



Response to PMPRB Draft Guidelines Consultation

August 4, 2020

Dr. Mitchell Levine
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Patented Medicines Prices Review Board
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Dear Dr. Levine:

Muscular Dystrophy Canada (MDC), Jesse's Journey and The Neuromuscular Disease Network for Canada (NMD4C) are thankful for the opportunity to respond to the Draft Guidelines Consultation.

EXECUTIVE SUMMARY & RECOMMENDATIONS

MDC, NMD4C and Jesse's Journey supports efforts to lower the costs of prescription drugs for Canadians. However, the PMPRB must conduct this in a way that ensures timely access by Canadians living with rare neuromuscular disorders to new medicines and opportunities for participation in clinical trials. Efforts to lower drug prices must be balanced in a way that encourages ongoing innovation and the launch of new medicines for neuromuscular disorders into the Canadian market. After careful review and analyses of the implications of the of the PMPRB guidelines (v. June 2020), **we believe the current draft of the PMPRB guidelines will severely limit and delay access to treatments and will negatively affect the health of Canadians with neuromuscular disorders.**

We respectfully request the following recommendations to be implemented:

Recommendation 1 | Take a step-wise phased approach to implementation of proposed changes and begin by initially applying changes to the comparator countries. All other changes aimed at further reducing prices should be put on hold until the PMPRB can fully understand the impact of implementing phase one including: determining if the objective of lowering Canadian prices has not been sufficiently met, and completing a thorough evaluation of the impact of the new economic criteria with recommendations by an independent third party.

Recommendation 2 | Have an independent third party knowledgeable in rare disease evaluate the impact of the revised economic criteria on the availability of medicines in Canada. Their role is to specifically inform any decision on whether, when and how to implement the use of the new economic criteria for innovative high cost medicines including medicines for rare diseases.

Recommendation 3 | Meaningfully and continuously engage disease-specific patient representatives in all aspects of decision-making processes to ensure patient voice, choice and representation. The PMPRB alone should not be weighing in on the economic value of patient lives: patients are the experts on their disease and need to be at the table to weigh in on the value of their lives too.

Recommendation 4 | Implement a distinct pathway for rare disease therapies so that the complexities specific to drugs in this space are considered in a meaningful way.



DETAILED BRIEF

MDC leads Canada's neuromuscular community as the central axis in complex health services, policy, and information ecosystem that surrounds and supports our core concern: Canadians with neuromuscular disorders. Muscular Dystrophy is the umbrella name used to cover the over-160 neuromuscular disorders which are known to exist. While the disorders we represent are individually rare, they together impact a large number of Canadians. In fact, more than 50,000 Canadians from coast to coast. These disorders can weaken the body's muscles, or the communication between the nerves and the muscles. The causes, symptoms, age of onset, severity and progression vary depending on the individual and the exact diagnosis. For many individuals, neuromuscular disorders can be fatal. Currently, there is no cure for these disorders. However, as emphasized in a 2017 paper¹ published in the Journal of Medical Genetics: *“many exciting treatment approaches are currently in clinical trial, and several have achieved conditional or full market approval in various regions of the world. Many other treatments are in the pipeline, and we predict that over the next decade meaningful therapies will become widespread across the neuromuscular disease spectrum.”*

Jesse's Journey is Canada's leading charity in the fight to defeat Duchenne muscular dystrophy – the most common fatal genetic disease diagnosed in childhood. For the past 25 years, Jesse's Journey has empowered patients, families, and caregivers living with Duchenne through education and resources, provided a collective voice to advocate for access to treatments in Canada, and has become the country's largest funder of Duchenne research investing more than \$13.1M in projects around the world.

NMD4C is the new pan-Canadian network that brings together the country's leading clinical, scientific, technical, and patient expertise to improve care, research, and collaboration in neuromuscular disease. Launched in January 2020 with funding from the Canadian Institutes of Health Research (CIHR) and MDC, NMD4C builds on existing national initiatives such as the Canadian Neuromuscular Disease Registry (CNDR), the Canadian Pediatric Neuromuscular Group (CPNG), and the former neuromuscular disease network CAN-NMD. The mission of NMD4C is to improve the care, research and treatment of NMDs for all Canadians. Its vision is to be a comprehensive, inclusive, open and enduring network through which Canadian stakeholders can share expertise and data, and collaborate on joint activities and research for the benefit of Canadian patients.

