Building Toward a Potential Pan-Canadian Formulary: A Report From the Advisory Panel

June 2022

CADTH recognizes the inherent and treaty rights of all First Nations, Inuit, and Métis peoples across this land. We acknowledge the harms and mistakes of the past and are committed to moving forward in partnership with Indigenous communities in a spirit of reconciliation and collaboration. CADTH staff work across Canada, residing on various traditional lands and collaborating with Indigenous governments, health care providers, and community members. Our Ottawa offices are located on the unceded, unsurrendered Territory of the Anishinabe Algonquin Nation. Our Toronto offices are located on the traditional territory of many nations, including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee, and the Wendat.

Acknowledgements: CADTH would like to acknowledge the Canadian Institute for Health Information, CADTH's Health Economics Advisory Council, Non-Insured Health Benefits, and the Patented Medicine Prices Review Board for their contribution in providing advice and data to support this work. CADTH would specifically like to acknowledge the Panel members and is grateful to the members, who like so many other exceptional people who work with CADTH have helped Canadian healthcare decision makers, health care professionals, health system leaders and policymakers make well-informed decisions and improve the quality of health care services.

Disclaimer: This material is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose; this document should not be used as a substitute for professional medical advice or for the application of professional judgment in any decision-making process. Users may use this document at their own risk. Care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up to date as at the applicable date the material was first published. Notwithstanding, CADTH is not responsible for any errors or omissions, or injury, loss, or damage arising from or relating to the use of this document and is not responsible for any third-party materials contained or referred to herein. This document is subject to copyright and other intellectual property rights and may only be used for non-commercial, personal use or private research and study.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

About the Panel Members

The panel comprises 2 co-chairs and 12 members. Its members were recruited from across Canada and represent diversity across gender, culture, race, and geographic region. The panel brings together members with a range of expertise and experience, including health care providers (nursing, pharmacy, and medicine), persons with lived and living experience, persons working with Indigenous and other communities often made vulnerable through a combination of social and economic policy, as well as those with designated representatives, and individuals with backgrounds in ethics, health policy, and drug plan leadership. The names, biographies, and conflict of interest declarations of the 14 members on the panel are available on the CADTH website.

Alexandra King (Co-chair), MD, FRCPC
Nipissing First Nation
Saskatchewan

Allen Lefebvre (Co-chair)
Saskatchewan

Stéphane Ahern, MD, FRCPC, PhD
Quebec

Shawn Bugden, BSc (Hons), BSc (Pharm), MSc, PharmD
Newfoundland and Labrador

Connie Côté, MA
Ontario

Elsie Duff, BScN, RN, NP, MEd, PhD
Manitoba

Bashir Jiwani, MA, PhD
British Columbia

Diane McArthur, BPR, MBA
Ontario

Andrew Pinto, MD, CCFP, FRCPC
Ontario

Sheri Roach, RN, MN, MHA
Nova Scotia

Adil Virani, BSc (Pharm), PharmD
British Columbia

Cornelia (Nel) Wieman, MD, FRCPC[a]
British Columbia

Sam Wong, MD, FRCPC
Alberta and the Northwest Territories

Yan Yu, MD, MPP, MBA, CCFP
Alberta

[a] Dr. Cornelia (Nel) Wieman stepped down in March 2022 due to very significant competing commitments. On behalf of the panel, the co-chairs would like to acknowledge Dr. Wieman's significant contributions to the panel's work.

Table of Contents

List of Tables

List of Figures

Abbreviations

ACE	angiotensin-converting enzyme
AHFS	American Hospital Formulary Service
ATC	anatomical therapeutic chemical
CIHI	Canadian Institute for Health Information
CPG	clinical practice guideline
EML	essential medicines list
FPT	federal, provincial, and territorial
HEAC	Health Economics Advisory Council
HTA	health technology assessment
INESSS	Institut national d'excellence en santé et en services sociaux
MCDA	multicriteria decision analysis
NIHB	Non-Insured Health Benefits
pCPA	pan-Canadian Pharmaceutical Alliance
RWD	real-world data
RWE	real-world evidence

Executive Summary

Significant gaps in access to prescription drugs exist in Canada. These gaps have been noted in the literature, including the report by the Advisory Council on the Implementation of National Pharmacare[1] entitled *A Prescription for Canada: Achieving Pharmacare for All* (hereinafter referred to as the council report).[2] Even when insured, some people living in Canada still do not have sufficient or equitable access to medications. Some of the reasons reported include differences in which drugs are included on different formularies, delayed access, and out-of-pocket costs.[3] A pan-Canadian formulary within a national pharmacare program could help to address inequitable access to prescription drugs and to those products that directly support the delivery, administration, and optimal use of drugs (i.e., related products) for people living in what has become known as Canada.

The goal of developing a potential pan-Canadian formulary is to include a broad range of safe, effective, evidence-based drugs and related products that meet the health care needs of peoples living in Canada. Developing a framework for the design and implementation of a potential pan-Canadian formulary is complex. The panel considered what would serve all people living in Canada today and years into the future. The panel strongly feels that, while policies need to respond to the issues of today, a lasting framework must be resilient, agile, sustainable, and adaptable to the unforeseen but inescapable changes of tomorrow. It is our belief that our recommendations will provide decision-makers with the framework and tools necessary to initiate the steps to creating and implementing a potential pan-Canadian formulary.

The following elements were outlined in the council report[2] to develop a potential pan-Canadian formulary:

- terms of coverage (i.e., eligibility criteria or who may be covered)
- processes for creating a list of drugs and related products (i.e., what is covered and why)
- ways to manage the formulary (i.e., how to maintain the list)
- how it could be financed (i.e., who or what group funds it)
- who makes the decisions (i.e., whether the listing decision is made by a group, organization, or designated individual such as a health minister or an executive officer of a drug program).

CADTH was engaged to **support 2 of the 5 named elements**; specifically, **to develop processes for creating a list of drugs and related products and to highlight best practices for managing a formulary.** At the request of Health Canada, CADTH convened a time-limited multidisciplinary advisory panel to provide non-binding recommendations regarding a framework for a potential pan-Canadian prescription drug list, or formulary. Specifically, the mandate of the panel was to:

- develop principles that could guide the development of a potential pan-Canadian formulary

- create a proposed sample list of commonly prescribed drugs and select related products as a test case based on a subset of the therapeutic areas that could be included on a potential pan-Canadian formulary
- establish criteria and a transparent process that could expand the proposed sample list to other therapeutic areas, and guide how new products could be added to the list and how a proposed list could be maintained over time
- engage with interested parties to solicit broad perspectives to inform the panel's recommendations.

Working within the mandate given to them, the panel's recommendations are based on their interpretation of the council report,[2] review of the comments shared by respondents to the consultation, and other assumptions noted in this report. The panel understood that the process to develop and implement a potential pan-Canadian formulary is complex and would require attention to a wide range of issues, not all of which were within the panel's mandate to consider. As a result, the panel's work did not include:

- assessment of current drug plan processes or expectations about whether or how coverage on existing drug plans might be impacted by a potential pan-Canadian formulary
- identification of governance structures to implement a potential pan-Canadian formulary (e.g., which organization or entity should oversee implementation of a potential pan-Canadian formulary or make funding decisions)
- consideration of financing issues (e.g., funding allocation; financial contributions; funding models; budget scope, size, and amount; or individual drug plan budgets or projected estimates for those budgets)
- review of the terms for coverage (e.g., patient contributions such as copayments or deductibles) and patient eligibility, including status (e.g., international workers or refugee status [undocumented])
- consideration of the interplay between public and private insurance plans (i.e., coverage as first and second payer)
- consideration of other ongoing pharmaceutical initiatives (e.g., Health Canada's Drugs for Rare Diseases Strategy).

Although out of scope, the panel recognizes the importance of these elements to address as part of the future design and implementation of a pan-Canadian formulary, and advocates for their consideration as part of future work. It is anticipated that the recommendations in this report could inform the discussion on a decision-making framework for other pharmaceutical initiatives. Throughout their discussions, the panel was challenged by the out-of-scope elements and made assumptions to proceed (e.g., if a potential pan-Canadian formulary is intended to be an add-on or overlaying model, it would work with existing structures and systems, and be synchronized with existing drug programs across the country). Further clarity of these elements could result in the recommendations being refined or enhanced.

