begins, there is little to no previous scientific or technical knowledge available to build on, so research must essentially begin at a standing start. It is hard to find data on long-term progression of these diseases. And with many unique rare and ultra-rare disorders, the pathology is profoundly diverse.

All these factors result in trials that take longer, leading to higher relative costs to develop rare disease treatments. Just as important, these factors result in longer review and approval times.

In order for innovators to recoup their investments from very small patient populations, they have no choice but to price their medicines on a per-patient basis much higher than more common treatments, though overall budget impact remains relatively lower than for more common conditions. And as a result, rare disease treatments struggle to meet cost/benefit thresholds that have been applied in the approval process to address pharmaceuticals designed for larger populations.

## **Challenges with the Current Regulatory, Pricing, HTA & Reimbursement Processes**

The regulatory environment, pricing and HTA review processes, or reimbursement process make only limited provisions for the additional challenges that must be overcome to successfully bring a rare disease treatment to market.

## **Regulatory Environment**

Other jurisdictions have established intellectual property (IP) frameworks to encourage the development of rare disease treatments. These policies have provided a range of incentives to pharmaceutical manufacturers. Conversely, Canada has no separate regulatory framework.

The previous federal government suggested it would finally develop a framework for rare disease treatments, with regulations planned between 2017 and 2019. However, with a new government taking power in 2015, Health Canada has since removed any reference to this framework or rare disease-specific policies from its website.

The federal government did launch a new website in August 2018 to provide guidance to rare disease innovators on the current review and approval process. But, by not including any tools or incentives to bring rare disease treatments to Canada, it is of limited use.

## **Pricing**

Under the current system, it is difficult for a rare disease treatment to pass the PMPRB's tests for excessive pricing. The proposed PMPRB guideline changes will exacerbate this issue.

Traditional pharmacoeconomic tools and analyses are biased in the way that they address rare disorder treatments. Requiring them in the context of HTA reviews represents an unnecessary barrier to access and negatively affects the timing of adoption by public drug plans as it is. The proposal to apply the same flawed pharmacoeconomic models to PMPRB reviews would be even more problematic for patient access and time to listing.

The proposed PMPRB reforms would raise the price threshold to a level that rare disease treatments realistically cannot meet. Overall, it will be even more difficult for the price of a rare disease medicine to be deemed "non-excessive". As a result, it will be uneconomical for manufacturers to seek market access in Canada for new rare disease treatments, which will further limit patients' access to these treatments.

In fact, it is likely that innovative pharmaceutical manufacturers would delay launches significantly in Canada in response to these reforms because of the uncertain pricing environment and the lengthy public reimbursement processes relative to other countries with similar health care systems. It must be noted that Canada is a reference country for other countries pricing frameworks and lower pricing in Canada would impact global pricing practices negatively.

## **Health Technology Assessment**

The Canadian Agency for Drugs and Therapeutic Health (CADTH), fails to account for the small clinical trial sizes associated with rare disease treatments, or that randomized, double-blind studies cannot be conducted on patients with life-threatening conditions. Essentially, existing review processes discriminate against treatments for small, extremely at-risk patient populations. In addition, CADTH reviews tend to be conducted with too much emphasis on academic methods instead of informed therapeutic and/or current patient management knowledge in a specific therapeutic area or for a given condition.

It is no surprise then, that CADTH positively recommends only 34% of rare disease treatments<sup>4</sup> – a result which is almost always required before a manufacturer can enter negotiations with the pan-Canadian Pricing Alliance (pCPA).<sup>5</sup> Moreover, a comparison of the treatment of rare disease medicines by the CADTH’s Common Drug Review versus other medications indicated that orphan medicines were not recommended 65.5% of the time, while other medicines were rejected in only 47.6% of the cases.<sup>5</sup>

Even when CADTH positively recommends a rare disease treatment, there is still only a limited chance that negotiations at pCPA will be successful because it has no special pathway for these treatments, either to set terms or ensure timely access for patients. In fact, applications and negotiations for rare disease treatments often take longer than those for less innovative medications, forcing patients to wait even longer for access for what would often be the only approved treatment for their disease.

