Canadian Organization for Rare Disorders

Submission by the

CANADIAN ORGANIZATION FOR RARE DISORDERS

to the Public Consultation on

Canada's National Strategy for High-Cost Drugs for Rare Diseases

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What are we trying to solve in Canada?

The Canadian Organization for Rare Disorders (CORD) is pleased that the time has come to move forward on the government's commitment to "improve patient access to high-cost drugs for rare diseases and ensure that access is consistent across the country." CORD welcomes the opportunity to provide feedback to the public consultation on Canada's National Strategy for High-Cost Drugs for Rare Diseases.

To be clear, we do not underestimate the complexity of the challenge nor the enormity of what we collectively are dedicated to achieving: the realization of a Rare Disease Drug Strategy that is state-of-the-art for patients. Across the globe, there is no single "best" rare disease drug plan but there are many plans with innovative solutions, adaptive pathways, and best practices that we can learn from.

CORD is Canada's national network for organizations representing all those with rare disorders. CORD provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders. CORD works with governments, researchers, clinicians and industry to promote research, diagnosis, treatment and services for all rare disorders in Canada.

In developing our recommendations, we have been guided by our "north star": the patients whose stories we hear day after day. We respectfully precede our response with examples of their gut-wrenching experiences, not to tug at heart strings but to paint starkly the harms patients do suffer as a result of systemic deficiencies in our treatment of rare diseases. Here's what some patient families shared at CORD's recent 2021 Rare Disease Day Conference:

- "I feel like a loser in front of my girls …" says Kimsaung, mom to Stephanie and Tiffany, two-year-old twins with spinal muscular atrophy (SMA), a progressive genetic disease that robs children of the ability to walk, eat, and even breathe on their own. In reality, Kimsaung didn't fail her children; our healthcare system did. The babies' early symptoms were dismissed by their physician; testing backlogs and errors led to a months-long delay in diagnosis, and the lack of urgency delayed referral to a specialist; meanwhile the children's condition was deteriorating. The parents are pleading for access to a life-altering gene therapy that has been approved by Health Canada but not yet funded by the provincial plan. The "treatable" window of opportunity is closing.
- What if you were a 17-year-old classical pianist, a black belt in taekwondo, and looking forward to attending university, but were told that you could lose your eyesight in the next four months without access to a new "one-time" gene therapy. The only problem: funding for the drug might not be approved in time. For Adam, this is not a hypothetical situation but a brutally real one. Adam's mom, Charmain, knows the therapy works because Jenna, his sister, also has retinitis pigmentosa, a rare disease that causes vision loss. Jenna was treated in one eye as part of a clinical trial and has retained her vision ten years later. Jenna wants treatment for the other eye before it is beyond stabilization but has directed all her energy toward advocating for Adam.
- Susi Vander Wyk, founder of CureSMA Canada, has advocated tirelessly for access to therapy for dozens of children with SMA. Sadly, because drug plans, public and private, are so disjointed, she has had to lead the battle on a plan by plan, province by province, and age cohort by age cohort basis. First, they won access for infants under two; then children up to age 10 in Ontario but not in other provinces; then in Quebec for all children but for adults only by special assessment. Paradoxically, even now with three approved therapies for SMA, Susi has not yet succeeded in getting treatment

for her 24-year-old daughter who is qualifying as a teacher and fighting to retain as much independence as possible.

- Thirty years ago, after years of frustrating misdiagnosis, when Christine White's daughter was finally diagnosed with Gaucher's Disease, a rare and potentially life-threatening metabolic disorder that affects the organs and tissues, she soon realized that it was the end of one journey and the beginning of another. The only effective therapy at the time was not listed on any provincial formulary but only available through case-by-case special access. So, she embarked on a journey of arduous advocacy, which continues to this day. When asked what has changed over the ensuing 30 years, she notes, "Sadly, not much." The fact that families have to fight tooth and nail to get access to a therapy is just shocking in this day and age.