This report is meant to present a potential pathway, including principles, values, and criteria to guide the development of a potential pan-Canadian formulary. Also included is a summary of the panel's work on a process for creating a list and evaluating products

for inclusion on a potential pan-Canadian formulary. Finally, this report outlines the panel's discussion on formulary management best practices (i.e., an approach to align formularies with current evidence), as well as how this work could move forward, and the elements that would need to be addressed.

Highlights From the Panel's Non-Binding Recommendations

1. The panel proposed 6 principles. The principles of the potential pan-Canadian formulary should be: Universal and integrated; equitable; effective, safe, and high quality; sustainable; efficient and timely; and inclusive, transparent, with fair process. The principles are presented at a high level and meant to act as guideposts; they are not listed in any specific order.
2. A potential pan-Canadian formulary should:
    a. be a dynamic and living system and involve multiple perspectives. The system to develop and operate a potential pan-Canadian formulary should be informed by multiple perspectives and involve patients, clinicians, and other health partners within the health care system. The potential pan-Canadian formulary should be a dynamic and living system.
    b. be aligned with, if not integrated into, other elements of the health system. The ideal of a universal pan-Canadian formulary would include a broad range of safe and effective medications and related products to meet the health care needs of all of Canada's diverse population. Access to medication is only one part of access to necessary health care, so in determining which drugs and related products should be included in a potential pan-Canadian formulary, the process design for such a formulary should be aligned with, if not integrated into, other elements of the health system.
    c. be equitable and support a distinction-based approach that promotes self-determination. A potential pan-Canadian formulary should contribute equal opportunities for health and wellness for people living in Canada with the desired result of equal outcomes. An equitable pan-Canadian formulary would list drugs available to people living in Canada in such a way as to make prescription drugs and related products more accessible to all who currently do not have access. To counteract barriers to access, a potential pan-Canadian formulary should be equitable and support a distinction-based approach that promotes self-determination.
    d. incorporate evidence that considers diverse populations, perspectives, and experiences. Central to effectiveness and quality are processes for monitoring, evaluating and improving performance against key commitments. Among other things, quality improvement will require analysis of evidence. As our understanding and use of real-world evidence evolves, it will incorporate evidence that considers diverse populations, perspectives, and experiences, as well as assessing value in a way that reflects the diversity and realities of Canada's population. Critically, this includes increasingly integrating Indigenous (i.e., First Nations, Inuit, and Métis) ways of knowing as part of our commitment to reconciliation. These elements will need to be considered and better integrated into a holistic evaluation

approach. However, given the panel's mandate, it did not pursue the methodological and epistemological analysis required in this regard; nor did it consider any form of multicriteria decision analysis. Before implementing any approach, these elements must be studied and clarified. This will require systematic methods for how decision-making should incorporate different levels and types of evidence, as well as a thoughtful policy and approach to evidence analysis. Research that lives up to these standards would be encouraged as a next step on this path.

e. be aligned with current evidence. Formulary modernization should be part of the process to reassess formulary listings. To derive true benefits, the panel noted that judicious resource allocation should be applied into formulary modernization as it can be a resource-intensive process. This process should be transparent and take a collaborative approach to meaningfully engage all partners in the health system (e.g., patients, clinicians, industry, decision-makers, and other interested parties).

f. be sustainable. A potential pan-Canadian formulary should be in the best interest of the people living in Canada. When considering sustainability, in addition to financial sustainability of health systems and prescription drug budgets, attention should be paid to the purpose of the formulary and how such decisions will allow the formulary to address other health system priorities. Cost-effectiveness is one of several important factors to fiscal sustainability and should be incorporated into any future work regarding a potential pan-Canadian formulary.

g. adopt systems and process efficiencies. Universality and integration of a pan-Canadian formulary will require a focus on system efficiencies and sustainability. This will include everything from minimizing process duplications and leveraging existing infrastructure and resources, to using cost-effective medications and related products. The principle of efficient and timely will require that decisions can be made well and in time to meet patient needs. These may include:

    i. providing simplified points of access for related products: In many Canadian jurisdictions, related products (devices that directly support the delivery, administration, and optimal use of drugs) are often covered through different programs within the health system. This makes navigating and accessing coverage difficult for patients and prescribers. A potential pan-Canadian formulary represents an opportunity to streamline processes, provide simplified points of access, and ultimately help patients, caregivers, and health care providers access these types of products. The process to identify which related products to include in a pan-Canadian formulary should be similar to the process followed for drug products (i.e., apply the same principles and criteria). The definition of related products should not be prescriptive but should include a set of criteria to enable a patient-oriented approach and allow for a continued focus on equity. A conservative approach should be established at the initial stage to test and evaluate the process before opening the criteria to allow for a wider selection of related products.

    ii. exploring a hybrid submission review model: For a new drug product to be considered for inclusion in a public drug plan, the sponsor (i.e., the submitter of the file) must complete 3 steps, (1) approval by Health

Canada that the drug may be sold in Canada, (2) health technology assessment (HTA) review (typically through CADTH or the Institut national d'excellence en santé et en services sociaux [INESSS]), and (3) pricing agreement via the pan-Canadian Pharmaceutical Alliance (pCPA) and/or federal, provincial, and territorial (FPT) payer. The sponsor decides when the initial application is made. HTA assessments are currently conducted using a "first-in, first-out" process based on when submissions are filed. A hybrid approach to submissions should be considered to allow for a standardized process to review drugs (i.e., first-in, first-out), as well as a fast-track mechanism to select drugs that meet an unmet need or have exceptional benefits. A similar approach should be considered for price negotiations (i.e., those products that are fast-tracked should continue as such downstream) to ensure a streamlined system.

3. Taking a staged approach to creating a potential pan-Canadian formulary. The panel established a 3-stage approach to creating a potential pan-Canadian formulary:

   - Stage 1: Approach to creating the proposed sample list of drugs and related products
   - Stage 2: Expanding to other therapeutic areas
   - Stage 3: Adding and maintaining a potential pan-Canadian formulary

   The panel explored different approaches for creating a proposed list of drugs and related products, including following an essential medicines list (EML) concept. According to WHO, "Essential medicines are those that satisfy the priority health care needs of a population," and an EML can be an integral component of treatment within the continuum of care.[4] WHO publishes a Model List of Essential Medicines every 2 years, which is meant to act as a blueprint for the development of national EMLs based on local priorities and treatment guidelines. The value of the EML approach is recognized, with increasing uptake in different jurisdictions globally to adopt or adapt the Model List of Essential Medicines based on local needs.[4] Notwithstanding the value that a national EML serves for some jurisdictions, the panel reviewed this approach by applying its proposed principles, and deliberated on the benefits and risks while considering the current formularies across Canada that already fund a broad list of drugs and related products. Because of numerous challenges that were observed, including the limited number of drugs in an EML, the panel did not pursue this approach (refer to Appendix 6 for details). Another approach involved conducting a comprehensive and comparative assessment of drugs; that is, comparing each individual product for the same indication by applying the criteria typically used in making listing recommendations. Although thorough, this type of comparative assessment requires more resources than were available to the panel to complete this work. Furthermore, the data needed to evaluate each drug against the criteria may not be easily available or available at all. The panel also did not simply build on an existing public formulary because of known gaps between the different formularies, including the significant differences in how these plans are administered and who may be eligible for coverage. By selecting a small

sample list of products as a proof of concept for the process, the panel's suggested method for arriving at a proposed sample list for a potential pan-Canadian formulary represents one possible approach to help address the current inconsistent and inequitable access to, and coverage for, drugs and related products, while recognizing there is still much work to be done. All 6 principles were adopted for inclusion in the assessment criteria to create the proposed sample list for the initial 3 therapeutic areas (cardiovascular diseases, diabetes, and psychiatric illnesses, which together represent approximately 62% of prescriptions dispensed). The 6 principles should also be applied for future expansion to other therapeutic areas. These guiding principles should be anchored in the evaluation criteria and deliberative processes for new products and/or indications and provide the basis for decision-making with respect to the evaluation of drugs and related products for a potential pan-Canadian formulary.

