

**Brief to House of Commons' Standing Committee on  
Barriers to Access Treatment and Drugs for Canadians Affected by Rare Diseases and Disorders**  
Submitted by pan-Canadian Pharmaceutical Alliance (Public Drug Plans)  
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## **I. EXECUTIVE SUMMARY**

Public drug plans, collectively as the pan-Canadian Pharmaceutical Alliance (pCPA) and individually as jurisdictions, have the role and responsibility to support the public by making appropriate drug funding decision that are evidence-informed, cost-effective, and affordable.

With expensive drugs for rare diseases (EDRDs), public drug plans in Canada and elsewhere around the world are experiencing significant challenges where the expectations and needs of the public drug plans from the pharmaceutical industry are not being met.

There are several challenges discussed in this paper. The three key challenges relate to: (1) Evidence Limitations – Often inadequate evidence around drug efficacy, safety, and cost-effectiveness to support drug coverage decisions; (2) High Drug Pricing - Extremely high drug prices and growing costs threaten drug program affordability, sustainability and subsequently access for patients; and (3) Gaps in national alignment and coordination of processes.

To address some of the barriers and challenges described with EDRDs, the pCPA and public drug plans request the following support from the federal government:

1. Federal funding support for EDRDs;
2. Federal implementation of pricing controls through the proposed Patented Medicines Pricing Review Boards (PMPRB's) proposed modernization changes; and
3. Federal government to continue to work with P/T public drug plans and the pCPA to better align, collaborate, and coordinate our respective approaches to address EDRD evidence and pricing issues.

## **II. BACKGROUND:**

1. Pan-Canadian Pharmaceutical Alliance (pCPA) :

Established in August 2010, the pan-Canadian Pharmaceutical Alliance (pCPA) conducts joint provincial/territorial/federal drug plan negotiations for brand name (patented) and generic drugs in Canada. The pCPA achieves greater value and consistent national drug coverage for publicly funded drug programs and patients through the use of the combined negotiating power of participating jurisdictions.

The pCPA member jurisdictions include public drug plan and/or cancer agency participation from: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland & Labrador, Yukon, Northwest Territories, Nunavut, Non-Insured Health Benefits (NIHB), Correctional Services Canada (CSC) and Veterans Affairs Canada (VAC).

The pCPA's mandate is to enhance patient access to clinically relevant and cost-effective drug treatment options. It serves this mandate by conducting collective, expert-informed, negotiations for drugs.

As of September 30, 2018, these collaborative efforts between provinces and territories have resulted in over 200 completed joint negotiations on brand name drugs and price reductions on over 60 generic drugs. The overall annualized savings from negotiations is estimated to be \$1.98B. Included in the numerous patented drugs negotiated, are both drugs for common and rare diseases. In 2018 (as of November 26, 2018), 9 negotiations for expensive drugs for rare disease (EDRDs) have been completed by the pCPA.

## **2. Public Drug Plans:**

Final coverage decisions for each drug are the responsibility of each individual public drug plan. Each public drug plan aims to deliver coverage that is accessible, appropriate, affordable, and contemporary to meet the needs of all of the beneficiaries it serves. In making drug coverage decisions, public drug plans rely upon national processes, including Health Canada (regulatory and the Special Access Programme), health technology assessments or HTA (e.g., Canadian Agency for Drugs and Technologies in Health (CADTH) for all provinces except Québec; Institut National d'Excellence en Sante et en Services Sociaux (INESSS for Québec)), the Patented Medicines Pricing Review Board (PMPRB), and the work of the pCPA.

Each year public drug plans review approximately 55-75 new drugs or new drug indications for potential coverage (includes drug submissions for both cancer and non-cancer uses). In addition to the demands of new drugs, most public drug plans are also responsible for funding other demands such as medical devices, medical supplies, and pharmacy services. Public drug plans strive to provide drug coverage that is contemporary and responsive to the needs of their citizens, while being accountable to the public, using the limited resources in a judicious, evidence-informed, fair, and cost-effective manner. As a result, public payers must make many difficult decisions associated with trade-offs and opportunity costs; deciding to fund one particular drug will mean another drug, device, and/or service cannot be funded.