Unfortunately, these stories are just a snapshot of what we are seeing broadly across Canada. A recent survey conducted by CORD showed that:

- 87% of rare disease patients received a delayed, wrong or no diagnosis for a rare condition
- 84% of rare disease patients have experienced delayed or no access to a rare disease specialist or clinic
- 86% of rare disease patients have experienced delayed or denied coverage for prescription medicines
- 84% of rare disease patients have experienced delayed or denied coverage for support services (therapy, medical devices, financial)

Ironically, the Canadian government has removed barriers and accelerated reviews to bring in the COVID-19 vaccines on an urgent basis, tactics they have not chosen to use for rare disease therapies. Said one patient, "I can get a vaccine for a virus that I probably won't die from but I cannot get access to a treatment for my rare disease, which I will certainly suffer and die from."

Canada, this is our opportunity to take the lessons we are learning from COVID to do better for patients and families with rare diseases.

The Time is Right—Right Now

Over the past 15 years, governments at both the federal and provincial/territorial levels have been inching cautiously toward a rare disease drug strategy. During this time, the rare disease patient community has been evolving from a marginalized, ill-informed, loosely organized collection of victims/supplicants to an engaged, informed, coalescent community as partner, albeit not yet equal. The challenge now is to move all of this talk into action on behalf of patients. Here is a brief recap of the rare drug movement to date:

- In 2004, CADTH recommended that the provinces not reimburse enzyme replacement therapy (ERT) for Fabry's Disease, a rare disease that primarily affects males causing kidney and heart failure and premature death. In 2005, CADTH recommended against ERT for Mucopolysaccharidosis Type 1, a progressive multi-system disease affecting young children. Patient advocates contended that CADTH's health technology assessment methods and cost-effectiveness criteria were not appropriate for rare diseases.
- In 2006, following a vociferous advocacy campaign, the federal-provincial-territorial (FPT) governments jointly funded a 10-year national research program to provide access to ERT for patients with Fabry's Disease while collecting data on outcomes and adverse effects.
- In 2006, the Conference of FPT Ministers of Health recommended: "a national framework for expensive drugs for rare diseases (EDRD) in collaboration with experts and move toward staged implementation."[1]
- This was followed in 2008 by a proposal for the establishment of a Canadian Access Program for Drugs for Rare Diseases that would "pool expertise and funding (based on 50/50 FPT funding formula) with centralized, transparent decision-making model with public involvement."[2] A draft framework was developed but not released publicly.
- In 2014, the provincial-territorial (PT) Ministers of Health set up the Expensive Drugs for Rare Diseases Working Group and in 2016 asked the EDRD WG, led by B.C., Alberta, and Ontario, to study issues of EDRD and to work toward more consistent assessments of drugs and coverage decisions, and a fair pricing strategy.[3]
- In 2018, the PT EDRD Working Group announced public consultations on a Supplemental Process for Complex/Specialized Drugs (SP_CSD) with the primary objective being "…to implement a proactive, consistent, fair and transparent process to assess complex/specialized drugs for the purpose of making responsive funding decisions." Key areas identified were: early drug identification, concurrent Health Canada, CADTH, PMPRB, and pCPA submission, CADTH review fully informed by drug plans and patient/clinical community with consideration of real-world evidence, pCPA negotiation with managed access/conditional funding considerations, RWE collected to inform

[1] Conference of Federal-Provincial-Territorial Ministers of Health, 2006. News Release: Health Ministers Continue Working on National Pharmaceuticals Strategy. https://scics.ca/en/product-produit/news-release-health-ministers-continue-working-on-the-national-pharmaceuticals-strategy/

[2] Annual Conference of Provincial-Territorial Ministers of Health, 2008. Backgrounder: National Pharmaceutical Strategy Decision Points. https://scics.ca/en/product-produit/backgrounder-national-pharmaceutical-strategy-decision-points/

[3] Annual Conference of Provincial-Territorial Ministers of Health, 2016. NEWS RELEASE – Improving health of Canadians the focus in wide-ranging health talks. https://scics.ca/en/product-produit/news-release-improving-health-of-canadians-the-focus-in-wide-ranging-health-talks/

continued usage and funding, individual patient access by national panel, and enhanced transparent communications. CORD surveyed its members and submitted feedback, mostly agreeing with an early (conditional), national, evidence-informed, expert-based, and patient-engaged managed access program BUT value-based assessment based on patient-centred, real-world outcomes analyzed at the appropriate time (for outcomes to be realized).