4. Building public trust through transparent decision-making. The panel recognized that the demand for health care is greater than the public health care system's resources (or ability to meet demand). Hence, difficult choices will need to be made to create a pan-Canadian formulary, which could have significant implications in terms of what access is provided and, consequently, what cannot be funded. Transparency of these choices is essential to building public trust.
5. Accountability and reason-driven decision-making. To ensure accountability and support reason-driven decision-making, the principle of transparency should apply to the creation and maintenance of a potential pan-Canadian formulary and part of the system in which it is embedded. To live up to the value of fair process, a potential pan-Canadian formulary will need to ensure appropriate conflict of interest guidelines are established and followed by all parties involved in the process.
6. Considerations for future work. Ongoing work and continued engagement will be required to refine the details of creating and maintaining a potential pan-Canadian formulary. It would be important to build based on key learnings that unfold as the plans for a potential pan-Canadian formulary advances, and out-of-scope items are addressed. The value of expanding the work could be diminished in the absence of clarity about the out-of-scope issues and this clarity would ideally be addressed before further work is undertaken or done in parallel for the work to be meaningful. This includes assessing the impact of other pharmaceutical initiatives (e.g., the drugs for rare diseases strategy) in an ongoing way to ensure synergies upon implementation. The panel members also highlighted that the existing variation in listing restrictions on a given drug across formularies leads to inequity. The panel recommended that harmonization of the eligibility criteria should be considered to ensure equitable access across Canada. Panel members also recognize that there are opportunities to improve and streamline the workflow for clinicians in navigating these restrictions, which would help reduce the amount of unnecessary, time-intensive, and costly administrative barriers for clinicians and their patients. The panel emphasized that patient outcomes and continuity of care should not be compromised in the process.

Setting the Context

Many Canadians cover the cost of their prescription drugs through a combination of public drug plans, private drug plans, and out-of-pocket payments. However, numerous individuals currently lack adequate coverage to afford the drugs they need. Significant gaps in access to prescription drugs in Canada have been widely described in the literature, including the report made by the Advisory Council on the Implementation of National Pharmacare[1] entitled *A Prescription for Canada: Achieving Pharmacare for All* (the council report).[2] For example, the council report[2] highlighted the following statistics.

- Nearly 3 million Canadians were not able to afford 1 or more of their prescription drugs.
- Almost 1 million Canadians cut back on food or home heating to pay for their prescription drugs or borrowed money to pay for them.
- The nature of work is also changing: More people are self-employed, part-time, or contract workers, and may face precarious employment. Only 27% of part-time employees have health benefits and others may not have health benefits at all. Women, young people, new Canadians, and recent immigrants are all more likely to work in part-time or contract positions, which could leave these groups without drug coverage simply because of the nature of their work.

According to results from a 2016 survey, the unaffordability of drugs prevented 5.5% of Canadians from taking 1 or more medications as prescribed.[5] Of the treatments not adhered to because of cost, most were drugs for treating psychiatric health conditions. The survey report also noted that many Canadians went without basic needs such as food (approximately 730,000 people), heat (approximately 238,000 people), and other health care expenses (approximately 239,000 people) to pay for their prescriptions. This disproportionately affects women, younger adults, Indigenous peoples, those with a poorer health status, those lacking drug insurance, and those with lower incomes.[5]

A recent report published by the Conference Board of Canada indicated that across the country, 1.1 million people, or 2.8% of the population, are uninsured for prescription drug coverage. Even when insured, some Canadians still do not have sufficient or equitable access to medications. Some of the reasons reported include differences in which drugs are included on different formularies, delayed access, and out-of-pocket costs.[3]

In view of these facts, introducing a pan-Canadian formulary within a national pharmacare program could help to address inequitable access to prescription drugs and related products for people living in what has become known as Canada.

Background

At the request of Health Canada, CADTH convened a time-limited multidisciplinary advisory panel (the panel) to provide non-binding recommendations regarding a framework for a potential pan-Canadian prescription drug list, or formulary. Throughout the process, CADTH provided oversight and facilitated the work of the panel. This report

is intended to contribute to the current dialogue by decision-makers and others on the development of a potential pan-Canadian formulary. This report includes the panel's consideration of the feedback received from respondents to the consultation. It should be noted that the work of the panel was, at times, restricted because of scope issues. In addition, it is anticipated that the recommendations in this report could also be used to inform the discussion on a decision-making framework for other pharmaceutical initiatives.

A formulary typically contains a list of medications and other products that are included within a health plan. It generally contains a description of each product that is listed and may also contain information to support prescribing, dispensing, and administration of the product, as well as any interchangeability between products.[6] The general purpose of a formulary is to ensure that the treatments that are used are safe, effective, and affordable. It also aims to include treatments that are cost-effective (i.e., takes into account how well a drug or technology works in relation to how much it costs).

The goal of developing a potential pan-Canadian formulary is to include a broad range of safe, effective, evidence-based drugs and related products that meet the health care needs of people living in Canada. Of note, this work includes "related products" (i.e., devices that directly support the delivery, administration, and optimal use of drugs, such as spacer devices for metered dose inhalers or blood glucose strips). Only a few select related products were discussed by the panel as a test case.

The exercise to develop a potential pan-Canadian formulary is complex. The following elements were outlined in the council report[2] to develop a potential pan-Canadian formulary:

- terms of coverage (i.e., eligibility criteria or who may be covered)
- processes for creating a list of drugs and related products (i.e., what is covered and why)
- ways to manage the formulary (i.e., how to maintain the list)
- how it could be financed (i.e., who or what group funds it)
- who makes the decisions (i.e., whether the listing decision is made by a group, organization, or designated individual such as a health minister or an executive officer of a drug program).

CADTH was engaged to support 2 of the 5 named elements; specifically, to **develop processes for creating a list of drugs and related products** and to **highlight best practices for managing a formulary**. Given its considerable experience and important role in the pharmaceutical management system, CADTH is uniquely positioned to act as a trusted source for high-quality, credible, and objective information in pharmaceutical decision-making processes to support FPT members and health organizations. CADTH has experience with developing options and implementing approaches to enhance HTAs, including the alignment of its drug review processes for common drugs, oncology, gene therapies, and plasma protein products. CADTH also collaborates on select projects with INESSS to ensure greater diversity of perspectives and insights into a condition and therapy under review by both organizations. CADTH has also previously supported the

work of the council.[1] CADTH was asked by Health Canada to establish a time-limited, multidisciplinary advisory panel to carry out the following:

- develop principles and a framework that could guide the development of a potential pan-Canadian formulary
- create a proposed sample list of commonly prescribed drugs and select related products as a test case based on a subset of the therapeutic areas that could be included on a potential pan-Canadian formulary
- establish criteria and a transparent process that could expand the proposed sample list to other therapeutic areas, and guide how new products could be added to the list and how a proposed list could be maintained over time
- consult with key stakeholders, including FPT governments, patients, clinicians, industry, and other interested parties.

Working within the mandate given to them, the panel's recommendations are based on its interpretation of the council report,[2] review of the comments shared by respondents to the consultation, and other assumptions noted in this report. The panel understood that the process to develop and implement a potential pan-Canadian formulary is complex and would require attention to a wide range of issues, not all of which were within the panel's mandate to consider. The panel recognized that this was an important yet initial piece of work and that the mandate included producing focused deliverables within defined timelines and resources. As a result, the panel's work did not include:

- assessment of current drug plan processes or expectations about whether or how coverage on existing drug plans might be impacted by a potential pan-Canadian formulary
- identification of governance structures to implement a potential pan-Canadian formulary (e.g., which organization or entity should oversee implementation of a potential pan-Canadian formulary or make funding decisions)
- consideration of financing issues (e.g., funding allocation; financial contributions; funding models; budget scope, size, and amount; or individual drug plan budgets or projected estimates for those budgets)
- review of the terms for coverage (e.g., patient contributions such as copayments or deductibles) and patient eligibility, including status (e.g., international workers or refugee status [undocumented])
- consideration of the interplay between public and private insurance plans (i.e., coverage as first and second payer)
- consideration of other ongoing pharmaceutical initiatives (e.g., Health Canada's Drugs for Rare Diseases Strategy).

Although out of scope, the panel recognizes the importance of these elements to address as part of the future design and implementation of a pan-Canadian formulary, and advocates that these elements be resolved or considered as part of future work. While the panel was not deliberating these aspects, some of these considerations have been highlighted at a high level in the Future Scope section for decision-makers to reflect on. A key part of the panel's work included stakeholder engagement, which provided an opportunity for broader perspectives and input into the panel's proposed approach and

recommendations. Many of the respondents also echoed the importance of addressing these key components of a potential pan-Canadian formulary. Throughout its discussions, the panel was challenged by the out-of-scope elements and made assumptions to proceed (e.g., if a potential pan-Canadian formulary is intended to be an add-on or overlaying model, it would work with existing structures and systems, and be synchronized with existing drug programs across the country). Further clarity of these elements could result in the recommendations being refined or enhanced.