### 3. Provincial/Territorial (P/T) Expensive Drugs for Rare Diseases Working Group (P/T EDRD WG)

In 2014, the provincial/territorial (PT) Health Ministers established the Expensive Drugs for Rare Diseases Working Group (EDRD WG), a separate entity from the pCPA. The working group represents all jurisdictions with Québec as an observer. The working group's mandate is to explore and develop strategies to improve the management of rare disease drug therapies with evidence-based approaches. In considering the significant challenges that exist in providing access to complex/specialized drug therapies, including those used to treat rare diseases, the EDRD WG has focused its efforts on four core areas: evidence, pricing, access and communication.

## III. KEY CHALLENGES WITH EDRDs:

### A. Pharmaceutical Manufacturers

Public drug plans fully recognize the critically important and valued role of the pharmaceutical industry to successfully discover, develop, and bring to market innovative medicines to meaningfully address unmet clinical needs. However, in doing so, public drug plans individually and collectively as the pCPA expect drug manufacturers to:

- Provide adequate evidence around their drug products' safety and efficacy to support coverage decisions;
- Provide fair, cost-effective and affordable prices;
- Follow the established national and PT processes; and
- Utilize their patient support programs and research programs (including clinical trials) in a responsible manner.

Many manufacturers are meeting these necessary requirements for their products as it relates to providing adequate evidence of clinical benefit and affordable cost-effective pricing, particularly with common diseases, where there are usually competing market alternatives. However, EDRD manufacturers are not meeting these expectations, resulting in significant challenges to public drug plans and the health care system. The challenges described are not unique to Canada, but exist globally and need to be addressed at an international level.

#### Evidence

Public drug plans are accountable for the appropriate use of public funds. Drug funding decisions are based on evidence of clinical benefit and fair pricing to ensure value-for-money and system affordability. For this, it is important to note that public drug plan coverage decisions consider both the evidence of clinical benefit/risks, pricing, and affordability together, and not separately.

It is acknowledged that for some ultra-rare diseases or highly complex conditions, it may be difficult to conduct the traditional clinical study design methods due to the small number of patients. Consequently, the clinical benefit may often be uncertain. Despite this, EDRDs have very high prices and there are few incentives for manufacturers to continue to appraise or demonstrate the value of

their drug. Ultimately, high prices and unclear clinical benefit challenge the sustainability of the health system.

In terms of the evidence, there are some drugs for rare diseases that have adequately demonstrated efficacy, effectiveness, and/or safety, to support an HTA recommendation with reimbursement conditions. The conditions for reimbursement define an eligible population through specific clinical criteria and usually also require a substantial price reduction. If there is a supportive HTA recommendation, the pCPA will usually proceed to negotiate with the drug manufacturer with the objective of successfully concluding a national letter of intent (LOI), which outlines the key agreement terms made between the pCPA and the drug manufacturer. Jurisdiction-specific product coverage or listing agreements can then be completed. When the evidence of clinical benefit has been adequate, jurisdictions have generally been successful in providing the therapy as a benefit in their programs.

Some drugs for rare diseases may have poor or unclear evidence of clinical benefit and/or harms. This could be due to one or a combination of factors, such as: poor study design, low number of study participants, highly variable patient types (disease heterogeneity), limited scope of patients studied (e.g., by age or degree of disease severity), use of surrogate outcomes measures (e.g., lab markers) rather than more clinically-meaningful outcomes (e.g., hospitalization), short study time periods, lack of or use of an irrelevant control group (comparator), lack of quality-of-life data, 'positive' results based on separate secondary analyses or only in a small subset of patients, etc. When drugs have been found to have poor or unclear evidence by independent expert committees, the HTA recommendation may be "do not reimburse" or may be limited to only a very specific patient group often with the condition of significant price reduction.

There are many drugs for rare diseases that have well-conducted clinical studies with clear results. Unfortunately, sometimes the studies conclude that the drug does not provide a clinically meaningful benefit in the studied population, which may result in a negative HTA recommendation. This also occurs for drugs developed for common diseases. The level of rarity of the disease being treated should not override the need for the drug manufacturer to provide adequate evidence of clinical benefit. For payers to fund therapies with unproven or poor efficacy is an irresponsible use of public funds given the large number of other competing health priorities.

