Towards a Value-based and Pan-Canadian Rare Disease Strategy

Innovative Medicines Canada

Submission to Health Canada Consultation on Drugs for Rare Diseases

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About Innovative Medicines Canada

Innovative Medicines Canada (IMC) is the national association of 45 biopharmaceutical and vaccine companies who are working steadfastly, with Canadian governments, to address the COVID-19 pandemic.

Guided by a strict Code of Ethical Practices, we work with governments, insurance companies, healthcare professionals and stakeholders to advance the field and enhance the wellbeing of Canadians. We are committed to being valued partners in Canada's healthcare system. IMC member companies produce the diagnostics, medicines and vaccines that will enable Canada to emerge from the global pandemic that continues to have devastating impacts on the health and prosperity of Canadians. According to Statistics Canada, in 2018 the sector added almost $15 billion in value added (GDP) to the Canadian economy and supported over 100,000 full-time equivalent jobs within Canada. Additionally, it invested nearly $2.0 billion on research and development. These investments directly benefit rare disease patients and constitute a critical component of our industry's contribution to Canada's innovation ecosystem.

Recommendations

1. *The federal government should work collaboratively with provinces, patients, clinicians, and industry to implement a value-based, pan-Canadian rare diseases strategy.*
2. *This policy should be developed and assessed according to several key principles outlined below, which include the need for timely patient access through innovative payer agreements. There are several international models discussed below that can be instructive to help create a made-in-Canada approach.*
3. *The strategy should be sensitive to the needs of provinces and patients and ensure that patients benefit directly from federal funds:*
    - *The federal government should work with provinces on an agile framework to meet provincial needs and province-specific gaps in coverage. For example, a flexible approach would provide federal support to jurisdictions with insufficient coverage to help improve coverage, while allowing those provinces with high out-of-pocket patient costs to direct funds to co-payment assistance.*
    - *The federal government should avoid creating new layers of bureaucracy and should instead focus on creating a dedicated and accelerated rare pathway for regulatory, assessment, and negotiation institutions. Any expert recommendation committees should involve rare disease experts, include direct engagement with patients and manufacturers, and de-emphasise the role of traditional pharmacoeconomics, which is poorly suited to assess drugs for rare conditions.*
    - *An office of an independent "Rare Disease Access Advocate", selected with patient input, could be engaged to help establish such a pathway and have a mandate to facilitate timely access.*
4. *The pending changes to the Patented Medicine Prices Review Board's (PMPRB) regulations are antithetical to the success of any rare disease framework. Health Canada has heard from numerous stakeholders through meetings and townhalls on the critical link between rare policy and the prejudice that will be caused by the PMPRB changes, particularly with respect to the new economic factors. At a minimum, the Health Canada should delay the implementation of PMPRB regulatory changes until the COVID-19 pandemic has abated and a pan-Canadian framework for rare disease has been established.*

Objective Analysis and Neutral Framing of Cost and Value are Needed

Canada remains one of the only developed countries without a rare disease policy.[i] Consequently, there are now many international learnings that can be instructive for Canada to help build a successful strategy. In additional to the international best practices discussed below, it is important that any pan-Canadian rare policy is based on a careful and objective assessment of the rare disease landscape. The Government of Canada should commission an independent and transparent assessment of the rare disease market in Canada. Reliance on non-transparent PMPRB analyses, which seem designed to paint a dire picture of costs in support of the pending regulatory changes, has resulted in the framing of rare disease medicines primarily with respect to their upfront costs (e.g., "Expensive Drugs for Rare Disease"), as opposed to long-term value within the health care system and particularly to patients. During the recent stakeholder townhalls held by Health Canada to discuss this issue, the message that the current consultation document is unduly focused on costs was a constantly repeated theme.