This report is meant to present a potential pathway, including principles, values, and criteria to guide the development of a potential pan-Canadian formulary. Also included is a summary of the panel's work on a process for creating a list and evaluating products for inclusion on a potential pan-Canadian formulary. Finally, it outlines the panel's discussion on formulary management best practices (i.e., an approach to align formularies with current evidence), as well as how this work could move forward, and the elements that would need to be addressed.

Advisory Panel Work Timeline

Details on the panel members can be found in the About the Panel Members section. The names, biographies, and conflict of interest declarations of the 14 members on the panel are available on the CADTH website. The panel is developing the work within this specific mandate. Further work on the implementation of a potential pan-Canadian formulary, should that decision be made, may require different panel membership and composition, particularly if there are opportunities to leverage existing processes.

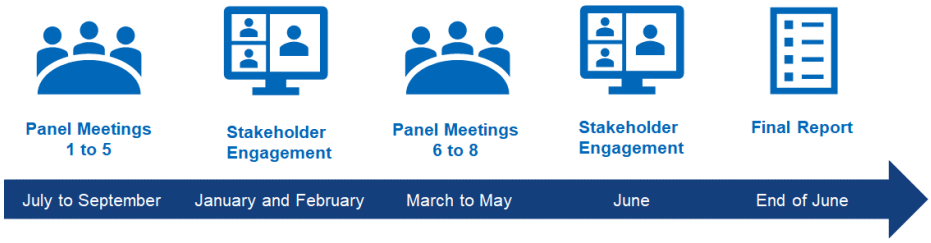
The panel deliberated over 5 half-day meetings held from July to September 2021 (Figure 1). It reviewed the recommendations in the council report,[2] published literature, and other references (e.g., listing status, utilization data). Panel members also brought their own experiences and considerable expertise. All this information was used to provide recommendations on the framework and proposed sample list of drug and related products for a potential pan-Canadian formulary.

A broad stakeholder consultation was conducted between January to February 2022. An online information session, web-based questionnaire, and a focus group were held to solicit feedback on the panel's work. A second online session was held in June 2022 to share the feedback received and key deliberations made by the panel. Refer to the Stakeholder Engagement section for further details.

Three additional half-day meetings were held between March and May 2022, after the consultation period. During these meetings, the panel reviewed the feedback received from the respondents, and, through careful discussion, identified how to address and incorporate the feedback and refine the draft recommendations.

This report will be submitted to Health Canada, shared with provincial and territorial governments, and made publicly available by June 30, 2022.

Figure 1: Timeline of the Panel's Work (2021–2022)



Note: Stakeholders were provided with an opportunity to submit feedback via written submission to CADTH from January 11 to February 25, 2022.

Stakeholder Engagement Process

Stakeholder engagement is an important aspect of the panel's work. The panel consulted widely with the support of CADTH, and worked diligently to ensure that a rich and comprehensive foundation of knowledge and perspective were incorporated into the recommendations.

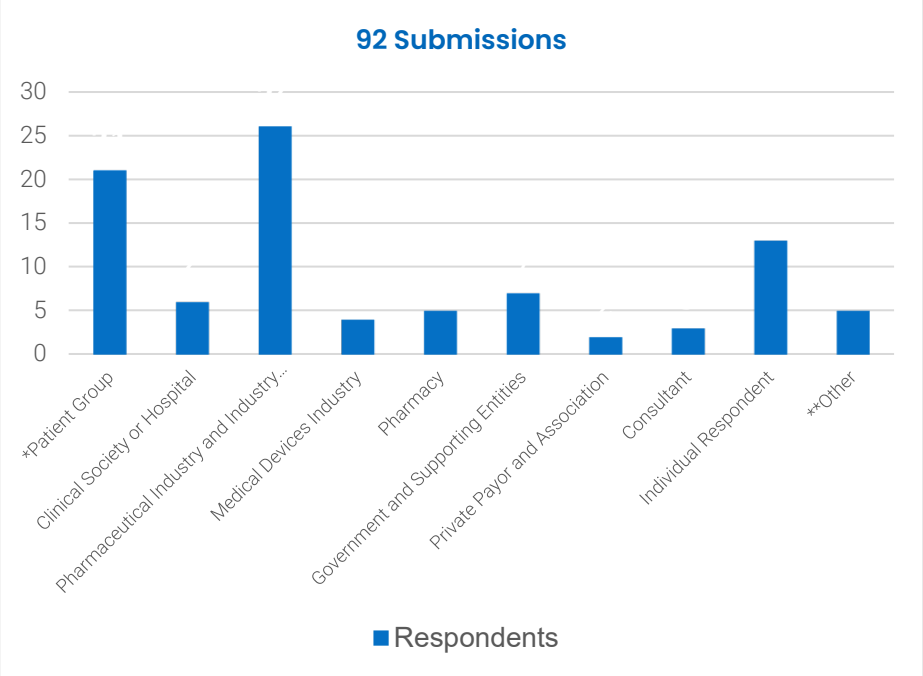
An online questionnaire was made available in English and French to solicit feedback on specific aspects of the panel's work. This online consultation was held between January 11 and February 25, 2022. In addition, an online information session was held for any interested parties on January 18, 2022. CADTH received 92 responses (refer to Figure 2) through the online questionnaire, reflecting feedback from a wide range of perspectives (e.g., patient groups, health care professionals, individuals from clinical societies, government and related agencies, associations, pharmaceutical companies, device companies, private insurance companies, researchers, consultants, and others).

To ensure the perspectives of populations made vulnerable by social and/or economic policies, particularly Indigenous peoples and those who have experienced the historic and ongoing impacts of colonization, are included in developing a potential pan-Canadian formulary, the panel (through CADTH), purposefully reached out to organizations that serve these populations for their input. The discussion that took place among representatives of the organizations that agreed to participate allowed for a shared experience and for the panel and CADTH to seek deep and meaningful input from groups that CADTH typically would not have the opportunity to engage with or that may have specific insights that would not typically be captured by CADTH's existing stakeholder network.

Careful thought and effort were also made to invite representatives from the Assembly of First Nations, Inuit Tapiriit Kanatami, and Métis National Council. The invitation remains open and CADTH is committed to engaging respectfully and humbly with First Nations, Inuit, and Métis peoples, communities, organizations, and governments — first to continue our initial efforts to listen and learn, and then to offer a role in supporting Indigenous health and wellness.

The panel and CADTH would like to thank all individuals, groups, and organizations that participated in the public consultation period. A summary of the key points raised by stakeholder consultation respondents have been included in Appendix 5 of this report. As part of CADTH's commitment to transparency, all comments received by the consultation deadline are publicly posted on the CADTH website. The entirety of this broad consultation informed this report.

Figure 2: Respondents to Online Questionnaire



* There were 2 patient groups respondents that represented 22 patient organizations.

** Other includes academia and research, community health centres, labour groups.

Organization of This Report

This report is presented in 2 parts:

Part 1: Formulating the Principles for a Potential Pan-Canadian Formulary

Part 2: Developing a Staged Approach to Create a Potential Pan-Canadian Formulary

- Stage 1: Approach to Creating the Proposed Sample List of Commonly Prescribed Drugs and Related Products
- Stage 2: Expanding to Other Therapeutic Areas
- Stage 3: Adding and Maintaining a Potential Pan-Canadian Formulary

Future scope: As previously mentioned, the panel acknowledges that the out-of-scope elements are important to address in the design and implementation of a potential pan-

Canadian formulary as part of future work. While the panel did not deliberate on these aspects, some of these considerations have been highlighted at a high level in the Future Scope section for decision-makers to reflect on, should this work progress.

