Stakeholder Consultation: Supplemental Process for Complex/Specialized Drugs Background Document

In 2014, the Provincial/Territorial (PT) Health Ministers established the Expensive Drugs for Rare Diseases Working Group (EDRD WG). The working group's mandate is to explore 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 communications.

Some of the current issues and challenges associated with complex/specialized drug therapies are outlined below, organized under the core areas of focus.

Evidence

- The lack of robust evidence to support efficacy, safety, and cost-effectiveness (due to small patient numbers and difficulties conducting well-designed clinical trials) makes decision-making difficult for clinicians, patients and payers.
- There are currently no best practices for generating or evaluating real-world evidence, which could help inform appropriate funding decisions in scenarios where there is high uncertainty with evidence available from studies.

Pricing

- High drug costs threaten drug program sustainability and access for patients.
- The rationale for high prices of EDRDs, even given their unique market dynamics, often does not appear to be justified.
- There are a growing number of drugs developed for the treatment of rare diseases, posing an increasing challenge for payers.

Access

- Complex/specialized drugs are often purported to address unmet needs in scenarios where no alternative therapies exist, leading to greater urgency from clinicians and patients to obtain timely access to these products.
- There is variability between jurisdictions both in terms of funding availability and criteria for treatment.

Communications

- There is a perceived lack of transparency and communication between the national drug review processes and patients and clinicians.

PROPOSED SUPPLEMENTAL PROCESS

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.

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The proposal has been supported in principle by PT Health Ministers, and the EDRD WG is now consulting with stakeholders to gather feedback and ideas in order to inform and refine the proposal.

The proposal includes modifications to the current national review process, which are outlined in the table below. A general overview of the current review and reimbursement process is available at https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2017/10/canada-reimbursement-profile. A figure depicting the current and proposed supplemental processes and their similarities and differences is included in Appendix A.

For clarity, the proposed supplemental process would not be an entirely separate pathway, and is not intended to allow eligible drugs to bypass regular processes. It is also not a guarantee of public funding for drugs that are eligible to be reviewed through the proposed process.

Table 1: Comparison of Current Process and Proposed Supplemental Process

Process Stage	Current Process	Supplemental Process
Early screening and identification of potentially eligible drugs	• No coordinated early national screening process • Some national agencies (e.g., CADTH, PMPRB) have screening mechanisms in place, but little systematic sharing of information with each other or with public drug plans	• Systematic early screening by a cross-organizational group that includes national agencies and public drug plans • Potentially eligible drugs identified based on pre-defined criteria; proposed primary criterion is Health Canada acceptance for review through an expedited pathway (e.g., Priority Review or advance consideration of conditional approval via the Notice of Compliance with Conditions [NOC/c] policy)*; screening criteria to identify additional drugs of interest to public plans could include disease severity, unmet need, cost per patient, budget impact, disease prevalence, potential for robust evidence generation • Manufacturers may request supplemental process pathway review; however, final decision rests with CADTH (considering drug plan feedback) • Eligible drugs targeted for parallel regulatory/HTA review
Concurrent submission	• Drugs generally submitted and reviewed separately/sequentially through Health Canada, CADTH, then pCPA; PMPRB review occurs after Health Canada	• Eligible drugs may be submitted concurrently to Health Canada, CADTH, PMPRB and pCPA to help reduce overall submission review time • Specific requirements for eligible submissions would be defined
Health technology assessment review	• Drug plan input to CADTH occurs relatively late in overall HTA review process • Drug plans review HTA information to identify issues before final recommendations issued • Limited number of clinicians engaged • Very limited consideration of RWE to address uncertainties	• Enhanced/earlier input to CADTH from drug plans • Enhanced clinician and patient/patient group engagement to ensure full understanding of all issues to inform HTA review/recommendation • Enhanced consideration of RWE to address uncertainties