### **Reimbursement**

In jurisdictions outside Canada, any therapy is usually publicly reimbursed after it is approved by the respective regulatory and/or HTA agency. This is not the case in Canada, where coverage depends upon public plans negotiating collectively through the pCPA with a manufacturer to establish acceptable financial terms. Even after a successful negotiation, a public plan will not necessarily add the medicine to its formulary. Adoption of new medicines on formularies by pCPA-participating plans after a letter of intent is concluded with pCPA is variable and the variation in timing is a barrier for conducting good faith negotiations in Canada.

Although some provincial / territorial drug plans have created processes for reimbursement of certain rare disease treatments, these are extremely specific to a very limited number of these treatments. In most jurisdictions, and for most rare disease treatments, no special provisions are made to ensure patients can access these medications.

## **2) The Need For a DRD-Specific Process Within National Pharmacare**

As previously outlined, we believe strongly that simply creating a system of national pharmacare that only extends existing coverage to all Canadians will have no discernible positive effect on patients’ access to rare disease treatments and not improve a system that is currently broken. A single, universal model – such as that introduced in New Zealand, and which some pharmacare advocates point to – will not suffice. In fact, adopting something similar to the system in New Zealand would likely reduce access to all medications, whether for rare diseases or common conditions.<sup>6</sup>

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<sup>4</sup> Menon D et al., Reimbursement of Drugs for Rare Diseases through the Public Healthcare System in Canada. Where Are We Now? *Healthcare Policy*. 11(1) August 2015. 15-32.

<sup>5</sup> Rawson N, Are the cost-effectiveness rules used by public drug plans denying coverage to Canadians with rare disorders? *Canadian Health Policy Institute*, August 4, 2015.

<sup>6</sup> A study by the Canadian Health Policy Institute examined prices for 248 drugs in nine clinical categories. It found that New Zealand approved 74% for marketing, compared to 90% in Canada. The number of approved medications that made the national formulary (the benefit listing rate) was lower in New Zealand than in seven of ten Canadian provinces. Rawson N, Fewer treatment options for patients if Canada adopts New Zealand's prescription drug policies, *Canadian Health Policy Institute* - <https://www.canadianhealthpolicy.com/products/fewer-treatment-options-for-patients-if-canada-adopts-new-zealand--s-prescription-drug-policies-.html>.

What is needed are separate funding mechanisms, processes, and/or distinct frameworks within the existing review processes, that assess rare disease treatments in a way that acknowledges their differences and gives patients a fairer chance of access with reasonable predictability and timeliness.

A separate process would:

- Assess the relative value of therapies differently depending upon the type of condition, the same principle behind special considerations given to oncology medications
- Consider societal good, that is, our obligation to patients with severe and debilitating conditions who have no alternative treatment options and
- Account for uncertainties in the evidence from clinical trials for rare disease treatments, due to smaller patient numbers, alternative endpoints and other challenges of rare disease

Unique treatment for rare disease treatments certainly has precedent. Most other high income countries recognize that rare diseases must be treated differently if all patients are to be treated equitably – Canada, however, has yet to make this distinction through either legislation or policy. To date, Canada has done less compared to other countries to address the unique needs of rare disease treatments, whether by updating innovation policy, regulatory approval or funding.

By introducing legislation and/or national plans specific to rare disease treatments, many countries have seen significant benefits.<sup>7</sup> For example, since the United States introduced the *Orphan Drug Act* in 1983, more than 541<sup>8</sup> distinct rare disease products have been developed (as of 2016). And in the European Union, since introducing collective policies for rare diseases member states saw the number of new medicines grow from eight to 70 in a little more than a decade.<sup>9</sup>

*“rare diseases must be treated differently if all patients are to be treated equitably”*

We advocate for a plan that meets our mutual goals. Our proposal provides an opportunity for patients to have timely access to therapies, provides payers and governments with relevant data on which to base funding decisions, and allows for industry to have a predictable system where they can bring innovative products to market and make a return on investment.

A new approach would provide immediate access to rare disease therapies at time of regulatory approval for a time-limited period. These therapies would need to satisfy specific criteria, and most importantly, would come with a commitment to evidence generation to demonstrate the value of these therapies to patients and the health care system.