Some countries in Europe are starting to explore the use of "managed access agreements" (MAA) to manage EDRDs. While the pCPA is open to explore this approach, it is still too early to know whether or not MAAs will be effective to address the evidence and pricing issues and this approach requires significant infrastructure and costs to support real world evidence collection.

### High Pricing

The high prices of drugs for rare diseases set by drug manufacturers represents the root cause that underpins many other challenges with the drugs for rare diseases. The list prices for these drugs now range from \$0.1M up to \$4.9 M per person per year. Since these therapies are generally for chronic illnesses, treating 1 patient for 10 years for example can cost payers from \$1M to \$49M. Pricing at these levels is well beyond what individuals can afford and well above the recent projection of annual

drug spending by Canadians of \$1,074 per capita <1>. The increasing number of therapies for rare diseases and the extremely high investment per individual patient will challenge the affordability and sustainability of public drug programs and divert investment opportunities away from other important areas of healthcare.

The pCPA supports a fair and reasonable return for manufacturers in order to cover research and development (R&D) costs and allow reinvestment to develop other new products. Manufacturers routinely argue that these high prices are justified due to the cost of investments to develop drugs for rare diseases and the relatively small market. However, while the pCPA requests that manufacturers transparently justify their extremely high pricing, there has been no transparent justification provided to date. Many of the world's highest revenue drugs are for those developed to treat rare diseases, with the number one top selling drug in the US being an orphan drug. A 2016 study found that orphan drugs are 5 times more profitable than non-orphan drugs <2>. A recent publication in JAMA Internal Medicine revealed that the R&D cost for 10 cancer and rare disease (orphan) drugs was \$7.2 billion and the revenue over 4 years was \$67 billion <3>. The extreme prices and demonstrated profitability without transparent justification, leaves payers and the public with the conclusion that the prices are set based primarily on profit maximization objectives rather than R&D recovery.

Many stakeholders cite that there are over 7,000 rare diseases and that 1 in 12 Canadians are affected by a rare disorder, though only 5% of these diseases have a treatment<4>. While the growth in treatments may result in much-needed health gains, the EDRD pipeline is expected to grow substantially. With this growth, the argument that EDRDs should all be funded because they comprise only a “small portion of the overall budget” is no longer valid. EDRDs, collectively, are accounting for a rapidly growing portion of government spending for a disproportionately small number of patients. In addition, this argument does not consider that these drugs are not priced cost-effectively resulting in significant opportunity costs of not funding other effective therapies for more common diseases.

Current industry pricing and business models are not aligned with payer expectations for value-for-money, quality of evidence, and cost-effectiveness. While the pCPA has successfully completed many negotiations with drug manufacturers and jurisdictions are covering many drugs for rare diseases, this should not be viewed as an indication that the pCPA has been able to adequately address the pricing concerns. The pCPA often negotiates under very challenging circumstances starting with an extremely high list price, severe untreated disease, no competing products, and high patient and care provider expectations to conclude negotiations quickly. As such, the pCPA remains very concerned that the prices achieved through negotiation remains largely unfair, excessive and not cost-effective and that pCPA needs collaborative federal support to manage.

Because of the pCPA's challenges around pricing and the limitations experienced using a negotiation approach, the pCPA strongly supports a legislated approach through the Patented Medicines Prices Review Board (PMPRB). The pCPA recognizes that the proposed PMPRB modernization changes are a reasonable, balanced, and necessary approach to protect all Canadians and payers from manufacturers who have excessive pricing. The proposed changes are an important step towards fairness, to not only bring Canadian prices more in line with international comparators but also by

introducing new pricing tests based on value-for-money (cost-effectiveness) and health system affordability (e.g., gross domestic product -based tests). The use of a value-for-money approach is needed as a more objective approach to assess the comparative evidence-based health benefits of a particular drug rather than relying solely on the current international price referencing test of drug prices which are arbitrarily set by drug manufacturers based on profit maximization objectives.