- In 2019, the EDRD produced a summary of all stakeholder comments on the SP_CSD. Responses across multiple stakeholders supported the need for a clearly defined process that is national, timely, transparent, and inclusive as well as agreement on consistent, equitable, fair, and sustainable outcomes. Stakeholders expressed support, in concept, for managed access plans to fulfill unmet needs while setting up mechanisms for monitoring and collecting real-world evidence and determining pricing. At the same time, while we recognize that a "managed access" process is an effective way forward for some rare disease drugs, it is not an appropriate, necessary, or feasible pathway for many other drugs for patients with rare diseases.

How will this consultation under the leadership of Health Canada move us collectively from talk to action? A major asset is the 2019 federal government budget commitment of $1 billion to set up Canada's Rare Disease Drug Strategy. Importantly, this investment and federal leadership will provide the opportunity to establish a strategic rare disease infrastructure essential to implementation of managed access, special access, compassionate access, early access, individualized access, clinical trials, and domestic research and drug development. In 2015, CORD launched Canada's Rare Disease Strategy in Parliament Hall and subsequently across the country.

These five components are essential to delivery of a Rare Drug strategy that is effective and cost-effective:

1. Diagnosis, including newborn screening, genetic testing, genetic counselling and patient registries
2. Timely, equitable, and evidence-based care through expert centres networked to local healthcare providers
3. Community support, including physical, psychosocial, and educational therapy and patient group empowerment
4. Sustainable access to promising therapies individualized to patient needs
5. Investment in innovative research including disease knowledge, therapeutic interventions, clinical trials, and real-world evidence

We are heartened by the fact that Health Canada has adopted key areas of the PT EDRD Supplemental "managed access" process as core elements in this consultation, increasing the likelihood that multiple stakeholders can coalesce around a national strategy. However, as our opening patient access challenges have illustrated, managed access is only one possible pathway and this Rare Disease Drug Strategy must consider multiple pathways. These issues are clearly illustrated when we take a case study approach to reviewing a policy, as follows:

- Managed access would be useless in the case of Stephanie and Tiffany, the SMA infants whose deteriorating disease status due to delayed diagnosis, requires urgent drug access to halt progression.

- Managed access will not serve Adam, the teen who has only a short time to access a therapy that will allow him to avoid blindness.
- The slow roll-out of managed access for the non-gene therapy SMA drug resulted in non-recoverable loss of function for many "less disabled" children who were denied access pending accumulation of "more evidence" and also has forestalled adult access in all provinces except Quebec, which provides for individualized review.
- With respect to Gaucher's disease, a comprehensive rare disease program with patient and family engagement would result in patients having access to their individually optimal therapy, which would improve adherence, patient outcomes, and return on investment for the system.

These examples are harbingers of the next generation of highly effective targeted therapies that will not be exclusive to rare diseases but typical of more common conditions where genetic and genomic testing will uncover highly specific variations that can be treated by targeted therapies. These treatments will provide tremendous healthcare outcomes by reducing disability, stopping and preventing symptom progression, and ostensibly eliminating the cause of a disease. Many of these will be infrequent or one-time therapies, reducing healthcare visits. Many of these will be digitally supported, allowing for self-management and even self-correction.

