Submission to the Patented Medicine Prices Review Board: Scoping Review

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Cystic Fibrosis Canada's Response

Cystic Fibrosis Canada supports efforts to lower the costs of prescription drugs for Canadians. We believe that this must not inhibit access to new drugs but can and must be done in a way that ensures timely access by Canadians to new medicines, especially innovative and precision medicines for rare diseases.

We also expect government to ensure that the regulatory environment in Canada does not unnecessarily limit Canadians' ability to access new life-saving therapies or therapies that can significantly improve outcomes and a patient's quality of life. Any efforts intended to lower prices must be made in a balanced way that continues to encourage innovation and does not result in the delay of launches and introduction of new medicines and clinical trials to Canada.

We appreciate the candor and approach of the current consultations. The roundtable sessions were inclusive of different perspectives, key to developing guidelines that serve both patients and payers.

Summary of Recommendations

Cystic Fibrosis Canada believes the PMPRB must:

- **Consider the impact these drugs have on the people who take them, and the overall value these drugs bring to people's lives, our health systems and broader society, and determine the value of a medicine by examining both cost and impact.** The PMPRB must absolutely view high-value drugs for rare diseases through a different lens than other types of medicines. The impact cannot be ignored when considering whether the prices of these medicines are excessive.

- **Provide timely access to new medicines that address unmet need, as measured against international comparators.** Regulatory frameworks and guidelines must facilitate and not discourage nor deter rapid introduction of a comprehensive range of medicines and vaccines as well as clinical trials, which provide willing patients early access to promising new therapies.

- **Improve the affordability of medicines for individual patients, health care systems, and public and private payers.** We support efforts that **reduce the burden of prescription drug costs** that these stakeholders bear, particularly in relation to international comparators.

- **Learn from the experience of innovative medicines that did not come to Canada or were slow to come to Canada due to market uncertainty.** The transformational cystic fibrosis therapy Trikafta entered the U.S. market two years before it entered Canada. By the time it came to Canada it had already been approved in almost 40 countries. This delay – created by market uncertainty caused by PMPRB's proposed pricing guidelines – cost Canadians with cystic fibrosis their health and, in some instances, their lives.

- **Learn from the experience of innovative medicines that moved quickly through the system and have had meaningful impact.** When Trikafta finally came to Canada it through the system with great speed, going from Health Canada application to being reimbursed by all public drug plans in just 11 months. In the short time that it has been available, most people on the lung transplant list are now off the list. Many people with cystic fibrosis are going back to work and school and are living lives they never thought they would have.

- **Utilize *in vitro* laboratory data from Canadian and international patients, where it exists, as well as real-world evidence (RWE) from patients in other countries to access positive responses to precision medicines that help inform pricing decisions.**

- **Undertake an impact assessment of the draft guidelines, publicly release the assessment, and seek feedback through stakeholder consultations.** This is standard practice for new regulations and guidelines. It will ensure that the mutually beneficial objectives of patients and payers are met and will mitigate unintended consequences.

- **Engage patients and patient groups in meaningful and appropriate ways that reflect our capacity and expertise and provide us with ample time to participate in consultations.** Information must be provided in plain language, through multiple engagement methods, and ample time must be given to review information and provide feedback.

- **Improve the Board's transparency and embed greater accountability through rigorous monitoring and evaluation, conducted independently.**

Feedback: Scoping Paper

Cystic Fibrosis Canada is providing feedback on the themes below.

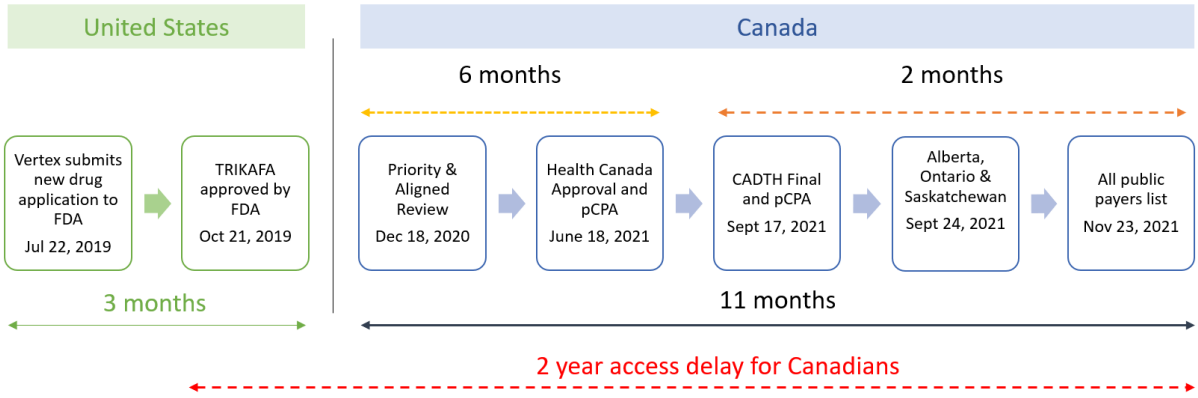
Pan-Canadian health partners, insurers and alignment with broader government initiatives