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<sup>7</sup> 27 of 35 countries in a 2015 survey had implemented legislation for DRDs (either independently or as part of the EU). 18 countries had national plans in place. Gammie T, *et al.*

<sup>8</sup> See slide deck online (slide 13): Lanthier M, Insights into Rare Disease Drug Approval: Trends and Recent Developments. *FDA*. 19. <https://www.fda.gov/downloads/forindustry/developingproductsforrareconditions/ucm581335.pdf>.

<sup>9</sup> The Canadian Rare Disease Therapies Landscape: Bridging Opportunities to Reality. *BIOTECCanada*. 2015. 10 - [http://www.biotech.ca/wp-content/uploads/2016/03/white\\_paper\\_mar\\_2.pdf](http://www.biotech.ca/wp-content/uploads/2016/03/white_paper_mar_2.pdf).

## Will Properly Funding DRDs Overwhelm National Pharmacare?

When looking at the high per-patient cost and the number of rare disease treatments currently under development in innovators' pipelines, some payers may worry that routinely reimbursing these treatments will overwhelm already strained health care budgets. This worry likely extends to creating a separate process, which would lead to greater coverage of rare disease treatments by public payers.

These worries, however, are unfounded. If one looks closely at rare disease treatments within the health system as a whole, it is improbable that they will have the kind of budgetary impact that some fear. In coming years, rare disease treatments will not affect drug budgets in any significant way. Although the per patient cost of rare disease treatments can be relatively high, the overall effect on budgets is low because rare diseases affect such small patient populations.

The actual numbers bear this out. Spending on rare disease treatments represents only a small fraction of medication expenditure in Canada: 5.6% of all medication spending in 2013. In the United States, which approves more medicines generally, the percentage in 2013 was 8.9%.<sup>10</sup> This is even more manageable when one considers that publicly-funded prescription medicines costs represent a relatively small share of health care costs generally.

Our forecasts suggest that in future years the rate of spending on rare disease treatments will not increase unsustainably in Canada. As well, despite the number of rare disease treatments in manufacturers' pipelines today, many will not be approved, and soon generics will begin to replace innovative versions, limiting future spending.

## Summary

In addition to recognizing and addressing the specific challenges in developing rare disease treatments, any national pharmacare model should adequately address the needs of rare disease patients. This is true regardless of whatever model of pharmacare the federal government eventually establishes.

First, we want to emphasize again that any form of national pharmacare that looks like existing pharmacare will do nothing for rare disease patients. We recommend building a unique national regulatory and reimbursement framework for patients living with rare disease. Even plugging "gaps" in the existing system to cover those with inadequate insurance, rather than adopting an entirely new universal system of coverage, will do little for rare disease patients unless changes are made with a specific eye to these conditions and treatments.

This is why we strongly advocate for separate approval and reimbursement processes for rare disease treatments throughout the system. Only with a separate process can rare disease treatments be assessed fairly, and in a way that will improve patients' timely access and encourage further innovation in Canada. It is important to note, however, that a separate process, which should improve access to rare

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<sup>10</sup> Divino, Victoria, et. al., Pharmaceutical expenditure on drugs for rare diseases in Canada: a historical (2007–13) and prospective (2014–18) MIDAS sales data analysis, *Orphanet Journal of Rare Diseases*, 2016; 11: 68 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4875716/>.

disease treatments, will not force provinces to significantly increase spending on medications. The actual effects on budgets should be negligible.

Rare disease innovators are open to working with payers to explore innovative ways to reimburse rare disease treatments. This includes exploring the potential of managed entry agreements and conditional approvals to help payers manage budgets while improving timely access to such treatments.

For many years, Canadian governments have grappled unsuccessfully with how to manage rare disease treatments. Now, with a national conversation underway to create pan-Canadian public coverage for medications, opportunity has knocked. By building a system of national pharmacare that recognizes the unique needs of rare disease treatments, Canada can accelerate innovation in this country while alleviating the suffering of many thousands of Canadians with life-threatening or life-altering conditions.

On behalf of our group of rare disease innovators in Canada, thank you again for the opportunity to share our collective view. If you have any questions or wish to discuss any element of this submission, please do not hesitate to contact me.

Sincerely,

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