While the prices of drugs for rare diseases (DRDs) reflect the high development cost and capital risk which must be amortized over time and small patient populations, spending on rare disease medicines is not "out of control" nor necessarily a cause for undue concern. Recent analysis conducted by IMC from a custom dataset developed by IQVIA suggest that in 2019 (the most recent year available) non-oncology DRDs represented 2.9% of total drug spending by all payers. Private payers covered one-third of that cost, with public payers and hospitals covering the remaining two-thirds.[ii] This is proportional to the patient population affected by rare disease which is estimated by Dr. Alex Mackenzie of CHEO to be approximately 2% to 3% of the population.[iii] CORD estimates a significantly higher figure, citing 3 million impacted Canadians. The differences in both scope and spending trends speak to the importance of definitional issues and the need for clarity regarding future policy approaches. See the table below for additional context on a rare disease definition.

Rare medicines bring tremendous value to patients and the health care system. The true costs to the system, patients and caregivers are felt most when *not* treating patients with the medicines they need.[iv] Our industry supports a broader and more value-focused discussion on DRDs. We remain open to provincial policies that are connected to the real-world value that rare disease medicines provide to patients and the health system. Canadians also recognize that addressing health challenges requires investment and rare disease policy cannot be predicated on an optimistic view that Canadian governments will automatically have access to the world's highest-quality innovations without paying for a share for the cost of those innovations through pricing comparable to international peer jurisdictions (see discussion of PMPRB below).

Given recent trends and the promising future research pipeline for new rare disease treatments, the innovative industry recognizes the need for balance and affordability due to significant innovations and high unmet patient need which remains a challenge in Canada. For these reasons, **our sector is strongly supportive of value-based reimbursement frameworks to ensure good value for money** (see principles and examples below).

Principles for a Value-based and pan-Canadian Framework Leveraging International Best Practices

Existing clinical trial and Health Technology Assessment (HTA) processes are ill-equipped to assess value and manage uncertainty at the time of rare disease product launch. This is due to the inherent limitations of small patient populations which result in evidence limitations and the need for ongoing real-world evidence generation. Furthermore, current product listing processes and agreements could evolve to better reflect a value-based process where products are funded at time of launch but then reassessed after some period of time on the market (please see the examples below). To facilitate such a value-based framework, the federal government should consider supporting provinces and patients through targeted investments in real-world data infrastructure.[v]

Our innovative industry is supportive of lifecycle management approaches that focus on providing patients with early access to needed medicines. For many rare disease medicines, Real World Evidence (RWE) can play a role through conditional assessments contingent upon follow-on RWE or other evidence being submitted. This could result in improved and more timely access for patients to innovative new therapies while addressing payer concerns with respect to uncertainty and risk. Canadian governments should establish a pan-Canadian rare disease framework based on the following principles:

Key Principle	**Illustrative Example**
Federal rare disease policy must be sensitive to provincial and patient needs – Success will be dependent on collaboration including collaborative decision-making	Greater involvement of all stakeholders is needed at the decision-making table. *Example of collaborative decision-making:* The Scottish Medicines Consortium which offers inclusive advice on the funding of new medicines and carefully considers evidence from patients, clinicians and pharmaceutical companies when making decisions.[vi] *Example of meeting provincial needs*: Federal funds could be distributed on the basis of province-specific needs for use in a manner determined by provinces, based on a transfer model (e.g., a rare disease transfer, similar to the *Canada Health Transfer*).

Key Principle	Illustrative Example
Clarity on a predictable definition of rare diseases	Canada should clearly define what qualifies as a rare disease for the purposes of aligning approaches and interpretations across all regulatory and reimbursement reviews. IMC would welcome further consideration of international practices in this area and would suggest Canada look to the European prevalence-based approach (currently no more than 1 in 2000) as a constructive point of departure. For clarity, due consideration should also be given to the inclusion of other appropriate qualifying criteria including disease severity and extent of unmet need. From an implementation standpoint, the same definitions, scope, and criteria for identifying rare diseases should be applied consistently across all agencies and levels of government and processes. This would promote a more consistent and predictable approach for patients and other stakeholders and enable more integrated, pan-Canadian approaches to improving data collection, screening and detection, and the timeliness and consistency of coverage across funders.
Public payer policies must include a predicable pathway for timely access with fair value for patients, payers and companies	Example: Germany has immediate coverage on product launch and free pricing at a temporary level followed by a value review tailored for rare and also provides dedicated reimbursement-related incentives.[vii] For some rare disease medicines with ongoing evidence generation needs, France has a mechanism for a comprehensive study/registry of all patients treated to provide data from real-world outcomes to be submitted for a reassessment within five years[viii] Leveraging these best practices, a made-in-Canada approach could include: • A streamlined rare disease pathway; • A dedicated rare disease expert committee to replace CADTH's generalist HTA committee. The cancer system and the former Pan-Canadian Oncology Drug Review (pCODR) could be an instructive model for a dedicated review path;