Developing a Framework for a Potential Pan-Canadian Formulary

Overview of the Proposed Framework

The overall goal identified by the panel is to create a pan-Canadian formulary that includes a broad range of safe, effective, evidence-based drugs and related products that would be reflective of the health care needs of Canada's diverse population. To create the framework to achieve this goal, the panel built on 3 foundational concepts: patient-oriented; meaningful and thoughtful multi-stakeholder consultation; and transparency of process (i.e., who makes the decisions, as well as how and why the decisions were made). Patient-oriented is focused on patient-identified priorities and improves patient outcomes.[7] This framework is guided by the panel's principles and the Quadruple Aim framework. The Quadruple Aim framework is used to guide the redesign of health care systems and the transition to population health that is centred on 4 overarching goals: improved population health outcomes, improved care and patient experience, improved provider satisfaction, and lower costs or better value.[7]

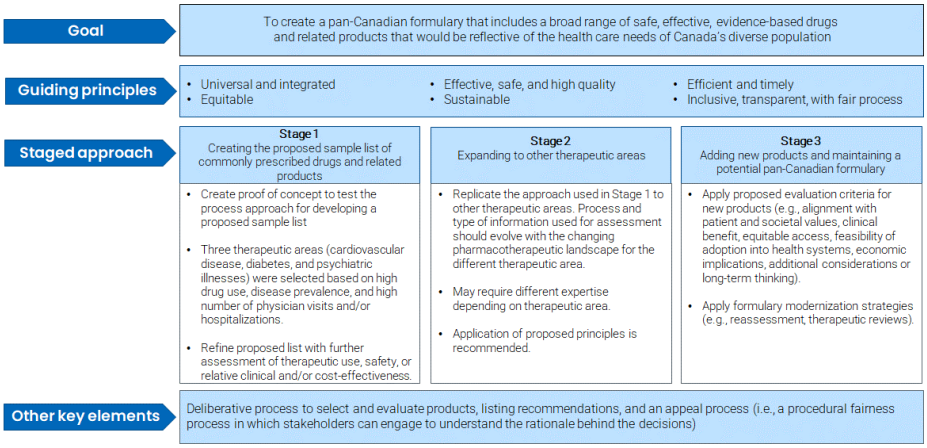
Figure 3 provides an overview of the proposed framework for a potential pan-Canadian formulary developed by the panel. It outlines the goal, guiding principles, and approach to creating and testing a proposed sample list and scaling the process (i.e., stages to grow the process over time). It also indicates how to add new products to a potential pan-Canadian formulary and maintain the formulary over time, if a pan-Canadian formulary is implemented.

Other key elements of the framework, which are discussed in detail subsequently, include:

- a deliberative process to evaluate products
- formulary modernization strategies (i.e., an approach to align formularies with current evidence)
- a listing recommendation and reasons that are clear, publicly accessible, and easy-to-understand
- rules of procedural fairness that can be followed throughout the decision-making process.

This proposed framework is only intended to provide a roadmap; additional policies, procedures, and operational steps would need to be further explored and consulted on with interested parties if decision-makers consider moving forward with the recommendations.

Figure 3: Proposed Framework for a Potential Pan-Canadian Formulary



Part 1: Formulating the Principles for a Potential Pan-Canadian Formulary

The Process

The panel's first task was to establish a set of principles to guide the selection and management of a proposed list of drugs and related products for a potential pan-Canadian formulary. As part of the initial meeting preparation and orientation, the panel was provided with a set of principles and definitions from the published literature. The principles were sourced from key Canadian documents, such as the *Canada Health Act*[8] (CHA) and the *Act Respecting Prescription Drug Insurance* (Quebec),[9] as well as a limited literature search.

To inform the panel's discussions on this topic, a limited literature search was conducted by an information specialist on key resources, including Medline, the international HTA database, and the websites of Canadian and major international health technology agencies. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search keywords were formulary, pharmacare, essential medication, universal plan, national plan and framework, management, implementation, policies, processes, principles, practices.

The Medline search was completed on June 17, 2021, and limited to English- and French-language documents published since January 1, 2016. No filters were applied to limit the retrieval by report.

This information was supplemented by a focused internet search for relevant grey literature (literature that is not commercially published) and publications of principles

regarding prescription drug access in the Canadian context. Grey literature was identified by searching sources listed in relevant sections of the Grey Matters: A Practical Tool For Searching Health-Related Grey Literature checklist.[10] The grey literature search was conducted between June 14, 2021, and June 18, 2021. The main search keywords were formulary, pharmacare, essential medication, universal plan, national plan and framework, management, implementation, policies, processes, principles, practices. The grey literature search was limited to English- and French-language documents published since January 1, 2011.

Examples of the identified literature include policy statements or recommendations from Canadian professional[11] or patient advocacy associations,[12] policy research papers,[13] and published HTA deliberation principles.[14] The panel recognized that there are no standard guiding principles for formulary management in Canada. However, various organizations and committees have made recommendations on key principles; for example, principles outlined under the CHA[8] and guiding principles for the pan-Canadian Pharmaceutical Alliance process, among others.

The panel acknowledged that a potential pan-Canadian formulary's principles should align with those that have been created for the Canadian health care systems, but must remain independent. Although the principles outlined under the CHA serve as a strong foundation, the panel felt that adopting them directly or from those of other organizations and initiatives may impact the pan-Canadian formulary's principles in the long term if the principles of these organizations or initiatives change in the future. As work with the pan-Canadian formulary progresses, a more careful assessment and accounting over time of the principles against other key values statements within the health system may enable closer alignment and identification of tensions that require resolution.

Proposed Principles

Upon review and discussion and then deliberation on the feedback received through the consultation, the panel recommends 6 guiding principles. A potential pan-Canadian formulary should be: universal and integrated; equitable; effective, safe, and high quality; sustainable; efficient and timely; and inclusive, transparent, with fair process. The principles are presented at a high level and meant to act as guideposts; they are not listed in any specific order. Ongoing work will be required to refine the detailed interpretation and application of each principle, and to build upon them based on key learnings that unfold as the plans for a pan-Canadian formulary advance, and out-of-scope items are addressed. The panel emphasized that in any event, patient outcomes and continuity of care should not be compromised in the process.

Discussion Highlights

The following highlights are not listed in any specific order.

Universal and integrated: Providing access to prescription drugs and related products is part of the basic commitment to health care that is a defining feature of Canadian

society. In this way, formulary decision-making is not just about economics. It is a central investment to advance and maintain the health and wellbeing of the people of Canada, and society as a whole.

The ideal of universality includes the population covered — Canadian society in all its diversity; it also covers the breadth of health care — the different types of health care needs.

The ideal of a universal pan-Canadian formulary would include a broad range of safe and effective medications and related products to meet the health care needs of all of Canada's diverse population. Access to medication is only one part of access to necessary health care, so in determining which drugs and related products should be included in a potential pan-Canadian formulary, the process design for such a formulary should be aligned with, if not integrated into, other elements of the health system.

The panel recognized that the demand for health care will be greater than the public health care systems resources (or ability to meet demand), and that difficult choices will need to be made to create a pan-Canadian formulary, which could have significant implications in terms of what access is provided and, consequently, what cannot be funded. Transparency of these choices is essential to building public trust.

Equitable (equal outcomes, equitable access): The people of Canada are equally deserving of having their health care needs met. A potential pan-Canadian formulary should contribute equal opportunities for health and wellness for people living in what has become known as Canada with the desired results that would lead to equal outcomes.

The existing system may not serve several subgroups or subpopulations in Canada for a variety of reasons and consequently, they face variable degrees of access to necessary resources. This can be due to a variety of practices and factors, including those that may be considered discriminatory, such as experienced by First Nations, Inuit, and Métis peoples. It is also due to bias and stigma, such as is experienced by people with mental illness and addictions issues. Others face barriers to access because of the way the system is organized and how care is delivered; or those who live in rural and remote communities requiring them to travel very long distances to access treatments. These are only a few examples. To counteract these barriers to access, a potential pan-Canadian formulary should be equitable and support a distinction-based approach (i.e., acknowledge the distinct histories, interests, and priorities of First Nations, Inuit, and Métis peoples) that promotes self-determination.

An equitable pan-Canadian formulary would list drugs available to all people living in Canada in such a way as to make prescription drugs and related products more accessible to all who currently do not have access. This includes filling gaps in access and ensuring that further gaps are not created or made worse.

Achieving equity requires looking at patterns of distribution of need and access and rectifying unfair distribution patterns. Distribution patterns should follow diversity characteristics. The Canadian Human Rights Commission suggests that these

characteristics include race, national or ethnic origin, colour, religion, age, sex, sexual orientation, gender identity or expression, marital status, family status, disability, and genetic characteristics.[15] Additional considerations that raise equity concerns include socio-economic status, housing security, and those who are affected by the social determinants of health. A potential pan-Canadian formulary should include a focus on those who are disadvantaged or people and populations that live in under-resourced communities, and make choices that create an equitable and sustainable formulary. The panel felt that being mindful of what determines the health of a population, as well as the need to reduce inequities within the population are important. These considerations align with the definition by the Public Health Agency of Canada, which states that "population health is an approach to health that aims to improve the health of the entire population and to reduce health inequities among population groups."[16]

Effective, safe, and high quality: For a potential pan-Canadian formulary to live up to the commitments to improve health, it must encompass products that are effective, safe, and of high quality.