Cystic Fibrosis Canada agrees that the "development of new guidelines presents an opportunity for the PMPRB to reduce the uncertainty of the path to market for innovators, and to coordinate with and offer better support to existing regulatory and pricing bodies, as well as support initiatives of federal, provincial, and territorial activities within the pharmaceutical sector", as noted on page 12 of the scoping paper.

It was this uncertainty that caused delays in bringing game-changing drug Trikafta to Canada at a time when most other OCED countries had done so. During this time, Canadians with CF grew sicker, irreversible damage was done to their bodies, and people died while waiting for the drug, lives that may have been saved had the drug gotten to them sooner.

When the drug finally did come to Canada, it moved through the system with great speed, going from Health Canada application to being reimbursed by all public drug plans in just 11 months. With this in mind, our response to **Question 5.1** in the scoping review is that **we can learn from this experience**, with a delay in Trikafta entering the Canadian system due to uncertainties in the system and then rapid (by Canadian standards) progress through the review and reimbursement.

TRIKAFTA 12+: POINT OF ENTRY TO PUBLIC REIMBURSEMENT



Once the Health Canada review commenced, Trikafta moved quickly through the system largely due to the following:

- Health Canada's priority review designation, through which the drug was reviewed within 180 days.
- CADTH and INESSS' aligned review process, which harmonizes the HTA review with Health Canada's priority review.
- pCPA and manufacturer negotiations were completed within the Health Canada priority review window with a clause that stated the drug would be added to the funding agreement for two other therapies pending a positive Health Canada review and HTA assessment.

The Canadian drug review process is slow and highly complex, but this does not relate to the quality of the review or additional rigor. Drug reviews can occur more quickly as the Trikafta experience, and especially the COVID vaccine experience demonstrates, when there is a will and coordinated effort by all bodies. Canadians expect and deserve a system where manufacturers aren't dissuaded from making applications due to uncertainty in the system, and where all review bodies routinely coordinate efforts to ensure that all drugs, and especially life changing and lifesaving drugs for rare diseases, reach patients without delay.

Engaging with patients, health practitioners, pharmacy and other stakeholders

The lead for this theme notes that high-cost medicines ($10k/year) made up 57.1% of total patented medicines sales in 2021, up from 17.3% in 2012 However, the other side of the equation – impact – is not mentioned. How expensive is too expensive to save and/or change a life? Is box 5 an indicator that medication pricing is out of control and excessive, or is it an indicator that precision medicines are changing the lives of Canadians? A purely cost-based analysis can't answer this question and is therefore only one portion of the needed analysis.

To determine the value of a medicine, both cost and impact must be considered. What have these drugs done for people? How have these medicines impacted their lives? How have these drugs impacted the lives of caregivers? Do the people taking these drugs have improved quality of life?

In examining past pricing trends and projecting future cost impacts, the PMPRB must consider the current trends in the actual drug development pipeline. There is a significant emphasis on precision medicines and personal medicine, especially for rare and fatal diseases, and this is only anticipated to increase in the coming years. In 2012 there were approximately 80 precision medicines commercially available, and as of 2020 that number more than tripled.

Exponential growth will likely continue to characterize this space. There will be more stem cell-based and nucleic acid-based therapies that are partially or fully tailored to individual patients. Many of these therapies will be life changing or lifesaving, including some that may be fully curative. This future, which is already upon us, will require very different thinking about the cost of medicines, the value of medicines and what is an acceptable pricing level for these types of medicines. A curative therapy for a rare disease such as cystic fibrosis or sickle cell disease, or one that restores vision in a blind person can't be thought of the same way as a me-too therapy for a common ailment, such as a new antibiotic, statin or minor pain reliever, so we need to stop treating them as such.