Actually, we are already there. So, it is urgent that we implement the Rare Drug Strategy and the concomitant Rare Disease Strategy as soon as possible, since these will serve as the pilot and model for more common conditions. Moreover, these examples warn us that we cannot afford a "supplemental" process that sits within or alongside the current process but, instead, need an "alternative" process that is managed by its own agency with agile pathways that are customized to the specific disease and drug context.

The leadership of Health Canada is essential in the establishment of a Canadian Rare Drug Agency (CRDA), which must have self-contained jurisdiction, similar to Canadian Blood Services/HemaQuébec (CBS/HQ) with a board of directors, budgetary control, transparent decision making, patient/clinician engagement, and public accountability. However, to learn from the errors of the CBS/HQ, the CRDA must also have its own network of experts, with disease-specific panels, to assess appropriate criteria for access, outcome measures, clinical networks, and value/pricing. The CRDA must be guaranteed sufficient budget to ensure optimal access and management of current and future therapies.

CORD supports Health Canada's continued modernization of its regulatory processes to support a "life-cycle" approach to innovative medicines, including advice regarding clinical trials design, patient-centred outcome measures and the collection of data that is relevant to values assessment and real-world data collection and analyses. We have commented on and urge the increased collaboration of Health Canada with other regulators on review, approval, and patient engagement in regulatory processes to promote a harmonized and more timely process.

CORD supports the option to invest in Canadian research and development toward discovery, testing, and marketing of innovative therapies. Canada has been notably absent in the years since the 1983 passage in the United States of the Orphan Drug Act and the European Union's directive on Orphan Medicinal Products in 2000, which ushered in decades of research and new treatments. Indeed, on Rare Disease Day 2021, the FDA announced new requests for applications to its Orphan Products Grants program and a Bespoke Gene Therapy Consortium to develop individualized therapies.[4]

However, we reiterate our concerns that, the recent changes to the Patented Medicine Prices Review Board (PMPRB) regulations are working counter to the announced Drug Strategy goals to improve access to "high cost" rare disease drugs. Indeed, CORD calls upon the federal government to balance its rhetoric and exercise leadership by acknowledging the tremendous savings that early access to treatment can generate in the long run. Timely access can help slow down or reverse the damage caused by disease and help reduce the long-term costs to families and the health system.

To these ends, CORD also calls upon the federal government to exercise its jurisdictional responsibility for "fair" drug pricing. CORD calls for assurance that rare disease drugs will not be priced excessively but also that legislated pricing restrictions do not risk limiting or delaying entry of innovative therapies or clinical trials to Canada. The rare disease community is very concerned that the revised PMPRB regulations and the proposed guidelines are premised on inaccurate analyses that have been conducted with biased, limited, and just plain wrong information. CORD has presented all of this feedback to the PMPRB consultations and we are discouraged to see these premises repeated without correction in this consultation on "High-Cost Drugs for Rare Diseases."

In brief, there has been unwarranted fear raised about the prices of rare disease treatments without considering their relatively low budget impact (because of the very low number of patients) and the value they bring to patients and the health system. A recent study found that non-oncology related drugs for rare diseases only made up 1.9% of total public medication expenditure in Canada in 2019. These expenditures are a small drop in the bucket compared to other areas of our health system.[5]

In summary, while a National Strategy for High-Cost Drugs for Rare Diseases is an important step forward, this strategy cannot be achieved if we focus only on improving access to treatments. Addressing rare diseases requires a broader and more holistic approach that ensures research and development happens here in Canada, clinical networks of excellence are established, and supports are provided for both patients and those they care for.