Currently, the range of treatments and therapies available to support impacted individuals comes with a heavy financial burden and a significant economic impact. In fact, MDC recently conducted a 'cost-of-illness' study to evaluate the impact of neuromuscular disorders on the finances, productivity and quality of life of children, adults and family members with neuromuscular disorders (n=1100+).

Preliminary analyses of the data we obtained indicated:

(1) living with a neuromuscular disorder in Canada is associated with enormous direct and indirect costs;

(2) there is limited and fragmented access to therapies and treatment for most neuromuscular disorders;

(3) individuals face a range of extraordinary challenges, including misdiagnosis, social isolation, financial hardship, reduced educational and job opportunities and lack of treatment options.



Beyond PMPRB, we recognize that Canada's system of regulation, review and reimbursement of drugs for neuromuscular disorders presents difficulties for the approval of treatments useful to people affected by diseases that attack small populations. It is not designed for these kinds of drugs and treatments, and thus inherently presents an almost insurmountable hurdle for them. For this very reason, our organizations are strongly committed to raising awareness and strongly advocating for fair and patient-centric policies, investing in innovative research that has potential for real-world impact and providing programs and support services for those impacted by neuromuscular disorders, their caregivers and families, healthcare professionals and researchers. As patient organizations, we are passionate in the belief that every Canadian with a neuromuscular disorder deserves to benefit from leading-edge discoveries in the research field in a timely manner, which can ultimately lower the overall cost of illness. **MDC together with Jesse's Journey and NMD4C have studied the PMPRB guidelines carefully and are of the strong belief that the proposed PMPRB guidelines will have serious consequences on clinical trial opportunities and access to new medications for individuals living with neuromuscular disorders such as Duchenne muscular dystrophy (DMD) in Canada.**

DMD is a childhood, muscle degenerative disease, affecting 1 in 5000 Canadian males. If left untreated, DMD will render these children wheelchair bound by their early teens and leave them with a life expectancy in their late 20s. Currently there are 4 therapies approved for DMD in the USA and EU. **None of these therapies are approved in Canada. This includes current standard of care: corticosteroids.** The investment in DMD drug discovery and clinical trials is on the incline globally, there are currently 36 molecules under investigation from pre-clinical to Phase III. This brings a lot of hope to Canadians living with a devastating disease like DMD. DMD clinical trial participation is competitive and Canadian families affected by the disorder are at a disadvantage already due to limited trial sites and enrollment space nationally. As noted in our 'cost-of-illness' study, families often find themselves competing for international spots where travel is burdensome or faced with disappointment because preference is given to local families with established relationships with the trial sites. Clinical trials for DMD are on the decline in Canada²:

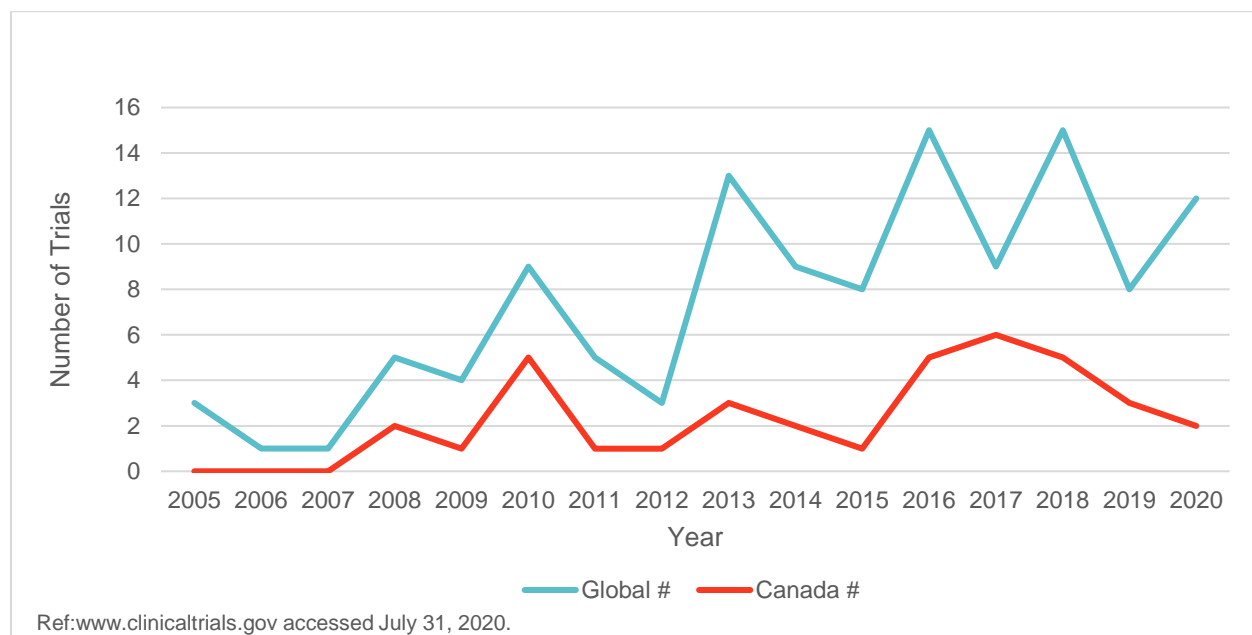


Table 1. Trends in Industry Sponsored Interventional DMD Clinical Trials Over Time



In Canada there is a direct correlation between clinical trial participation and new drug submissions/approval. For example, in 2016, the US approved Sarepta's exon 51 skipping therapy Eteplirsen for DMD. However, Sarepta did not even run a clinical program for Eteplirsen in Canada, and has given no indication it even intends to apply for a new drug submission for Eteplirsen here in Canada. Thirteen percent of the Canadian DMD population carry the mutation that make their disease amendable to exon 51 skipping therapies, and cannot access this medication. Some of these individuals may be fortunate enough to qualify themselves for a foreign clinical trial, or are able to pay out of pocket for foreign medications through Health Canada's Special Access Program. However, as we know, neither of those solutions is sustainable or a long-term solution for Canadians.

The new pricing guidelines have already begun to influence and amplify these challenges Canadian DMD families are already facing. Canadians donate millions of dollars to organizations that fund research around the world and yet when treatments are approved elsewhere, we cannot access them. **Not having access to a treatment that is available in another country is worse than having no treatments at all.** It kills all hope of our promising future in DMD research and the potential to improve the quality and extension of life of our patients. **We are profoundly concerned about the impact the pricing changes will have on the health research infrastructure of Canada.** Although PMPRB confidently notes that pricing is not a significant determinant to bringing clinical research to Canada, we are not so sure. A Life Sciences Ontario (2019)³ survey says otherwise. In that survey, 91% of pharmaceutical executives said the changes would have a negative effect on clinical research in Canada, with 44% saying the negative effect would be "significant." Labrie (2020)⁴ conducted a detailed literature review and found that there is in fact a large body of evidence directly linking prices and price regulations to R&D investment and new drug access. Of 49 studies that reviewed this specific issue, 44 found there was a significant negative relationship between drug price controls with each or both of R&D investment and drug access, or a significant positive relationship between drug price levels with each or both of R&D and drug access. There will be significant adverse impact of the proposed changes on research incentives and investments, which is crucial as we are on the verge of life-changing therapies and treatments for individuals with neuromuscular disorders. Patient organizations like MDC and Jesse's Journey are here to support the future for neuromuscular research and we want to work with government agencies to find solutions that will give Canadians fair and equal opportunities to have a better quality of life.