Key Principle	Illustrative Example
	• Exempting some smaller budget products from initial HTA review, to be reviewed later in the product lifecycle, should also be considered; • Dedicated pCPA negotiation stream for rare medicines that include pan-Canadian coverage with evidence development and innovative value-based reimbursement models and predictable timeframes for funding decisions; and • Managed access agreements with regular re-review - Canada could consider conditional uptake of products on the basis of Phase II trials with ongoing evidence generation. • Office of an independent "Rare Disease Access Advocate"
High quality evidence generation and analytics are needed to address clinical uncertainty and value	To facilitate the principles set out above, federal funding for disease registries, and RWE development for the purpose of informing product reassessments noted above. Germany has greater acceptance of this type of non-randomised or non-comparative data for rare disease drugs. France leverages a comprehensive study registry (see above). Secretariat and research support for clinical networks (e.g., metabolic disorder clinical groups) could also be beneficial.
Incentives for rare disease innovation are important but have not been part of the federal discussion to date	Example: US Orphan Drug Framework provides extended IP protection;[ix] There are also many incentives in Europe through EU Orphan Drug Legislation and extended IP provisions for orphan and paediatric medicines (See detailed EU information which includes up to 12 years protection)[x] The EU region has seen the strongest growth in clinical research on rare diseases since the mid 2000s globally: Annual activity has increased by 88% between 2006 and 2016, with the EU-5 countries experiencing an even bigger increase of 104% during that period.[xi] However, removing strong disincentives to introducing new rare disease drugs, such as the PMPRB's new economic factors, are a precondition for a successful Canadian rare disease strategy.

Key Principle	Illustrative Example
Public and private payers must both pay a fair share: avoid cost-shifting from private plans to public plans which would benefit for-profit insurers	There is an ongoing role for private payers to play in the reimbursement of drugs for rare diseases. Private insurers only fund approximately 1/3rd of Canadian rare disease medicines and have many tools at their disposal to address costs such as listing negotiations with manufacturers as well as expanded risk-pooling mechanisms similar to current Québec private market pooling mechanisms.[xii] It is important that unnecessary additional costs not be downloaded to the public payers.
Rare disease policy cannot be successful in context of the pending PMPRB regulatory changes, especially new economic factors	A successful rare disease policy and pending changes to the PMPRB cannot co-exist. Health Canada should amend *Patented Medicines Regulation* to remove "New Economic Factors"[xiii]. (See below and appendix)

Fundamental Inconsistency between DRD Policy and PMPRB Reforms

We are calling on the federal government to show leadership on behalf of all Canadians to improve the future prospects for rare disease patients and implement a pan-Canadian rare disease strategy as an alternative to more damaging elements of the PMPRB reforms. The principles and international best practices noted above can be instructive to help create a more balanced Canadian policy.

Future access to rare disease medicines is currently in significant jeopardy due to price regulation policy and the PMPRB's experimental new economic factors. PMPRB reforms would use binding HTA to drive prices to unsustainable levels. As demonstrated by documents secured under the *Access to Information Act*, Health Canada is aware of major reductions that exceed 90% given PMPRB's access to the new economic factors (see appendix). While PMPRB's Guidelines finalized in the Fall 2020 contain some possible price reduction caps, these caps may not be relevant at the PMPRB hearing level and do not provide manufacturers with basic price predictability and would require unsustainably low prices in comparison to international peer jurisdictions.

