Submission on Protecting Canadians from Excessive Drug Prices: Proposed Guidelines to the Patented Medicines Regulations

Submitted to:
Patented Medicines Regulations Consultations
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Executive Summary and Recommendations

Cystic Fibrosis Canada is pleased to provide feedback as part of the public consultation process on the revised PMPRB guidelines.

Cystic Fibrosis Canada is a national charitable not-for-profit corporation established in 1960, and is one of the world's top three charitable organizations committed to finding a cure for cystic fibrosis. Cystic Fibrosis Canada is committed to improving the health outcomes and quality of life for people diagnosed with cystic fibrosis in Canada. We are committed to pushing for change to improve the lives and livelihoods of Canadians living with cystic fibrosis.

Cystic Fibrosis Canada supports efforts to lower the costs of prescription drugs for Canadians. We believe that this can and must be done in a way that ensures timely access by Canadians to new medicines, especially precision medicines.

We believe the PMPRB can achieve reasonable pharmaceutical price reductions in ways that result in timely access. For example, it has been estimated that the change in comparator countries from the PMPRB 7 to the proposed PMPRB 11 will lead to price drops in Canada of approximately 20%. However, we are concerned that implementing measures to further reduce prices will only serve to make Canada an outlier with respect to its OECD counterparts, making our country an unfavourable market for launching medicines, thereby delaying or denying access to innovative medicines.

Cystic Fibrosis Canada recognizes that some measures have been added to the new guidelines that could better facilitate a Health Canada application for a game-changing drug that treats up to 90% of people with cystic fibrosis, Trikafta. However, these measures do not go far enough to get this drug and future precision medicines for cystic fibrosis to Canadians who need them.

Cystic Fibrosis Canada believes the reintroduction of the Therapeutic Criteria Level scale is a positive step toward recognizing and rewarding therapeutic innovation. However, it in and of itself does not pave the way for better access to innovative medicines. These medicines, for the most part, will still be subject to the application of economic factors that will drive away interest in launching innovative medicines in Canada.

Cystic Fibrosis Canada believes that the category of "Gap Medicines" is too narrowly defined and will not help Canadians with CF access Trikafta. The manufacturer will not be able to receive Health Canada approval for the drug before the designated January 2, 2021 approval deadline, even if the application was made on the date of this submission and received Priority Review.

While Cystic Fibrosis Canada supports pricing controls as a means to improve accessibility, we believe that the pricing pendulum has swung too far, too fast, with insufficient implementation of the feedback received, or insufficient change that reflects the feedback gathered to date on what these changes will mean to patients. These changes have already created a chilling regulatory, review and reimbursement environment, one in which manufacturers are questioning whether or not to launch their products in Canada.

The concerns of the cystic fibrosis community, people living with CF, families, clinicians and Cystic Fibrosis Canada, raised in the initial consultation process on the regulatory changes in 2017 and during the guidelines consultations in 2020, have not been fully addressed by the PMPRB.

While the PMPRB seemed to be engaged in weighing the concerns of cystic fibrosis and patient organizations like Cystic Fibrosis Canada, the consultation process has not been inclusive. The information presented during consultations for both the regulations and guidelines was not easy for the average Canadian to understand, and the consultation timelines were too short. These changes will impact access to medicines not only for Canadians with cystic fibrosis, but for all Canadians who need patented medicines. It is therefore troubling that little to no effort was made to meaningfully engage average Canadians in ways that helped them understand the impact of these changes, so that they too may make evidence-based decisions about how these changes may impact them and their health.

Cystic Fibrosis Canada is also concerned about the timing and scope of these guidelines being adopted during a pandemic, when most Canadians are focused on other issues, and at a time when the courts are weighing in on the legalities and reach of the PMPRB's mandate and methods. Until these cases are settled or all appeals have been exhausted, we will continue to have uncertainty in our drug regulatory and reimbursement environment, which does not bode well for drug launches.