We hope that you agree with us that Canadians need the ability to access therapies for rare diseases as soon as possible. We do not want to see a future where regulatory bodies are approving therapies in other countries, but pharmaceutical manufacturers elect not to come to Canada. Manufacturers must see Canada as a viable market to run clinical trials and pursue regulatory approval. 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 of new medicines in the Canadian market. Any changes to Canada's drug access pathway – including the PMPRB – must be flexible and responsive to the needs of rare diseases. In fact, we would like to use this opportunity to strongly urge for the implementation of the federally promised Rare Disease Strategy, for which guidelines by the PMPRB can be framed. **Canada stands out on its own with no strategy in place and without a strategy, it is impossible to develop pathways for drug pricing, approval and access.** The high prices of many drugs that treat rare diseases, as well as small populations that make it difficult for the manufacturers to collect clinical evidence needed to meet regulatory requirements, can lead to Incremental Cost-Effectiveness Ratios that exceed "willingness to pay" levels⁵. Budget restriction measures, especially around "expensive drugs" (as treatments and therapies for neuromuscular disorders often are), are becoming increasingly common⁶. Reference pricing methods (i.e., comparing and referencing to drug prices



in other countries or regions) can push manufacturers to postpone, or even avoid, entering certain markets to avoid a possible cascading price-drop effect elsewhere. Therefore, Canada must look at other countries with established rare disease strategies and policies specific to pricing and access to medicines.

We commend your efforts and fully support the PMPRB's mandate to lower the costs of prescription drugs for all Canadians, and for being flexible in making changes to the guidelines based on previous consultations. However, this is not enough. We believe that the guidelines can and must be crafted in a way that ensures timely access by Canadians to all new medicines in a simple way that is understood by Canadians.

RECOMMENDATIONS

Our recommendations are in line with those proposed by MDC in February 2020, but also by **Health Charities Coalition Canada (HCCC)**, **Cystic Fibrosis Canada (CF Canada)** and **ALS Society of Canada (ALS Canada)**. We strongly echo the discussions outlined in their thorough and carefully well thought-out submissions. We strongly encourage you to carefully review these submissions, and please take into account these four key recommendations:

RECOMMENDATION 1: MDC, NMD4C and Jesse's Journey urges the PMPRB to take a step-wise phased approach to its proposed changes implementation and begin by initially applying changes to the comparator countries. All other changes aimed at further reducing prices should be put on hold until the PMPRB can fully understand the impact of implementing phase one including: determining if the objective of lowering Canadian prices has not been sufficiently met, and completing a thorough evaluation of the impact of the new economic criteria with recommendations by an independent third party.

RECOMMENDATION 2: MDC, NMD4C and Jesse's Journey recommend that implementation of an independent third party knowledgeable in rare disease evaluate the impact of the revised economic criteria on the availability of medicines in Canada. Their role is to specifically inform any decision on whether, when and how to implement the use of the new economic criteria for innovative high cost medicines including medicines for rare diseases. Until this is completed and the value of these measures is demonstrated, no such measures should be adopted.

RECOMMENDATION 3: MDC, NMD4C and Jesse's Journey calls on the federal government to require that the PMPRB immediately establish a formal mechanism for meaningfully and continuously engaging disease-specific 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 such as the UK. The PMPRB alone should not be weighing in on the economic value of patient lives: patients are the experts on their disease and need to be at the table to weigh in on the value of their lives too.

RECOMMENDATION 4: MDC, NMD4C and Jesse's Journey recommend that the PMPRB implements a distinct pathway for medicines for rare diseases, recognizing the unique difficulties that they face. While a number of the adjustments in the June 2020 Draft Guidelines attempt to address the disadvantages of treatments for diseases that have smaller populations, the guidelines do not go far enough. The high cost and small market size of rare disease therapies mean the majority will exceed the thresholds and be subject to pharmacoeconomic assessments, which could be disadvantageous for future therapies for neuromuscular disorders. The use of the pharmacoeconomic assessments as proposed lengthen an already complicated process and do not take into consideration metrics relevant to patients of a specific rare disease. A distinct



pathway for rare disease therapies must be implemented so that the complexities specific to drugs in this space are considered in a meaningful way.

Thank you for the opportunity to review the guidelines and provide comments. We remain committed to working with the Federal Government and the broader stakeholder community in defining an implementation and evaluation process that will best address both the mandate to provide cost savings, but also and access to innovation that will optimally serve the needs of individuals with neuromuscular disorders in Canada, which may also ultimately save health care costs in Canada as well.

Please do take our feedback into consideration as you prepare the final guidelines and we would absolutely be happy to answer any questions you might have.

Kind Regards,

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Hanns Lochmuller
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