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Process Stage	Current Process	Supplemental Process
pCPA negotiations and implementation	• Negotiations conducted by pCPA and participating jurisdictions • Very limited consideration of managed access† agreements/conditional funding	• Negotiations coordinated by the pCPA Office according to set principles for eligible drugs • Enhanced consideration of managed access† agreements/conditional funding
Collection and assessment of real-world evidence	• Very limited use of RWE	• Leverage RWE to address evidence gap where appropriate • Enhanced use of RWE to inform continued funding, based on defined goals of therapy • Evaluation of RWE could lead to funding criteria changes (enhanced or restricted), price changes/renegotiations, or delisting
Individual patient access	• Adjudication and interpretation of reimbursement criteria at discretion of drug plans	• Where appropriate (specific circumstances TBD), and after a PT listing decision has been made, a national panel of experts would review individual patient cases and recommend funding eligibility, including patient goals, in order to increase equity and consistency between jurisdictions • Final funding decisions would remain the responsibility of individual jurisdictional decision makers
Communications	• Communications may be ad hoc and/or reactive	• Enhanced proactive communications and transparency with all stakeholders

CADTH = Canadian Agency for Drugs and Technologies in Health; HTA = health technology assessment; pCPA = pan-Canadian Pharmaceutical Alliance; PMPRB = Patented Medicine Prices Review Board; PT = Provincial/Territorial; RWE = real-world evidence; TBD = to be determined

* See Appendix B for information about Health Canada's Priority Review pathway and advance consideration of conditional approval via the Notice of Compliance with Conditions policy.

† Managed access programs have been described as programs "which are negotiated between manufacturers and payers, [to] provide access to a therapy with a requirement for additional specific data to be collected to fill an evidence gap." (Reference: Canadian Organization for Rare Disorders. Now is the Time: A Strategy for Rare Diseases is a Strategy for all Canadians. May 2015.)

Potential Benefits

Potential benefits of the proposed supplemental process include:

- More timely and transparent funding recommendations and decisions;
- Improved use of real-world evidence to inform evidence evaluations and funding decisions;
- Ability to enter into conditional managed access schemes with pre-set, clear expectations for governments, manufacturers, clinicians and patients;
- Improved negotiation co-ordination and mechanisms to ensure ongoing value and affordability; and
- Increased consistency of funding implementation between jurisdictions through use of a centralized panel of experts, when appropriate.

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CONSULTATION QUESTIONS

Questions that will be posed to stakeholders during consultations are provided in Appendix C.

NEXT STEPS

Stakeholder consultations will occur throughout fall 2018. Consultation feedback will be consolidated and used to refine the supplemental process proposal. The proposal will be brought back to PT Health Ministers for further review and discussion, with potential implementation of a supplemental process in spring/summer 2019.

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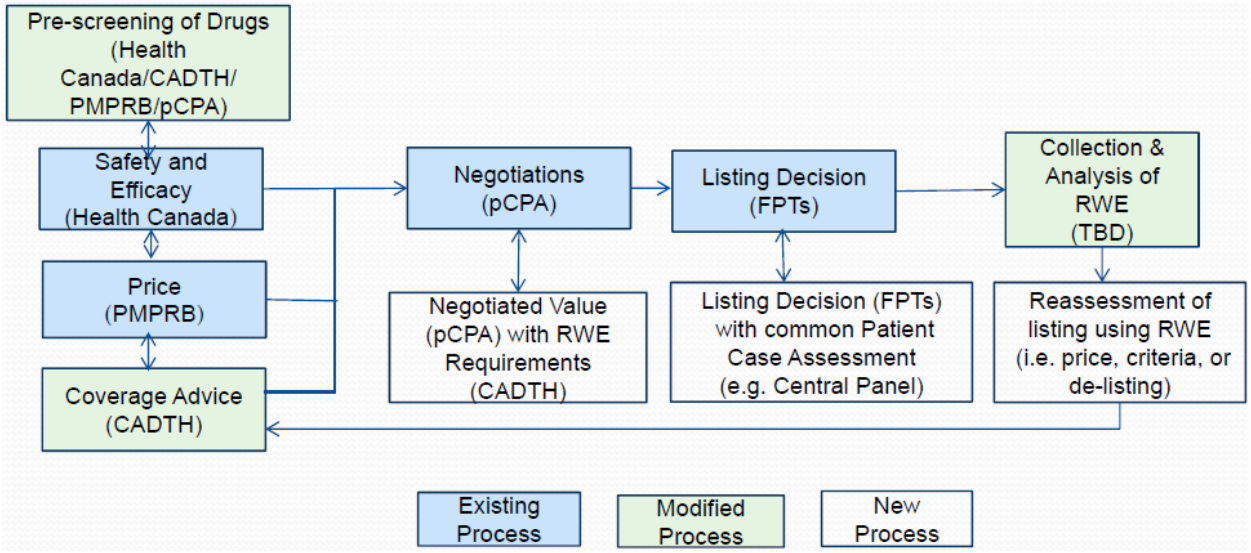
Appendix A: Current Process and Proposed Supplemental Process