The costs per patient for these therapies will be different, and in some cases a basket of comparator countries may be irrelevant if there are few to no precision medicines for rare diseases to compare prices to. A $1 per year drug is overpriced if there is no improvement in the health or quality of life of the patient. With this in mind, in response to Question 6.1, in the case of Trikafta we are seeing people come off the lung transplant list. Many are going back to work and school. Some have reduced the multitude of medicines people with CF must take on a daily basis. Some are having babies. Children have fewer sick days and can actively play with their friends. They have hopes and dreams their parents never thought they'd have. Caregivers have a reduced burden and can focus on other parts of their lives. Most of these experiences may seem like everyday things, but for Canadians affected by cystic fibrosis this drug is changing their lives dramatically.

With respect to **Question 6.3**, we are very fortunate that Canada and the world is experiencing a generation of new drugs for the treatment of rare diseases. Without this generation of rare medicines, many Canadians with cystic fibrosis would have never experienced all that is described above. They would be getting sicker instead of better, and some would no longer be with us.

So, while we support lower drug prices, price cannot be the sole variable that is considered. **In its efforts to drive down prices, the PMPRB can and must consider the impact these drugs have on the people who take them, and the overall value these drugs bring to people's lives, our health systems and broader society.** Therefore, in response to **Question 6.3 i the PMPRB must absolutely view high-value drugs for rare diseases through a different lens than other types of medicines. The impact cannot be ignored when considering whether the prices of these medicines are excessive.**

In terms of **Question 6.3 ii, the PMPRB, has** a drug pricing review mandate, not a mandate to conduct Health Technology Assessment (HTA). Canada already has HTA bodies. That said, the PMPRB should consider the recommendations and perspectives of international and domestic HTA bodies when determining how it will consider point of entry costs and in-market cost reassessments for life changing and lifesaving drugs for rare diseases. **When it comes to drugs for rare diseases it is important to consider real world evidence that is available or can determined**. **Very few rare disease populations are big enough to conduct randomized clinical trials (RCTs), let alone multiple RCTs.** Canada's cystic fibrosis population is no different.

For example, approximately 4300 Canadians live with cystic fibrosis and about 90% of them have at least one copy of the most common mutation that leads to cystic fibrosis, the F508del. It was possible to conduct both international and Canadian clinical trials on this population and, as a result, this is the population indicated by Health Canada.

Another 4-5% of the Canadian cystic fibrosis community have one of 176+ rare mutations that could or may benefit from Trikafta. Clinical trials were conducted on a subset of mutations in this population that had sufficient numbers to do so. However, there remain many mutations among this population for which there are so few people that clinical trials are not feasible. However, ***in vitro*** **laboratory data from Canadian and international patients, and real-world evidence (RWE) from patients in other countries shows that patients with many other mutations have positive responses to the drug.**

Over 200 Canadians with cystic fibrosis aged 2 years or older who have rare mutations are being left behind. They can't currently access this transformational therapy, even though their peers in other countries can, and it is all due to the nature of the evidence.

The US Food and Drug Administration (FDA) used *in vitro* data to expand Trikafta's label to include 177 mutations. The UK's National Health Services (NHS) and France's L'Agence nationale de sécurité du médicament et des produits de santé (L'ANSM) also used laboratory evidence to expand access for people with rare mutations.

L'ANSM is the program the CF world is watching, a model that we believe Canada should follow. Their compassionate use program covers CF patients aged 6+ who do not have two mutations deemed to be unresponsive to Trikafta. If patients have some clinical benefit, they may stay on treatment after the initial assessment period. Twenty-two of the 45 responders in the initial study have mutations not currently approved by the FDA, indicating that significantly more CF patients may benefit from treatment than have access in Canada or even the United States.

Canada already has infrastructure in place to capture and provide real world evidence (RWE) to support a similar program. The Canadian Cystic Fibrosis Registry was created in the early 1970s with the goal of monitoring important clinical trends in the Canadian CF population. The Registry has played an invaluable role in helping to improve the quality and length of life of people with cystic fibrosis. Since its inception the median age of survival of Canadians with cystic fibrosis has tripled, thanks to ever evolving medical interventions and the introduction of infection prevention and control measures.