The industry has offered an additional $1 billion to help address rare diseases and a made-in-Canada manufacturing and commercialization accelerator. We also put billions of dollars in savings on the table for all patented medicines as an alternative to more damaging and unpredictable PMPRB reforms. Third party analysis suggest that Canadians could realize $19.8 billion in savings over ten years on international basket changes alone (i.e., through price comparisons with other countries). This significantly exceeds Health Canada's estimate of $13.2 billion in savings. However, Health Canada has not engaged in meaningful dialogue on policy alternatives and has consistently ignored concerns of many stakeholders, including

patients, the rare disease community, life sciences groups, provinces including Québec and Ontario, and producers of innovative medicines and vaccines.

A suspension of the July 1st, 2021 scheduled implementation of changes to the PMRPB is needed to allow all parties to address the COVID-19 pandemic and to provide more time to discuss alternative PMPRB changes that will still meet government's policy objectives including affordability and rare diseases. The pending PMPRB changes will not make "drugs more affordable for those with rare diseases". To the contrary, it is widely acknowledged that these changes will impact the timely launch of new medicines in Canada and make fewer rare disease medicines available to those Canadians who urgently need them.

Even under the current regime, CORD estimates that even under the current regime only 60% of treatments for rare disorders are submitted for approval in Canada, and most get approved up to six years later than in the U.S. and Europe. CORD concludes that 'people with rare disorders in Canada are missing out on treatments that could save or significantly improve their lives.'[xiv]

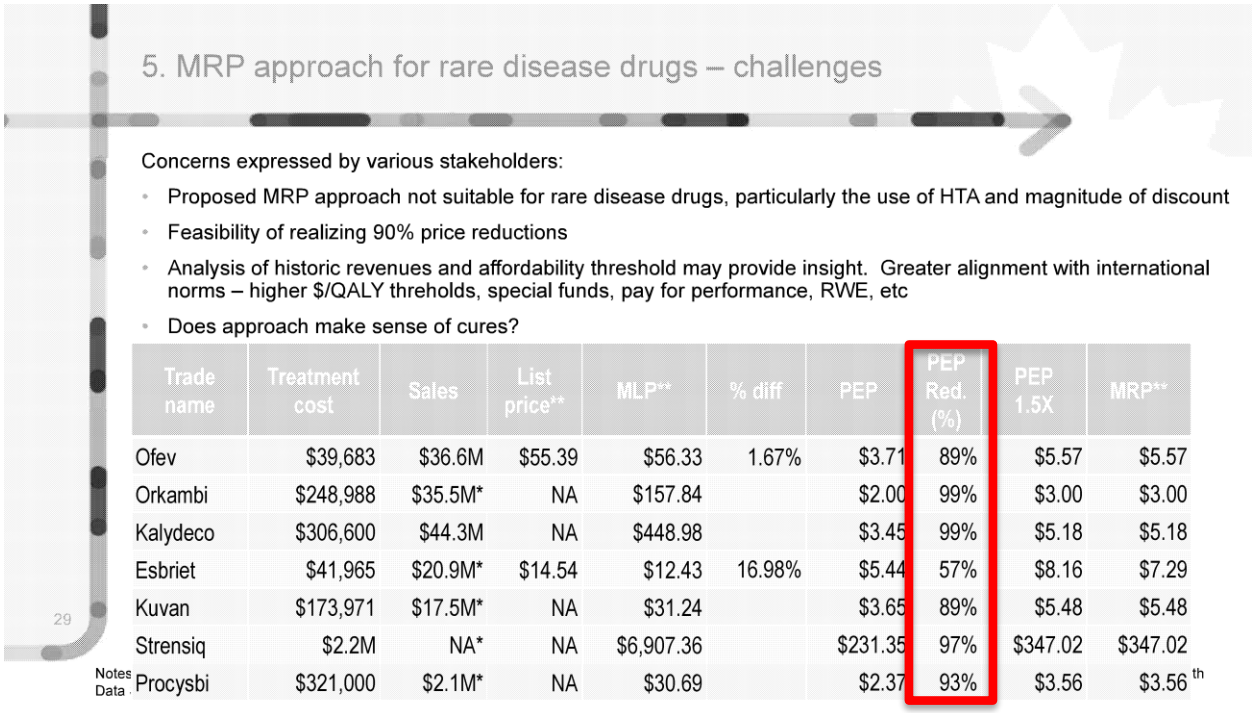
The imposition of flawed and controversial policy changes during a national health crisis is inappropriate and unreasonable given the need for governments, industry, and other stakeholders to prioritize resources to address COVID-19 and move forward with a rare disease policy framework.