In our February 14, 2020 submission on the first draft of the PMPRB guidelines, Cystic Fibrosis Canada made similar recommendations to the ones noted below, which have been revised to reflect updates to the June 2020 draft guidelines. In reviewing the latter set of guidelines, we applied our February 2020 recommendations to determine to what extent our recommendations have been met. This information is available in the full brief section of this submission.

RECOMMENDATION 1:
As a commitment to lowering drug costs to reasonable levels, Cystic Fibrosis Canada urges the PMPRB to take a phased approach to implementation and begin with implementation of the changes to the comparator countries. All other changes aimed at further reducing prices should be put on hold until the PMPRB can learn about the impact of implementing phase one and until the impact of the new economic criteria can be thoroughly evaluated by an independent third party.

RECOMMENDATION 2:
As a commitment to improving access to innovative medicines for Canadians who need them now, Cystic Fibrosis Canada calls on the PMPRB to immediately amend the Health Canada *approval* deadline for Gap Medicines to an *application* deadline. Under this amendment manufacturers would have until January 2, 2021 to *apply* for a Drug Identification Number (DIN), rather than *secure* a DIN by that time.

RECOMMENDATION 3:
Cystic Fibrosis Canada recommends that implementation of an independent third party evaluate the impact of the revised economic criteria on the availability of medicines in Canada specifically to inform any decision on whether, when and how to implement the use of the new economic criteria for innovative, precision and other high cost medicines. Until this is completed and the value of these measures is demonstrated, no such measures should be adopted.

RECOMMENDATION 4:
Cystic Fibrosis Canada calls on the federal government to require that the PMPRB immediately establish a formal mechanism for meaningfully and continuously engaging patient representatives in its drug decision-making processes to ensure patient voice, choice and representation. Patient Advisory Councils aimed at improving access for themselves and others are utilized in many of Canada's comparator countries. Now that the PMPRB will be weighing in on the economic value of patient lives, patients need to be at the table to weigh in on the value of their lives too.

DETAILED BRIEF

Cystic Fibrosis Canada

Cystic Fibrosis Canada is a national charitable not-for-profit corporation established in 1960, and is one of the world's top three charitable organizations committed to finding a cure for cystic fibrosis. As an internationally recognized leader in funding cystic fibrosis research, innovation, and clinical care, we invest more funding in life-saving cystic fibrosis research and care than any other non-government agency in Canada. Since 1960, Cystic Fibrosis Canada has invested more than $261 million in leading research, innovation and care, resulting in one of the world's highest survival rates for people living with cystic fibrosis. Cystic Fibrosis Canada is committed to ensuring people diagnosed with cystic fibrosis in Canada have increased health outcomes and quality of life.

About Cystic Fibrosis

Cystic fibrosis is the most common fatal genetic disease affecting Canadian children and young adults. There is no cure. Cystic fibrosis causes various effects on the body, but mainly affects the digestive system and lungs. The degree of cystic fibrosis severity differs from person to person, however, the persistence and ongoing infection in the lungs, with progressive loss of lung function, will eventually lead to death in the majority of people with cystic fibrosis. Other typical complications caused by cystic fibrosis are:

- Difficulty digesting fats and proteins;
- Malnutrition and vitamin deficiencies due to poor absorption of nutrients;
- Sinus infections;
- and CF-related co-morbidities including CF-related diabetes and CF-related liver disease.

Cystic fibrosis is a complex disease caused by mutations in the gene for the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR). There are over 2,000 known mutations. Cystic fibrosis has a huge impact on the people who live with it, their loved ones, and on society. Every week in Canada, two people are diagnosed with cystic fibrosis, one of them through newborn screening. Approximately one in every 3,600 children born in Canada has cystic fibrosis.