Effectiveness should consider not only clinical effectiveness and cost-effectiveness but also effectiveness in equitable access to treatment. For example, adding the option of oral drug administration in addition to IV administration may improve access for those who would have to travel a significant distance at potentially high cost to reach an IV clinic. How this will be operationalized will required further evaluation of the current systems to ensure that it is harmonized. For example, INESSS first determines if a drug has therapeutic value (i.e., identification of the unmet health need in the intended patient population and the determination of the level of this need, and the drug's ability to provide a clinical benefit) before determining the reasonableness of the price charged for a drug and the drug's cost-effectiveness.[17] In contrast, CADTH currently applies a framework that includes all the elements that should be considered by its expert committee during its review, and reinforces that no single element overrides another, but rather that the expert committee uses the sum of all elements to formulate a reimbursement recommendation.[18]

As such, a framework should be flexible and consider the impact on and needs of diverse patient populations, such as including treatments that require less testing or that are easier to administer and use. This may require cost-effectiveness analyses for specific subgroups where health care costs and implications may differ; for example, the impact of geographic location and living situations, given the differences in rural or remote locations from densely populated regions.

Central to effectiveness and quality are processes for monitoring, evaluating, and improving performance against key commitments. Among other things, quality improvement will require analysis of evidence. As our understanding and use of real-world evidence evolves, it will incorporate evidence that considers diverse populations, perspectives, and experiences, as well as assessing value in a way that reflects the diversity and realities of Canada's population. Critically, this includes increasingly integrating Indigenous (i.e., First Nations, Inuit, and Métis) ways of knowing as part of our commitment to reconciliation. These elements will need to be considered and better

integrated into a holistic evaluation approach. However, given the panel's mandate, it did not pursue the methodological and epistemological analysis required in this regard; nor did they consider any form of multicriteria decision analysis. Before implementing any approach, these elements must be studied and clarified. This will require systematic methods for how decision-making should incorporate different levels and types of evidence and a thoughtful policy and approach to evidence analysis. The encouragement of research that lives up to these standards would be a next step on this path.

Sustainable: A potential pan-Canadian formulary should be in the best interest of the people living in Canada. When thinking about sustainability, in addition to financial sustainability, attention should be paid to the purpose of the formulary and how formulary decisions will allow the system to live up to the key commitments of the formulary. There should be a focus on creating value to support a sustainable health system. The system should remain flexible and adaptable to new ways to move forward and work toward improving access to medications, as well as improved health outcomes and quality of life.

Efficient and timely: Universality and integration in a context of using limited public resources wisely will require a focus on system efficiencies wherever possible. This will include everything from minimizing process duplications and leveraging existing infrastructure and resources, to using cost-effective medications and related products. This principle will require that decisions can be made well and in time to meet patient needs.

Inclusive, transparent, with fair process: A potential pan-Canadian formulary would require the partnership of multiple stakeholders, from patients and clinicians, to policy-makers and administrators, researchers, manufacturers, and disease-specific patient advocacy groups. To enable access to the different types of information and perspective needed to live up these principles, the system design to develop and operate a pan-Canadian formulary should be informed by multiple perspectives. This will require early, inclusive, and meaningful engagement. This is also an opportunity to codevelop and take a collaborative approach that acknowledges the distinct nature and lived experiences of First Nations, Inuit, and Métis peoples. This engagement should be characterized by safe deliberation spaces where there is room for informed and candid sharing of perspectives about how criteria are defined, interpreted, and applied to formulary decisions.

A potential pan-Canadian formulary would be there to serve the need of patients. Patients are not just stakeholders but the end users of the formulary. A potential pan-Canadian formulary must reflect the values of people living in Canada — including patients, clinicians, and their representatives, and also citizens who will be affected by the resource allocation decisions made related to the formulary. The approach to the formulary will have to be clear about the purposes and nature of patient engagement and public engagement and include appropriate methods for both.

To ensure accountability and support reason-driven decision-making, the principle of transparency should apply to the creation and maintenance of a potential pan-Canadian formulary and part of the system in which it is embedded. Decision-making structures

and processes on how decisions are made should be transparent to all vested parties, including a full disclosure of every stakeholder involved. Fair process and reason-based decisions will also require a predictable and transparent review and appeal process.

Living up to the Principles

As mentioned, the principles that should guide a potential pan-Canadian formulary will impact not only access to drugs and related products, but also the broader health system. The panel has attempted to model its work, including how it analyzed information and drew conclusions, so that it upholds each of the 6 principles. The panel also recognized that additional work may be necessary to ensure a values-based approach to such impacts.

Philosophical analysis: A deep analysis of the principles that should guide formulary decisions, the relationship between and relative importance of different parties within the health system, the appropriate understanding of relevant and justified knowledge and information, and in particular, the most justified way to consider the principle of equity and how to balance commitments to smaller subgroups with the needs of the broad population are all beyond the scope of the panel's work and remains to be done.

Equity-advancing methods: The panel's suggested method for arriving at a proposed sample list for a potential pan-Canadian formulary demonstrates an approach to address the current inconsistent and inequitable access to, and coverage for, drugs and related products. This initial effort will require supplementation by other methods of identifying and responding to the needs for drugs and related products of these subgroups.

Tools and methods for interpretation, prioritization, and application of principles and criteria: The principles reflect commitments that will at times be in tension. Meeting unmet needs of patients facing high barriers to access may not in every instance align with timely, evidence-informed decisions. In these cases, careful interpretation and balancing will be required. As stated, the principles are meant to act as guideposts. But to ensure that the interpretation of these principles is well-justified and in the spirit of the commitments described here overall, it will be crucial that the values-analyses that underpin trade-offs when hard choices must be made are transparent and well-justified and documented in a manner that allows ongoing learning and improvement. Systems and processes to enable this will have to be part of the structure of a potential pan-Canadian formulary.

Related to this, both content and process values will have to be anchored in clear values-driven practices (i.e., make decisions based on one's values, and that the values are a core part of how one operates as an entity). For example, the values and criteria outlined in Table 1 (or even those that are settled on if this work moves ahead) should be discussed and applied in safe spaces; tools and decisions structures will also be required. A multicriteria decision analysis (MCDA) approach embedded within an explicit and intentional values-based deliberation process is the kind of process that can help committees make formulary decisions, focus discussion on key values, and ensure that

safeguards are built into discussion methods. In addition to new methods, critical reflection on the biases of existing methods should also be undertaken. Using concrete tools where possible can assist with interpretation, weighing, and balancing of principles as tensions are reconciled. The panel has not analyzed these methods in-depth, and this work will need to be done in the future.

Conflict of interest guidelines: To live up to the values of fair process, a potential pan-Canadian formulary will need to ensure appropriate conflict of interest guidelines are established and followed by all parties involved in the process. It is important to recognize that being in a conflict of interest is not in itself unethical — it is simply a condition one finds oneself in and is to be expected given the diversity of perspectives required for an effective formulary. What matters is how these situations are dealt with. Beyond transparency, guidelines need to provide direction on how conflicts might be balanced and what constraints need to be put in place in deliberation forums to appropriately mitigate these issues.