The federal government, who regulates drug pricing through the PMPRB and at the same time grants market authorization for the same products, should responsibly implement the necessary regulatory adjustments needed to protect consumers against the pharmaceutical industry's unfair and excessive market prices. If excessive pricing concerns are not addressed, then all F/P/T governments will continually be challenged with making difficult patient funding decisions and needing to trade off extreme opportunity costs for other health priorities, including other new innovative medicines.

#### National and P/T Processes:

Health Canada's Special Access Program (SAP) programme provides an important pathway for patients to access drugs (including drugs for rare diseases) that have not been reviewed or approved by Health Canada. This process is intended as a last-resort process where other options are not available, and the process assumes that safe effective drugs available outside Canada will be submitted for review by Health Canada in due course. However, some manufacturers do not submit their SAP drugs for Health Canada's market authorization review. As a result, these SAP drugs bypass the conventional processes of HTA evaluations and pCPA negotiations. Sometimes SAP drugs or SAP competing drugs are submitted for Health Canada's review and approved. Unfortunately, there are numerous instances when the new product introduced carries a significantly higher drug cost than the previous or comparator SAP drug.

An additional challenge is that for new drug products (or new indications for existing drug products) that receive Health Canada NOC, some companies do not routinely make submissions to the national HTA bodies. Without a submission to HTA, public drug plans cannot properly review drugs for coverage decisions. Other times, Health Canada will issue an NOC with Conditions (NOC/c) for indications with limited data, but with limited consequences for companies who do not fulfill their conditions. Some conditions, such as the need to collect more evidence, may be left unaddressed for significant periods of time, with HTA and payers, who are being asked to fund the full indication, left unable to evaluate the efficacy of the drug where data is missing or limited.

#### Clinical Trial and Patient Support (Compassionate Access) Programs

There is a growing concern that some manufacturers are increasingly using their clinical trial programs and "compassionate" drug access programs as a mechanism to influence decision processes or leverage public drug coverage. Patients who agree to be part of a clinical trial program are usually provided drug supply at no cost. However, when the study ends the provision of continued drug supply is variable. Similarly, through manufacturer "compassionate" drug access programs, patients may be provided no-charge (or financially assisted) coverage to drugs. The pCPA has experienced numerous situations where manufacturers threaten to stop "compassionate" supply of drug to

patients in order to leverage their negotiation position. This is very concerning to the pCPA as this practice creates significant issues for the patients receiving the medication and the patient's care providers. Although there are a great many benefits to these access programs, manufacturers who start supplying drug for such patients should act responsibly to fulfill their commitments to support patients and not misuse programs for market access purposes.

## **B. National and Provincial Processes**

There are currently several separate federal, national, P/T or regional, and provincial review and decision-making process frameworks focused on managing pharmaceuticals in Canada for the public. Each has its own separate mandate, goals, objectives, processes, budgets, accountabilities etc. Over the past 5-10 years, through increased national and inter-provincial collaboration on initiatives such as with CADTH and the pCPA, there is now greater recognition by all of the public entities that there are significant opportunities to further improve alignment and collaboration on various pharmaceutical issues of national interest.

### Gap in Needs Between Regulatory Review and Public Funding Review

One important unresolved challenge relates to the differences in mandates and decision making considerations between Health Canada's market authorization process and the public drug plans' HTA/pCPA-based drug coverage decision process.

Health Canada's market authorization review process is focused on drug safety (benefit vs risk), efficacy (does it have a clinical effect), and manufacturing quality. Health Canada's review is also singularly focused on the individual drug under review without need to demonstrate comparative value over other available drugs or treatment options.

Public drug plans consider drug efficacy and safety, but include cost-related considerations (e.g., budget impact, cost-effectiveness, opportunity costs, and affordability). Further, public drug plans with the support of HTA and independent expert committees determine with as much specificity as possible, where the drug fits compared to other options (comparative efficacy), what specific clinical outcomes are expected (with preference for more clinically meaningful endpoints like morbidity and mortality instead of surrogate endpoints like lab measures), and the specific patient and clinical circumstances when the drug is found to work best.