As exists already in almost all other developed nations, a cohesive and comprehensive strategy is needed to cover all aspects of rare disorders in Canada. Such a strategy should not depend on just one level of

[4] US FDA. FDA's rare disease day 2021: FDA shows sustained support of rare disease product development during the public health emergency. (2021). https://www.fda.gov/news-events/fda-voices/rare-disease-day-2021-fda-shows-sustained-support-rare-disease-product-development-during-public

[5] Forte L et al, The current and future cost of orphan drugs in Canada, Poster at ISPOR Europe 2019, Copenhagen, Denmark,
November 2019. https://www.ispor.org/heor-resources/presentations-database/presentation/euro2019-3122/96632; and updated in the submission by RAREi to the PMPRB: https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/submission-received/june2020/June%202020%20submission_RAREi_EN.pdf

government to show leadership – it needs all Canadian governments and everyone in the rare community to help implement it. This requires the coordination of policymakers, health system leaders, patients, medicine developers, researchers and clinicians. Working together to implement the strategy would go a long way to helping millions of Canadians with rare disorders.

Since this work, and following the Budget 2019 announcement, CORD has undertaken a number of surveys of patients and caregivers and hosted virtual events with Canadian and international experts to identify key issues and potential solutions to improve Canadians' access to care and treatment.

Based on these extensive consultations, the present submission summarizes what we heard and outlines CORD's vision for what a Canadian national rare disease strategy can and should look like.

CORD's 12-Steps to a National Rare Disease Framework

We have chosen not to follow Health Canada's themed consultation guide and questions to respond, because we believe the questions are too narrowly focused and many of the themes are cross-cutting. In addition, much of the consultation document is too focused on access to treatments while not considering critical supports essential for effective drug usage. Verily, drug therapies harnessing health technology, microbiology, and genomic science are revolutionizing treatment from prevention to cure. Moreover, drugs for rare diseases are but the vanguard for targeted therapies for common conditions.

However, one could not state unequivocally that a life-saving therapy for ultra-rare disease patients should be assessed in the same way as a fourth-line therapy for a populous condition, thus justifying use of a "common" health technology assessment. In establishing a "national strategy for high-cost drugs for rare diseases", it is important, on the one hand, to start with some parameters, including the scope of the program, goals and desired outcomes, guiding principles, and alternative access pathways. On the other hand, given the dynamic and rapidly evolving environment for innovative drug development, a strategic framework must also be agile and adaptable to remain fit for purpose.

Now is the time for Canada to take bold action. CORD proposes the following 12 recommendations to set up a national program for "high-cost" (and not high-cost) drugs for rare diseases directed to fundamental goals of timely, consistent, and evidence-informed access with sustainable (values-based) budget impact. Each of the 12 recommendations is grounded in an incontestable foundational principle. We cite two exemplars which illustrate the value of a principles-driven approach.

In 1998, one year after the inquiry into the tainted blood scandal of the 1980s, the federal government, at the instigation of the patient community, rallied the provincial and territorial governments to collaborate on the creation of Canadian Blood Services and Hema Quebec. To restore patient and public trust, these were set up to be patient-centred, publicly accountable, transparent, evidence-based, independent agencies. We need to be at least this bold in terms of doing things differently after the pandemic.

In 2007, Joint Oncology Drug Review (JODR) was set up through a multi-stakeholder consultation process, to provide recommendations on reimbursements of cancer drugs separate from the Common Drug Review. Its successor, pCODR, has been subsumed administratively under CADTH but its deliberative framework is still

guided by the original four elements, which weigh equally patient values with clinical benefits, cost-effectiveness and implementation considerations.

It is in this context that CORD proposes 12 principles-based recommendations for Canada's Rare Disease Drug Strategy to be established within a Canadian Rare Disease Strategy. Canada should use this opportunity not just to provide access to new therapies but to aim to be a leader along every step of the rare drug life cycle.