Figure 4: Summary of Principles Identified in the Framework

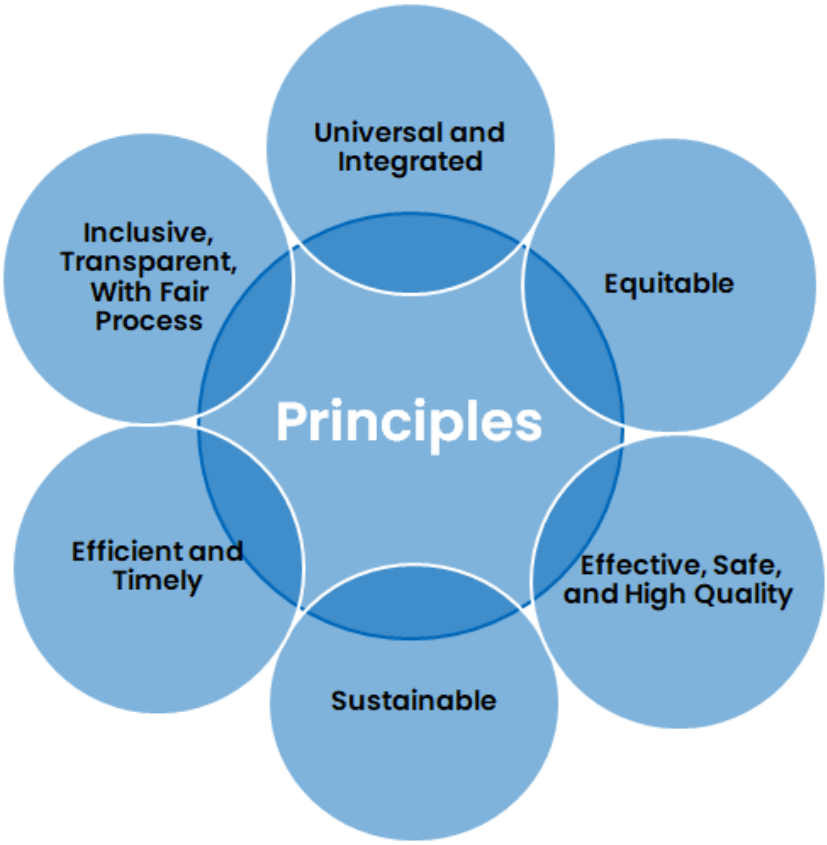


Table 1: Proposed Principles and Definitions

Framing the principles	Principles and definitions		Content or process values to support principles[a]
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	
Whose health care needs should the potential pan-Canadian formulary serve?	**Universal and integrated**	All people in Canada should have **access** to the prescription drugs and related products they need regardless of their diversity characteristics (which include, but are not limited to, race, national or ethnic origin, colour, religion, age, sex, sexual orientation, gender identity or expression, marital status, family status, disability, and genetic characteristics). Additionally, the needs of all people should be served regardless of geographical location within Canada.	**Content values** • **Coherence:** Formulary decisions should align with the broader system for both drug selection and overall health system goals. • **Integrity:** Structures and systems and formulary decisions should align with the values of users and Canadian society at large (recognizing this will require balancing of competing values). **Process values** • **Comprehensiveness:** Drugs for all types of health care needs should be considered in the overall process. • **Harmonization:** Structures and systems should be synchronized with existing drug programs across the country.
Whose needs should be prioritized?	**Equitable**	**Equity recognizes that individuals have different circumstances** that require variable allocation of resources to provide opportunities to achieve equal outcomes. Policies and processes for a potential pan-Canadian formulary should **close gaps in access** to prescription drugs, especially when the gaps arise from unintended consequences of policies that may create variation in access.	**Content values** • **Equal outcomes:** Structures and processes should improve equality of outcomes for the Canadian population, which will improve health equity. Diversity competency and non-discriminatory lenses should be applied in system design and evaluation. • **Equitable access:** Listing criteria should include drugs that would (effectively) address health inequities in the system. **Process values** • **Data–driven approach to diversity:** Structures and

Framing the principles	Principles and definitions		Content or process values to support principles[a]
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	
			processes should include the identification of health and health care access data for relevant groups to enable application of the equity criterion in accordance with good data principles, including Indigenous data sovereignty and equity-promoting data.
What standard of effectiveness will be acceptable?	**Effective, safe, and high quality**	A potential pan-Canadian formulary should strive to provide access to people living in Canada to meet the **highest standard of health** and **patient experiences**. Choices should be based on an evaluation of the options and viewed in the context of benefit to patients and to the Canadian population as a whole. A potential pan-Canadian formulary should be monitored so that it can be continuously improved.	**Content values** • **Clinical benefit:** Listed drug products should address relevant health conditions, and benefits should sufficiently outweigh harms. Unmet health needs in the intended patient population should be met, and sufficient improvement to patient and caregiver quality of life should be provided. • **Effectiveness**: Considerations should include not only clinical effectiveness and cost-effectiveness, but also effectiveness in equitable access to treatment. **Process values** • **Evidence based:** The process of evaluating drugs for listing should be based on a solid and defensible understanding of acceptable evidence that includes clinical trials and real-world evidence. • **Quality improvement:** The formulary should be continuously reviewed, modernized, evaluated, and improved.
Who should benefit from the potential	**Sustainable**	The people of Canada should benefit from a formulary management system that	**Content values** • **Feasibility:** Listing criteria should include the impact of

Framing the principles	Principles and definitions		Content or process values to support principles[a]
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	
pan-Canadian formulary?		**maintains its own viability** and **supports long-term development and vision.**	a drug on resources for the therapy, if funded (including drug-only costs and costs of human and/or infrastructure resources for therapy administration and management of toxicities and/or side effects). • **Long-term thinking:** Structure and processes should allow for anticipating and planning for future health care challenges, from new health trends to drug treatments for emerging diseases. • **Economic implications:** Formulary decisions should consider the value for money and the cost-effectiveness of drugs to maximize benefit for unit of expenditure, opportunity costs, and overall systems costs.
How should the system operate?	**Efficient and timely**	The process should **minimize duplication of steps** and ensure access to prescription drugs on the potential pan-Canadian formulary is provided in a seamless manner to ensure the right drug gets to the right patient at the right time.	**Process values** • **Streamlined:** Decision processes should be efficient and reduce duplication. • **Timeliness:** Decision processes should ensure timely access to drugs and related products to meet relevant patient health goals.
Whose perspectives should be considered in system design and decision-making?	**Inclusive, transparent, with fair process**	A potential pan-Canadian formulary should be developed and managed in **collaboration with partners**, such as patients, people with lived and living experience (including caregivers), health care providers, health organizations, governments, and industry.	**Process values** • **Inclusive:** System operation and evaluation should be undertaken through the various lenses of the multiple stakeholders. • **Open to appeal:** The system should include a procedural fairness process in which stakeholders can engage to understand the rationale behind the decisions.

Framing the principles	Principles and definitions		Content or process values to support principles[a]
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	
			• **Reason driven:** Deliberation about a formulary listing should be based on reasons that are articulated in plain language. Deliberation should be open to different ways of knowing and sensitive to power dynamics that favour some perspectives over others without sufficient justification. • **Respectful:** Deliberation should create space for multiple viewpoints to be heard and engaged, with attention to implicit biases. • **Transparent**: The overall process of creating and managing a formulary should be explicit, clear, and accountable to people living in Canada.

[a] Content values are goals of the potential pan-Canadian formulary and the criteria used to determine products to be listed. Process values are standards that the overall structure and processes should meet.

Part 2: Developing a Staged Approach to Creating a Potential Pan-Canadian Formulary

The panel explored different approaches for creating a proposed list of drugs and related products, including following an EML concept. Some respondents to the stakeholder consultations had also suggested this approach, given that development of an EML was 1 of the recommendations of the council report.[2] According to WHO, "Essential medicines are those that satisfy the priority health care needs of a population," and an EML can be an integral component of treatment within the continuum of care.[4] WHO publishes a Model List of Essential Medicines every 2 years, which is meant to act as a blueprint for the development of national EMLs based on local priorities and treatment guidelines. The value of the EML approach is recognized, with increasing uptake in different jurisdictions globally to adopt or adapt the Model List of Essential Medicines based on local needs.[4] Notwithstanding the value that a national EML serves for some jurisdictions, the panel deliberated on this approach, and considered its benefits and risks in the Canadian context. Specifically, the panel reviewed this approach by applying its proposed principles, and considered the current formularies across Canada that already fund a broad list of drugs and related products. Given the limited number of

drugs in an EML across all 14 WHO Anatomic Therapeutic Chemical (ATC) categories, the panel determined that an EML would not align with the principles established by the panel; particularly, the principles of equitable; efficient and timely; and inclusive, transparent, with fair process. An overview of the EML-based approach considered by the panel, and its benefits, risks, and limitations, is presented in Appendix 6.

Another approach involved a comprehensive and comparative assessment of drugs, that is, comparing products for the same indications by applying the criteria typically used in making listing recommendations (e.g., clinical benefit, equitable access, feasibility, value for money, among others as noted in Table 1). Although thorough, this type of comparative assessment requires more resources than were available to the panel to complete this work. Furthermore, the data needed to evaluate each drug against the criteria may not be easily available or available at all. The panel also did not simply build on an existing public formulary because of known gaps between the different formularies, including the significant differences in how these plans are administered and who may be eligible for coverage. A recent report issued by the Patented Medicine Prices Review Board conducted an analysis of agreement rates for listings across public formularies (i.e., received a recommendation to list on public formularies). The findings show that the reimbursement of selected medicines was fairly consistent across most of Canada's public drug plans. However, listing rates on public drug plans ranged across jurisdictions, with an average of 65% (up to 88% weighted) across the formularies analyzed.[19] This points toward inconsistencies in drug listing status that remain across Canada. Therefore, the panel determined that this approach would be a particular challenge with the "equitable access" criterion.