As a result, there are usually significant differences between the evidence that is needed for Health Canada to grant market authorization compared with the level of evidence the HTA and public drug plans require to fund. Tremendous tension in our healthcare system is created when drugs with very high costs are granted broad market authorizations but the HTA recommendations are negative or only supportive for a selected subgroup of patients with unmet need and the drug costs are extreme. The need for adequate evidence by drug plans is further disadvantaged since the drug manufacturers primarily develop their drugs' clinical study research and development program to satisfy the needs of market authorization regulators (such as the FDA) rather than the needs of the drug payers or

clinicians. Canadian and international HTA bodies have programs and advice available to manufacturers to assist in planning clinical trials that can meet the needs of all stakeholders. Drug manufacturers should be designing their clinical study programs to satisfy the needs of regulators, funders, clinicians and ultimately patients.

#### Public Agency Coordination and Communication

In order to better manage the challenges associated with EDRDs in Canada, the key public agencies should better align their mandates and processes while improving coordination where possible. This includes public agencies like Health Canada, HTA agencies (CADTH/INESSS), PMPRB, and public drug plans. There is also insufficient objective public-facing information on the challenges around EDRDs.

#### **IV. P/T EDRD Working Group Initiative to Improve Management of EDRD**

To address some of the challenges identified above, the EDRD WG has developed a proposal for a supplemental process for complex/specialized drugs that builds upon the existing national and jurisdictional drug review processes.

The primary objective of the proposal is to implement a proactive, consistent, fair and transparent process to assess complex/specialized drugs for the purpose of making responsive funding decisions.

The proposal includes modifications to the current national review process, including greater alignment, coordination and prioritization to identify complex drugs earlier for supplemental processes, improved use of real-world evidence to inform regulatory/HTA evaluations and funding decisions, and implementing centralized panels of experts for consistent implementation decisions where appropriate.

The EDRD WG is now consulting with a broad group of stakeholders to gather feedback to inform and refine the proposal. The stakeholders include health system partners (e.g., Health Canada, CADTH and PMRPB), researchers, clinicians, patient groups, pharmaceutical industry, and private insurers. Once the results of the consultation are gathered and considered, further direction on potential changes are expected in the spring/summer 2019.

## V. SUMMARY AND KEY RECOMMENDATIONS

Public drug plans, collectively as the pCPA and individually as jurisdictions, have the role and responsibility to support the public by making appropriate public drug funding decisions that are evidence-informed, cost-effective, affordable and sustainable.

With drugs for rare diseases, there are several significant challenges for public drug plans in Canada and elsewhere around the world. Public drug plans expect drug manufacturers to follow the established national and P/T processes, to provide adequate evidence around their drug products' safety and efficacy to support coverage decisions, to provide fair, cost-effective and affordable prices, and to utilize their research (clinical trial) and patient support programs in a responsible manner.

The extreme high pricing set by manufacturers is a principle cause of the many payer challenges for drugs for rare diseases and will continue to challenge drug program sustainability. Besides supporting PMPRB's modernization efforts, the pricing and evidence issue identified needs to be resolved together with industry and there should be greater alignment and collaboration among the key health partners and stakeholders.

To address some of the barriers and challenges described with expensive drugs for rare diseases, the pCPA and public drug plans request the following support from the federal government:

1. The federal government should provide funding for drugs for rare disease, either through its recent and ongoing consideration of a national pharmacare approach or through an alternative national mechanism.
2. The federal government must better protect Canadians from excessive drug pricing by not only implementing the PMPRB's proposed modernization changes with new pricing tests, but also explore collaborations with other international governments to jointly address this growing global issue.
3. The federal government should continue to work with P/T public drug plans and the pCPA to better align, collaborate, and coordinate our respective structures and policies wherever possible to improve the management of drugs for rare diseases. This includes working together with the industry and other stakeholders to address the evidence and pricing issues, establishing a coordinated screening and prioritization mechanism to nationally identify complex drugs that may require supplemental support, and providing support to expand the research and evaluation capacity for real world evidence (RWE) for these drugs.

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