Conclusion

The innovative pharmaceutical industry is committed to working with governments at all levels and with stakeholders to co-develop a value-based and pan-Canadian rare disease strategy to ensure patients have better coverage for treatments. We believe that all governments and stakeholders want to ensure that critical medicines that can make the difference between life and death are delivered to Canadian patients in a timely manner. The principles and examples above can be used to help create a made-in-Canada strategy that is sensitive to the unique features of Canada's federation while at the same time leveraging international best practices. A true partnership among all interested parties and with common goals is key to ensuring patients have access to the drugs they need not just to survive, but to live longer, healthier lives. Such equitable access cannot be dependent on income, age, or postal code. Together, we can build a framework to support innovative agreements which measure the fair value and contribution of medicines for patients and payers through value-based reviews and enhanced predictability for payers and all stakeholders. We look forward to continuing the dialogue with Health Canada and other stakeholders once additional information regarding the government's DRD policy intentions become available.

Appendix: Government aware of "Challenges" regarding PMPRB and Rare Disease Medicines

In January 2020, PMPRB provided its government Health Partners with a summary of several concerns expressed by stakeholders regarding the impact of PMPRB pharmacoeconomic price (PEP) and analyses of required discounts on rare disease that exceed 90% in many cases. These analyses were not made public but were obtained through requests under the *Access to Information Act*. With PMPRB reforms becoming effective in a matter of months on July 1, 2021, industry and stakeholders have significant ongoing concerns regarding the negative impact the reforms will have on access to rare disease medicines. Federal rare disease policy can offer a more reasonable and value-based alternative to the PMPRB's new economic factors.



5. MRP approach for rare disease drugs – challenges

Concerns expressed by various stakeholders:

- Proposed MRP approach not suitable for rare disease drugs, particularly the use of HTA and magnitude of discount
- Feasibility of realizing 90% price reductions
- Analysis of historic revenues and affordability threshold may provide insight. Greater alignment with international norms – higher $/QALY threholds, special funds, pay for performance, RWE, etc
- Does approach make sense of cures?

Trade name	Treatment cost	Sales	List price**	MLP**	% diff	PEP	PEP Red. (%)	PEP 1.5X	MRP**
Ofev	$39,683	$36.6M	$55.39	$56.33	1.67%	$3.71	89%	$5.57	$5.57
Orkambi	$248,988	$35.5M*	NA	$157.84		$2.00	99%	$3.00	$3.00
Kalydeco	$306,600	$44.3M	NA	$448.98		$3.45	99%	$5.18	$5.18
Esbriet	$41,965	$20.9M*	$14.54	$12.43	16.98%	$5.44	57%	$8.16	$7.29
Kuvan	$173,971	$17.5M*	NA	$31.24		$3.65	89%	$5.48	$5.48
Strensiq	$2.2M	NA*	NA	$6,907.36		$231.35	97%	$347.02	$347.02
Procysbi	$321,000	$2.1M*	NA	$30.69		$2.37	93%	$3.56	$3.56 th

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Notes Data

[i] McMillan and Campbell, "We need a 'made in Canada' orphan drug framework" CMAJ, Oct 2017 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5647165/#b1-189e1274

[ii] These are based on DRD's that meet either the US or EU definition of rare.