1. **Patient empowerment:** Empower patient organizations and patient advocates to participate as active full partners in all aspects of Canada's Rare Drug Strategy and Rare Disease Strategy. To this end, allocate positions of decision-making and responsibility to patient representatives nominated by the patient community and provide the training, support, and resources to enable effective participation. Enforce policies and practices of open, transparent, and accountable communications. Patient organizations should be allocated appropriate financial resources to engage as equal partners.
2. **Creation of a Canadian Rare Drug Agency**: Establish the Canadian Rare Drug Agency as an independent, transparent, publicly accountable agency with responsibility for all aspects of the review of drugs for rare diseases, in coordination with Health Canada and their regulatory procedures and PMPRB pricing procedures (not including economic assessment).
    a. A potential model is Canadian Blood Services and Hema-Québec, which jointly manage all aspects of the blood system from procurement to distribution, including conditions/criteria for product use, price negotiation, monitoring, and patient outcomes data collection, and patient registry.
    b. Like CBS, the CRDA shall be a pan-Canadian agency established by federal and all provincial/territorial governments (with a potential separate Quebec entity). It shall have an independent governance structure, governing board, budget, operations, and reporting functions.
    c. Like CBS/HQ, the provinces, along with the federal government, may determine which therapies should be managed by the CRDA. [N.B. Not all products used by patients with blood disorders are managed by CBS/HQ and not all products managed by CBS/HQ are "blood-based" or "blood-replacement" therapies.] However, all drug products managed by CBS/HQ are available to all patients, regardless of their geographic location and drug plan enrollment. CORD proposes similar "rules of operation" for the CRDA, whereby criteria are developed to determine which rare disease drugs should be managed by the CRDA on behalf of all drug plans and all Canadians (with potential exceptions where appropriate). [N.B. The designation of a "rare disease" not based on population prevalence but on circumstances is consistent with many jurisdictions and indeed is typical of most funding authorities whereby "orphan" designation conveys no specific reimbursement preference or status.]
    d. The CRDA, like CBS/HQ shall be guaranteed sufficient budget to carry out its mandate, with funding from the PT and federal governments with no direct interference in operations and accountability through reporting and oversight.

3. **Create R&D incentives:** Invest in Research and Development, which in the short term should support therapeutic product accessibility, monitoring, and evaluation through clinical trials, patient registries and real-world data collection as well as best practices for usage and support. Over the long-term, R&D investment should build capacity for drug discovery, technological innovation, manufacturing and production, and (global) distribution. To these ends, Health Canada along with Industry Canada should develop and implement incentives for research and development of therapies and diagnostics for rare diseases, including grants, comparable to those of the USA and some European Union countries. Research and development should be coordinated through existing institutions, such as CIHR, National Research Council, Genome Canada, CCRM, Regenerative Medicine Alliance of Canada, and Maternal Infant Child Youth Research Network.
4. **Speed up access to treatment:** Ensure timely availability of new treatments in Canada by establishing a competitive and viable environment for early drug launches, including supportive mechanisms for clinical trials, early access programs, clinical site development, patient registries, and patient support programs. Recognizing that status as a preferred location for early drug entry not only benefits patients but also the clinical and research communities, Canada should support public-private initiatives, similar to the European Union's Innovative Medicines Initiatives, to foster pharmaceutical investment in collaborative programs in drug development, testing, and patient support.
5. **Address regulatory barriers:** Ensure that the regulations and guidelines of the PMPRB are directed, per its mandate, on ensuring that the list prices of pharmaceutical products in Canada are not excessive, that is, do not exceed a "reasonable" threshold of fairness compared to comparable countries, in keeping with the goals and objectives of Canadians for new drug availability. To that end, CORD calls for Health Canada to roll back the 2019 PMPRB regulatory changes by removing the proposed use of economic factors. If implemented in their current form, these regulatory changes will lead to prices far below the OECD average. Even in advance of implementation, these changes have led to reduced clinical trials[6] and new drug launches[7] over the period of time since their announcement in 2017. To promote transparency and accountability, PMPRB should establish an Advisory Board that includes patient and clinician representation.
6. **Improve regulatory approvals process:** Ensure Health Canada continues to update its regulatory process to encourage clinical trial and new drug submissions for rare disease drugs, including those designated as "orphan drugs" by the US FDA and EMA. To these ends, Health Canada should actively collaborate and coordinate with other jurisdictions to promote harmonization in procedures, thus reducing barriers to entry in Canada and expediting approvals from drug registration to clinical trial approvals to notices of compliance. Health Canada should establish a process to officially acknowledge foreign orphan designations, as appropriate. Health Canada should also expand its program of joint approvals with other regulatory agencies to include drugs for rare diseases whenever feasible and appropriate. Health Canada should develop and implement an official