More than 4,300 children, adolescents, and adults with cystic fibrosis attend one of 42 specialized multidisciplinary cystic fibrosis clinics in Canada. Cystic fibrosis is still often considered a paediatric disease because survival in the 1960's was in the single digits. However, progress in combating cystic fibrosis has been exceptional. Now, because of our ability to manage care through specialized multidisciplinary clinics and the availability of therapies to treat CF symptoms, the median age of survival of a child born in 2018 is 52.1 years; people diagnosed with cystic fibrosis in Canada have a 50% chance of living beyond that age. Over sixty percent of people living with cystic fibrosis are now adults. They are finishing school and university, launching careers in areas such as law, science, and business and starting families. Yet, their ambitions are still far too often cut short. Half of the people with cystic fibrosis who died in 2018 were under the age of 33.

Cystic fibrosis remains relentlessly progressive, comorbidities accumulate with age, and quality of life declines. Canadian cystic fibrosis patients attended over 18,900 CF-specific outpatient clinic visits in 2018. People with cystic fibrosis experience episodes of infection and acute inflammation called

pulmonary exacerbations (PEx) that frequently require in-patient IV antibiotics. PEx typically increase in frequency with age and in concert with declining respiratory function. In 2018, 1,209 individuals with cystic fibrosis cumulatively spent almost 26,500 days in the hospital. To put things in perspective, that adds up to over 70 years.

Existing cystic fibrosis medications have helped with the symptoms of the disease, but highly effective modulator therapies (HEMTs) now exist. These drugs, also called CFTR modulators, are different—they target the cause of cystic fibrosis by correcting the defective CFTR protein and don't just manage the symptoms. HEMTs can dramatically improve the health of people with cystic fibrosis.

Kalydeco, the first generation HEMT was approved for a specific mutation by Health Canada in 2012 and in 2014 for additional mutations, that altogether capture about 5% of the cystic fibrosis population. The second-generation drugs, Orkambi and Symdeko, were approved by Health Canada in 2016 and 2018, respectively. They treat about 50% of the cystic fibrosis population that carry two copies of the most common mutation, delF508. Finally, a third-generation drug called Trikafta was approved six-months ahead of schedule and labelled a breakthrough therapy by the FDA in October 2019. Trikafta can treat patients with a single copy of delF508, or up to 90% of the Canadian cystic fibrosis population. The manufacturer has yet to apply for Health Canada approval of this drug. The clinical benefit of Kalydeco and Trikafta in particular has been nothing short of spectacular, with patients and physicians alike describing them as life-changing. Evidence shows that amongst other changes, lung function is dramatically improved, PEx are significantly reduced and quality of life significantly improves[1,2].

In spite of Health Canada approval, and largely because our system of approving and reimbursing drugs for rare diseases is so cumbersome and convoluted, our population's ability to access these new, life- changing drugs is severely limited.

Health Canada first approved Kalydeco in 2012. As of February 7, 2020, six years after it was first approved, Canadians still don't have public coverage for Kalydeco for all mutations.

Orkambi was approved by Health Canada in 2016. Almost four years later, this drug is only publicly available in four provinces: in Quebec under the 'patient d'exception' program, and in Saskatchewan, Alberta, and Ontario under extremely restrictive access criteria. As of February 2020, to our knowledge, only one child with cystic fibrosis has been able to access Orkambi under those conditions in those provinces.

Symdeko, was approved by Health Canada on June 27, 2018. Currently the drug is only available through private insurance, as the manufacturer has thus far declined to put the medicine through Canada's challenging drug review and reimbursement system for precision medicines.

Trikafta is the single biggest innovation in cystic fibrosis care since the disease was first identified in 1938. The drug can treat up to 90% of Canadians with cystic fibrosis and is not yet available in Canada. Due to concerns over the new PMPRB regulations, the manufacturer has yet to apply for Health Canada approval. Cystic Fibrosis Canada is lobbying the manufacturer to submit the drug as soon as possible. It was fast-tracked for and has received approval in the U.S. and through the European Medicines Association (EMA).

It is important to note that the HEMTs described above are at the forefront of precision medicine.