Since the majority of CF patients attend one of 40 accredited CF clinics (paediatric and adult) within Canada, the Registry is very complete. It includes data on virtually all Canadians with cystic fibrosis, giving a comprehensive picture of the CF population in this country.

The Registry is used both by CF clinicians and researchers to improve their knowledge of disease patterns and care of patients with cystic fibrosis. The data collected within the Registry can be used to better understand clinic populations, respond to emerging health care issues, develop quality improvement initiatives and track clinical outcomes over time. These efforts will ultimately translate into improved outcomes for people with cystic fibrosis.

In addition to the Registry, the Program for Individualized Cystic Fibrosis Therapy (CFIT) is well positioned to improve access for people with rare mutations now. partnership of Cystic Fibrosis Canada and The Hospital for Sick Children, CFIT is creating a bank of nasal epithelial cells and stem cells (iPSCs)

from CF patients. With these cell samples available as models for researchers, new therapies can be tested and perfected to treat CF patients in the future.

The Israeli Ministry of Health used CFIT data and organoid data to grant off-label short-term access to Trikafta for those with rare mutations. That Canadian *in vitro* data was used to inform decision-making by a foreign ministry but is not accepted in Canada shows how absurd our current evidence practices are.

It's time for our regulatory and reimbursement systems to catch up with their peers. Cystic fibrosis can't wait.

In response to **Question 6.4**, the PMPRB can better engage with patients and patient groups by:

- **Engage patients and patient groups in meaningful and appropriate ways that reflect our capacity and expertise.** This includes providing information in plain language and seeking input through multiple engagement methods.

- **Provide patients and patient groups ample time to participate in consultations.** Patients and patient groups do not have a lot of resources and must plan for participation. Giving them a few weeks notice about consultations is a barrier that makes it very difficult for them to actively participate.

- **Undertake an impact assessment of the draft guidelines, publicly release the assessment and seek feedback through stakeholder consultations.** This is standard practice for new regulations and guidelines. It will ensure that the mutually beneficial objectives of patients and payers are met and will mitigate unintended consequences.

- **Improve the Board's transparency and embed greater accountability through rigorous monitoring and evaluation, conducted independently.**

General feedback

Canada needs effective and balanced pharmaceutical pricing guidelines that help sustain and improve the health and wellbeing of today's patients, as well as tomorrow's. To achieve these objectives the PMPRB must ensure that the guidelines:

- **Provide timely access to new medicines that address unmet need, as measured against international comparators.** Regulatory frameworks and guidelines must facilitate and not discourage nor deter rapid introduction of a comprehensive range of medicines and vaccines as well as clinical trials, which provide willing patients early access to promising new therapies.

- **Improve the affordability of medicines for individual patients, health care systems, and public and private payers.** We support efforts that **reduce the burden of prescription drug costs** that these stakeholders bear, particularly in relation to international comparators.

Thank you for the opportunity to provide feedback. We look forward to participating in future consultations.

About Cystic Fibrosis and Cystic Fibrosis Canada

Cystic fibrosis is the most common fatal genetic disease affecting 4,338 Canadian children and young adults. There is no cure. Of the Canadians with cystic fibrosis who died in the past five years, half were under the age of 38.7 years of age. Cystic fibrosis is a progressive, degenerative multi-system disease that affects mainly the lungs and digestive system. In addition to the physical effects of the disease anxiety and depression are rampant in this population. Double lung transplants are the final option for patients with end-stage disease; most fatalities of people with CF are due to lung disease.

Cystic Fibrosis Canada has dramatically changed the cystic fibrosis story. We have advanced research and care that has more than doubled life expectancy. Since being founded by parents in 1960, Cystic Fibrosis Canada has grown into a leading organization with a central role engaging people living with cystic fibrosis, parents and caregivers, volunteers, researchers and healthcare professionals, government and donors. We work together to change lives for the 4,338 Canadian children and adults living with cystic fibrosis through treatments, research, information and support.

Despite our remarkable progress together, we are not yet done. We will keep pushing, keep going further until all people with cystic fibrosis can and do experience everything life has to offer – and enjoy everything life has to offer. Learn more at www.cysticfibrosis.ca.