[6] Rawson, N., Clinical Trials in Canada: Worrying Signs Remain Despite PMPRB's Superficial Response, Canadian Health Policy Institute, 2021: https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada--worrying-signs-remain-despite-pmprb---s-superficial-response.html

[7] IQVIA data prepared for Life Sciences Ontario, New Medicine Launches: Canada in a Global Context, 2020: https://lifesciencesontario.ca/wp-content/uploads/2020/06/EN_LSO_Global-Launch-Benchmarking_Webinar-June22-20_Final.pdf

program of patient engagement that includes training, support, and resources, compatible and in collaboration with those of the US FDA and the EMA.

7. **Ensure pathways for special cases:** In cases of urgent need, timely access should be provided through the federal Special Access Program (SAP), even prior to Health Canada approval. We need to create a pathway through Early Access Programs (EAP), like those used in the USA, European countries and elsewhere. Assure early access to urgently needed therapies for patients reliant on public plans by pre-NOC negotiation of access and funding through the CRDA "special access fund" that may be repaid after the drug funding has been finalized. In all cases of urgent or emergency need, the request is initiated by the treating physician and approved by an expert (individual or panel) based on best available evidence and the physician's acceptance of responsibility for care. Where agreed upon reimbursement has not been concluded, the drug could be paid for through a "special access" fund. Where a patient has private drug coverage, the EAP provisions should also be followed.
8. **Need for multiple funding options**: Multiple separate pathways for rare disease drugs with early differentiation based on population size, disease severity, unmet need, evidence uncertainty, potential therapeutic value, budget impact, annual unit price, and industry. The determination of need for a distinct rare disease pathway shall be undertaken by the CRDA, upon submission by the manufacturer, clinical community, or patient community or determined by the CRDA on its own initiative. The pathways should be universally applicable to all patients accessing the specific drug regardless of where they live and their drug plan. Therefore, like the CBS/HQ, the CRDA should undertake the pricing negotiation, purchasing agreements, distribution and payment for drug products procured through a distinct rare disease pathway. Like the CBS/HQ system, the drug plan (public or private) that is responsible for the patient shall be required to reimburse the CRDA based on actual drug usage.
9. **Leverage Managed Access Programs (MAPs):** MAPs are a specific type of drug pathway. There are many in place in Canada for access to rare disease therapies, especially those receiving an NOC-C where there is uncertainty about the evidence at the time of approval but where the unmet needs and benefits outweigh the risks.
    a. MAPs should be anticipated and pre-planned at the earliest possible time, that is, at the time of clinical trials, regulatory submission, HTA submission, or whenever there is a recognition that an MAP may be optimal. The CRDA should take the lead in coordinating the process, including by taking responsibility for putting together a drug-specific expert committee that includes treating clinicians and patients to determine the criteria for access, defining patient outcome measures, setting up a monitoring plan, and putting in place data collection mechanisms, and establishing the evaluation protocol.
    b. The MAP should also identify all components of the rare disease care and treatment that need to be in place to implement the program, including diagnostic and other testing, (specialist) clinical care, other supportive care services and care team personnel, patient education on benefits, risks, and potential outcomes, and commitment to management responsibilities, and community support services, as appropriate.
    c. An MAP should facilitate patient access to the therapy at the optimal time, usually when their physician deems it appropriate based on best available evidence and the patient's characteristics. To that end, the process for setting up an MAP must be efficient and agile

and be able to accommodate, for example, limitations in clinical trial data, uncertainties with respect to long-term outcomes, and extrapolations to the broader patient population.

d. The MAP process should be designed to be iterative, so criteria for access are updated as new data are collected. The negotiated MAP should apply to all patients accessing the specific therapy regardless of where they live and the type of drug plan that they have.