Precision medicine, also sometimes referred to as personalized medicine, is where therapy is tailored to the individual characteristics of each patient, often on a genetic basis, and is broadly acknowledged to be the future of medicine, not just for cystic fibrosis, but for all of medicine. It is the nature of precision medicine that patients are stratified by the biological root cause of their condition, and therefore many
precision medicine drugs target ever smaller patient populations and face many of the same challenges as drugs for rare diseases, including high cost. This is evidenced even within the rare disease space by looking at the stratification of cystic fibrosis patients according to the above-described HEMTs.

Impact of Pricing

The limited and delayed access to precision medicines like Kalydeco, Orkambi and Symdeko, and Trikafta are examples of system failure. Canada's system of regulating, reviewing and reimbursing drugs that treat small populations is unfavourable to innovative precision therapeutics.

Drug pricing is an issue of vital importance to all Canadians since it directly relates to accessibility. But affordability is only one aspect that impacts accessibility. Timeliness to access and availability of medications throughout Canada's healthcare systems are also important considerations.

Cystic Fibrosis Canada supports policy efforts aimed at reducing drug prices and managing pharmacare costs. However, such efforts need to consider the broader context of availability and access to innovative medicines, like precision drugs, that are at the forefront of medicine.

We agree with the PMPRB that changing the basket of comparator countries used by the PMPRB will have the desired effect of lowering the costs of drugs in Canada to or below the median of Organization for Economic Cooperation and Development (OECD) countries, a price drop of 20% or more. However, implementing additional measures to further reduce prices will only serve to make Canada an outlier with respect to those same OECD counterparts and an unfavourable target for the pharmaceutical industry, which in turn puts Canadians at risk for further delays in accessing innovative and precision medicines.

RECOMMENDATION 1:
As a commitment to lowering drug costs to reasonable levels, Cystic Fibrosis Canada urges the PMPRB to take a phased approach to implementation and begin with implementation of the changes to the comparator countries. All other changes aimed at further reducing prices should be put on hold until the PMPRB can learn about the impact of implementing phase one and until the impact of the new economic criteria can be thoroughly evaluated by an independent third party.

As some of these issues were not addressed in the June 2020 draft guidelines, this recommendation remains outstanding and is even more urgent now than it was then. If the Government of Canada really wants to lower drug costs, it should implement this measure while the rest of the measures are evaluated by the independent third party.

Impact on Access

Even before the recommended PMPRB changes, Canada was not on par with other developed nations when it comes to providing timely, equitable and publicly-funded access to new treatments. In Canada, the wait from Health Canada approval to public drug plan reimbursement for life-sustaining and life-

changing medicines for cystic fibrosis was 449 days across provinces, comprising 80% of the eligible national public drug plan population and ranking Canada 15th of the top 20 OECD countries[3]. This is why Canada needs a fair and fast process to get game-changing medicines to the people who need them.

According to Innovative Medicines Canada, between 2011-2016 Canadian jurisdictions covered far fewer new medicines than most comparable OECD countries. In the best-case scenario[1], Canada covered 70% of available medicines. But country-wide[2] this figure fell to 39%. For rare disease medicines, the gap was even larger: only 29% were publicly reimbursed in Canada, country wide, while the OECD20 sat at a staggering 95%.

Canada, as a whole, represents only 2-2.5% of the global pharmaceutical market. But as revealed above, Canada isn't a single market. At Cystic Fibrosis Canada we are painfully aware of the broad disparities in access to specialized cystic fibrosis drugs across multiple Canadian jurisdictions.

Medicines, and therefore maximum prices, were previously categorized based on clinical impact: breakthrough, showing substantial improvement, moderate improvement or slight/no improvement over current therapy. Maximum prices were allowed accordingly. Under the new regulations, medicines will be classified as either Category I or Category II based on market characteristics, including affordability measured by its market size with little regard to innovation except what is suggested by the pharmaco-economic value. It must be noted however that cost-effectiveness methods do not work well when evaluating drugs for rare disorders. Models are known to perform poorly for rare or precision medicines[4,5,6], are based on assumptions and results can vary widely even when using the same data [7,8]. The new regulations provide no consideration for precision drugs, drugs for rare disorders or other high- cost specialized therapies.