[iii] https://www.ourcommons.ca/Content/Committee/421/HESA/Reports/RP10349306/hesarp22/hesarp22-e.pdf

[iv] It should be noted that rare disease medicines are discounted as part of confidential product listing agreements which provide significant value to Canadian public and private payers.

[v] A pan-Canadian rare disease policy must be thought of in broad terms and should address a range of pan-Canadian issues such as incentives for innovation which are important to attract early-stage venture capital, clinical trials which can experience challenges in recruitment, investment, and gathering evidence, as well as issues related to screening and detection, such as the availability of diagnostics and testing at birth for "at risk" populations.

[vi] See "How We Decide" which includes a dedicated Patient and Clinician Engagement (PACE) meeting. This additional step allows Scotland "to hear more evidence from patient groups and clinicians on the added value of a medicine which may not always be captured in the company's submission. At this stage, the company can also submit or improve a Patient Access Scheme (PAS), which can help to improve the value for money of the medicine. The output from a PACE meeting is a major factor in SMC decision making." https://www.scottishmedicines.org.uk/how-we-decide/ Special treatment for "ultra-orphan" drugs is also available https://www.scottishmedicines.org.uk/how-we-decide/ultra-orphan-medicines-for-extremely-rare-conditions/ ; Similarly, in Germany patient representatives participate in all decision making sessions; https://8c3e11d9-5f36-452f-abe3-c95befd6e85d.filesusr.com/ugd/e1a359_3ce53a1d83e84d6d83866c55195d1056.pdf

[vii] Germany provides a "guaranteed additional benefit for orphan drugs [which] ensures a strong negotiation position or strengthens the negotiation position of the company when negotiating the reimbursement price paid by the statutory health insurance funds. Consequently, it ensures a reasonable reimbursement for medicines for rare diseases, taking into account the possible limitations that medicines for rare diseases might face in the development and marketing process." Also, the acceptance of non-randomised or non-comparative data is greater for drugs with orphan designation and "the rarity of the disease or a special target population (e.g., children) are taken into account also for assessment of new medicines without orphan designation." https://8c3e11d9-5f36-452f-abe3-c95befd6e85d.filesusr.com/ugd/e1a359_3ce53a1d83e84d6d83866c55195d1056.pdf

[viii] Glennie, J, "International HTA Approaches to Rare Disease Medications: Case Study and Lessons for Canada" *Provincial Reimbursement Advisor,* vol 23, issue 4, 2020.

[ix] U.S. Orphan Drug Act includes, exclusive marketing rights, tax credits for certain clinical development expenses, grant support, and other incentives for sponsors to develop drugs for people with rare diseases. https://www.ncbi.nlm.nih.gov/books/NBK56185/

[x] See EMA summary of incentives: https://www.ema.europa.eu/en/documents/presentation/presentation-data-exclusivity-market-protection-orphan-paediatric-rewards-s-ribeiro_en.pdf

[xi] "Benchmarking Success: Evaluating the Orphan Regulation and its impact on patients and rare disease R&D in the European Union" https://www.pugatch-consilium.com/reports/Benchmarking_success.pdf

[xii] All group insurers in Québec contribute to a pooling plan that protects private sector plan sponsors against the financial impact of large claims for drug costs. https://www.sunlife.ca/workplace/en/group-benefits/focus-updates/advisors-and-consultants/quebec-group-insurance-pooling-update-for-2021-whats-changing/

[xiii] Unless fundamentally altered, PMPRB changes will limit access to new medicines and vaccines in Canada. The PMPRB has essentially acknowledged that the proposed regime will have negative access consequences by creating exemptions from the Guidelines for COVID-19 medicines and vaccines. Why is this special treatment needed for some products, but no similar measures provided for other Canadian patients who will be negatively impacted, such as those suffering from cancer, cystic fibrosis, and a range of other severe illnesses? Regardless of PMPRB policy declarations, the industry and patients do not have ultimate assurances that PMPRB changes will not impact COVID-19 patented products, because these exemptions are non-binding and subject to change by the PMPRB at any time.

[xiv] See CORD https://www.raredisorders.ca/about-cord/