e. Other financial arrangements negotiated as part of an MAP may be included to help address inherent or perceived financial risks to either payers or manufacturers, or both. These include free "initial" doses, capped dosing (number of doses or duration of treatment), capped number of reimbursements, free product, and straight pricing discounts. An important option used in many countries for therapies that have long-lasting benefits (a.k.a. durable therapies such as cell transplant or gene therapy) but come with large (one-time) prices may be managed through a combination of "outcome monitoring" and an amortization scheme whereby scheduled payments are contingent on the continued effectiveness of the treatment.

10. **Facilitate concurrent Health Canada and HTA reviews:** Joint Health Canada and HTA application (where appropriate), where Health Canada data, analyses and conclusions on benefits and risks, patient outcomes, and appropriate treatment cohorts are made available to the HTA body for their review. However, payers should not be engaged during this stage.

11. **Support real-world evidence generation**: The CRDA shall be responsible for real-world monitoring, data collection, and evaluating the benefits, risks, and uncertainty for each drug. Patient data relevant to drug use should be directly linked to other health information and, therefore, best collected as part of an overall electronic health record. However, the implementation of a data management program for drug monitoring should not be contingent on setting up an electronic health data platform where one does not yet exist. Moreover, while the specific drug monitoring data should be collated and analyzed nationally and even internationally, it is not necessary to have a single patient registry or data platform across all clinical sites.
Patients may be required to provide data as a condition of receiving a specific therapy; however, they shall always be informed and give consent as to how their data will be used. Patients must be engaged not only to collect and submit data but also to receive back not only their own data but also relevant population data.

12. **Enhance centres of clinical expertise**: The CRDA shall partner in developing Networked Centres of Expertise for specific rare diseases related to management of a therapy. If feasible, the treatment of rare disease patients should be directed by an expert and an appropriate support team. The expert centre shall establish linkages to the patient's local healthcare providers for day-to-day management. Expert centres should serve as resources for patients, be linked nationally and internationally, funded to develop best practices, provide opportunities for skills development and mentorship to non-specialists, and participate in research. Canada should move toward establishing National Rare Disease Centres of Expertise that include multiple specialists and multiple disciplines.

Application to Address Patient Access Challenges

- Challenge: Stephanie and Tiffany, two-year-old twins with spinal muscular atrophy (SMA), are seeking access to a life-altering gene therapy that has been approved by Health Canada but not yet funded by the provincial plan. The "treatable" window of opportunity is closing.
  Solution: While the Managed Access Program is being set up, request access through the Emergency Access Plan that provides therapy and funding to patients with urgent needs, based on their physicians' prescription.
- Challenge: Adam, a 17-year-old musician and athlete, is seeking access to a "one-time" gene therapy that could keep him from going blind … but only if he gets access in the next four months. It is approved but not yet funded.
  Solution: Obtain treatment through the Emergency Access Program and funding mechanism. The provincial drug plan and the family's private plan can reimburse the EAP fund afterwards.
- Challenge: Susi's 24-year-old daughter with a progressive neuromuscular disorder is seeking access to a drug that could stabilize her condition and allow her to achieve her dream of being a teacher. There are three drugs approved but none available to her as an adult.
  Solution: Convene the Expert Treatment Panel to set up guidelines for treating adults based on "best evidence" through a "coverage with evidence development" program with criteria for starting an agreed-upon patient-centred outcome indicators for treatment continuance.
- Some 30 years after successfully advocating for a life-altering drug therapy for her young daughters, Christine finds herself waging the same battle for a new oral therapy that could significantly improve adherence over the original injection therapy. Now there is a one-time gene therapy in clinical trials.
  Solution: Request the Expert Treatment Panel to review the evidence and provide guidelines for access to the next-generation therapy. Negotiate pricing commensurate with patient-centred outcomes, including biophysical measurements, symptom management, and quality of life.