Much about the new economic criteria is experimental, in that these methods have never been tried anywhere before. The new regulations have injected a significant level of uncertainty for companies considering where to launch new innovative and precision medicines. Uncertainty represents risk, and businesses dislike risk. Given the uncertainty over price and even the ability to access the entire Canadian market there is great concern[9] that companies will defer launching drugs in Canada, if at all. We are already seeing this happen in the cystic fibrosis arena. The Canadian population should not be subjected to experimental processes that could impact their health without proper independent due diligence.

RECOMMENDATION 2:
As a commitment to improving access to innovative medicines for Canadians who need them now, Cystic Fibrosis Canada calls on the PMPRB to immediately amend the Health Canada *approval* deadline for Gap Medicines to an *application* deadline. Under this amendment manufacturers would have until January 2, 2021 to apply for a Drug Identification Number (DIN), rather than *secure* a DIN by that time.

RECOMMENDATION 3:
Cystic Fibrosis Canada recommends that implementation of an independent third party evaluate the

[1] Canada (Best-case) = Public reimbursement in at least one provincial reimbursement list covering at least 20% of the Canadian publicly-covered population.
[2] Canada (Country-wide) = Public reimbursement in a number of provincial reimbursements lists together covering at least 80%of the Canadian publicly- covered population.

impact of the revised economic criteria on the availability of medicines in Canada specifically to inform any decision on whether, when and how to implement the use of the new economic criteria for innovative, precision and other high cost medicines. Until this is completed and the value of these measures is demonstrated, no such measures should be adopted.

Cystic Fibrosis Canada called for this work to begin our February 14, 2020 submission to the draft guidelines. Until such a party is appointed and completes this work, this recommendation remains outstanding.

Stakeholder input

Cystic Fibrosis Canada appreciates that the PMPRB has tried to consult with patients. However, these efforts were not nearly enough and did not pay off. Given the complexity and technical nature of the guidelines, many patients and patient groups are still struggling to fully comprehend the impact that these changes will have on drug access to patented medicines and, ultimately, their health.

In its own words, "The PMPRB has committed to developing and conducting an extensive monitoring strategy, the Guidelines Modernization and Evaluation Process (GMEP), to track the impact of the Guideline changes on patients, health care providers, and other stakeholders"[10].

The PMPRB will use administrative, commercial and internal data sources in its decision-making but has not indicated how it will listen to patients and patient organizations, nor use the rich data available to such organizations like Cystic Fibrosis Canada in tracking the impact of the Guidelines.

Despite having one of the most robust and oldest CF patient registries in the world, Cystic Fibrosis Canada has yet to be approached by the PMPRB regarding utilization of this data as a means to demonstrate value in accessing innovative CF medicines. Cystic Fibrosis Canada is available to work in partnership on this front.

RECOMMENDATION 4:
Cystic Fibrosis Canada calls on the federal government to require that the PMPRB, along with other appropriate agencies, immediately establish a formal mechanism for meaningfully and continuously engaging patient representatives in its decision-making and processes to ensure patient voice, choice and representation. [11]

To our knowledge, no formal mechanism for meaningful and continuous engagement of patient representatives has been established since our mention of this recommendation in our February 2020 submission. This recommendation has not been met. There are many examples of meaningful patient engagement in drug access decision-making. Bodies like the Canadian Agency for Drugs and Technologies in Health (CADTH) and the pan-Canadian Oncology Review (pCODR) have patient advisory committees.There is absolutely no reason why the PMPRB can't involve patients in meaningful ways when so many other jurisdictions have and given the significant impact of the PMPRB's work on patient's health, it is essential they do so.

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