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Appendix B

Health Canada Priority Review of Drug Submissions

Below are excerpts from the Health Canada website regarding eligibility for a Priority Review.

> *This policy applies to a New Drug Submission (NDS) or Supplemental New Drug Submission (S/NDS) for a serious, life-threatening or severely debilitating disease or condition for which there is substantial evidence of clinical effectiveness that the drug provides:*
>
> - *effective treatment, prevention or diagnosis of a disease or condition for which no drug is presently marketed in Canada; or*
> - *a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies, preventatives or diagnostic agents for a disease or condition that is not adequately managed by a drug marketed in Canada.*

Further details regarding the Priority Review policy are available at https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html#a2.

Health Canada Notice of Compliance with Conditions (NOC/c)

Below are excerpts from the Health Canada website regarding the NOC/c policy.

> *The objective of the Notice of Compliance with Conditions policy is to:*
>
> a. *provide access to promising new drugs for patients suffering from serious, life-threatening or severely debilitating diseases or conditions for which no drug is presently marketed in Canada or for which a significant increase in efficacy or a significant decrease in risk is demonstrated in relation to an existing drug marketed in Canada;*
> b. *create mechanisms for the appropriate completion of confirmatory trials to verify the clinical benefit of a drug authorized under this policy; and*
> c. *ensure transparency of the conditions associated with the market authorization.*
>
> *The benefits of the NOC/c policy are twofold:*
>
> 1. *It facilitates earlier access to the drug by physicians and patients. The acceptance of promising evidence of clinical effectiveness allows for the filing of an eligible drug submission earlier than normally possible. Should the outcome of the review be positive, the time to approval and market for the drug may be shortened. It should be noted that the time to agreement on the acceptability of the contents of the "Letter of Undertaking" will affect the overall time to market.*
> 2. *It provides the means to effectively monitor, and report on, the safety and efficacy of promising new therapies through enhanced post-market surveillance initiatives.*

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> *A Notice of Compliance issued under the NOC/c policy may be granted for a drug product with promising clinical benefit, providing that it possesses an acceptable safety profile based on a benefit/risk assessment, and is found to be of high quality.*
>
> *In order to satisfy the intent of the policy, in providing accelerated access to life-saving therapies, submissions seeking advance NOC/c consideration are assigned a shortened review target to account for the Priority nature of the submission… NOC/c-eligible submissions, based on evidence including unvalidated surrogate markers or those lacking final outcomes data, are unlikely to meet the evidence requirements of the Priority Review Policy. Review targets for the NOC/c policy however, reflect the Priority status of the submission and following a comprehensive review of the information contained within the submission, the data may support NOC/c authorization.*

Further details regarding the NOC/c policy are available at https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/notice-compliance-conditions.html#a1.

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Appendix C: Stakeholder Consultation Questions

1. What do you perceive to be the current challenges and barriers facing expensive drugs for rare diseases?

2. From your perspective, does the proposed supplemental process address some or all of the current challenges encountered with complex/specialized drugs, including drugs for rare diseases? Why or why not?

3. What role could you or your organization play in working with others to achieve the stated objective of the proposed supplemental process?

4. Please provide your perspective on real world evidence (RWE) and how it could be incorporated into the current processes.

5. What challenges and/or opportunities do you see in obtaining and using RWE?

6. What is your perspective on having a national review panel to review patient cases? How do you believe this will impact access to EDRDs?

7. In considering the proposed process, have we missed anything?