Given its time limitations, the panel decided to apply the principles by taking a pragmatic approach to develop the initial list of commonly prescribed drugs. The panel proposed a sample list of prescription drugs and related products as a starting point while acknowledging the limitations associated with creating a proposed sample list. For example, when a comprehensive HTA methodology could not be used, whether because of resourcing or time constraints, the panel used available information when deliberating the development of the proposed sample list.

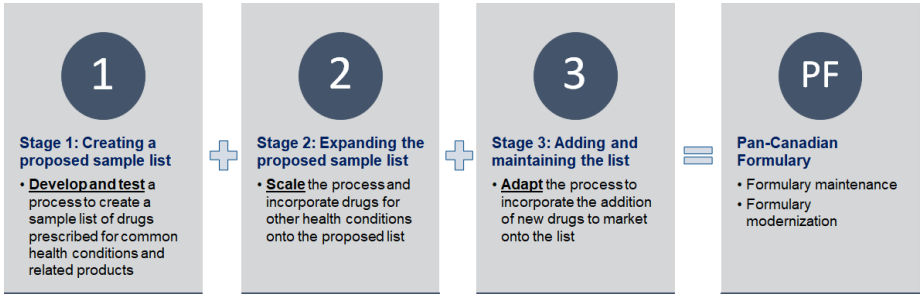
The panel established a 3-stage approach to creating a potential pan-Canadian formulary (refer to Figure 5). Of note, the panel has completed only a part of stage 1 based on its mandate. For the remaining stages identified in the following text, the overall process, concepts, and considerations have been discussed in this report. Importantly, guidance on other elements of the formulary that are beyond the panel's current mandate should also be addressed as part of the design and implementation of a potential pan-Canadian formulary.

Stage 1: Select a small sample list of products as a proof of concept for the process. Ensure that the guiding principles are followed while creating the proposed list.

Stage 2: Review and revise the proposed list as appropriate, then apply the proposed criteria to other therapeutic areas in a subsequent future step to scale the process and expand the proposed list.

Stage 3: Recommend criteria and processes for adding new drugs and related products once all therapeutic areas have been considered. Also suggest strategies to maintain a proposed list over time and to explore how this process could be integrated within the current health system.

Figure 5: Staged Approach to the Creation of a Pan-Canadian Formulary



The framework also included other key elements that are discussed in detail in the following section: deliberative processes to evaluate products; formulary modernization; listing recommendation and reasons that are clear, publicly accessible, and easy-to-understand; and that it follows the rules of procedural fairness throughout the decision-making process.

Stage 1: Approach to Creating the Proposed Sample List of Commonly Prescribed Drugs and Related Products

The Process

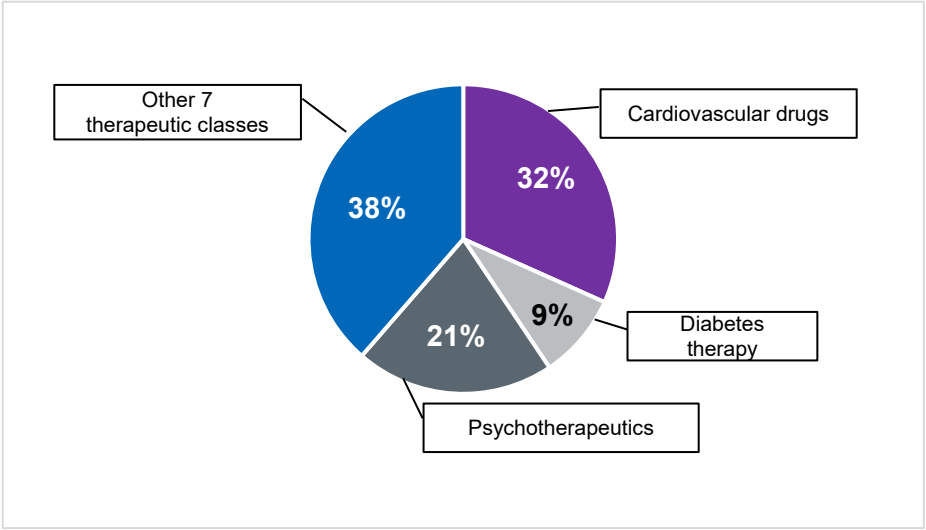
To develop the proposed sample list of commonly prescribed drugs and related products, the panel first identified therapeutic areas to focus on. The panel considered several factors in selecting the therapeutic areas, including therapeutic areas involving drugs with the highest utilization, disease areas with significant growth in prevalence rates, and conditions that account for high numbers of clinician visits and/or hospitalizations in Canada. For more details about the methodology, assumptions, and limitations, please refer to Appendix 1.

Based on these considerations, the panel selected 3 therapeutic areas: cardiovascular diseases, diabetes, and psychiatric illnesses. These areas were based on IQVIA's data (a global provider of health care–related data and analytics)[20] on Canadian Pharmaceutical Trends for 2020, in which the selected 3 therapeutic areas are reflected in the top 10 therapeutic classes of prescriptions dispensed in Canadian retail pharmacies. Out of the top 10 therapeutic classes of dispensed medications, prescriptions for cardiovascular drugs (including antihyperlipidemic drugs), diabetes drugs, and psychotherapeutic drugs together represent approximately 62% of prescriptions dispensed (refer to Figure 6).

To generate the proposed sample list, the panel was provided with a spreadsheet that included 277 drugs (cardiovascular diseases = 140; diabetes = 44; psychiatric illnesses = 93) and 10 related products (e.g., blood glucose strips). The following information was also provided for each drug or related product: listing status on identified FPT drug plan formularies, utilization data (claims and claimant by age and sex, if available), availability of a generic or biosimilar alternative for the drug molecule, pregnancy and breastfeeding considerations, and references summarizing available drugs and use in Canada. It was acknowledged that if other information becomes available in the future (e.g., from registries) and is appropriate, it should be incorporated to support the assessment criteria.

The panel reviewed drugs and related products that fell within these therapeutic areas and evaluated each using predetermined assessment criteria (refer to Table 2). The panel applied the assessment criteria on the basis of their alignment with the 6 principles. The principles of efficient and timely, and inclusive, transparent, with fair process are process-oriented and guided how the panel conducted their assessment. By applying the principles while reviewing the information for each drug (e.g., as obtained from listing status, utilization data, and other references), the panel determined whether the drug or related product should be included, flagged, or excluded from the proposed sample list. Some of the drugs were flagged because panel members recognized that additional expert consultation (beyond the panel's expertise) was required to decide if the drug should be included or excluded from the proposed sample list.

Figure 6: Prescriptions Dispensed in Canada (Based on Top 10 Therapeutic Classes in 2020)



Note: Reflects percentage of the total prescriptions dispensed for drugs within the top 10 therapeutic classes. Estimations are based on prescriptions dispensed in Canadian retail pharmacies, including new and refill prescriptions. Other 7 therapeutic classes include: analgesics, gastrointestinal, genitourinary, neurological disorders, vitamins, thyroid therapy, and hormones.
Source: Adapted from IQVIA, Top 10 Therapeutic Classes in Canada, 2020.[20]

Assessment Criteria for the Proposed Sample List for Drugs and Related Products

The panel used predefined assessment criteria that it developed to review each drug and related product to determine if they should be included or excluded from the proposed sample list, or flagged for further consideration by experts. "Flagged" means that the panel could not decide whether the product should be included or excluded at the point of deliberation because the panel felt that it did not have the expertise to make this determination. Table 2 outlines the predefined assessment criteria used by the panel to determine if a drug or related product should be included, flagged for expert consultation, or excluded from the proposed sample list.

Assessment of Drug Products for Sample List

Many drugs in the 3 selected therapeutic areas were commonly or universally included in the identified FPT drug formularies. The assessment was based on a review of the available information based on a point in time. Whether a drug was included was not based solely on its listing status. The panel compared the listing status of each product on the existing public drug plan formularies to identify gaps in access. These drugs were presumed to have demonstrated sufficient clinical benefit if they were listed, and the panel used this as 1 of the reasons (along with other information and applying the principles) to include them on the sample list. A key limitation to this approach is that the reason for inclusion on the FPT formularies may not coincide with the principles identified by the panel. That is, the decision-makers who selected the drugs for the FPT formularies might have used different principles to determine what to include on the lists for their respective jurisdictions.

When selecting drugs for inclusion in the proposed sample list, the panel paid special attention to drugs needed by specific subpopulations that would have improved access to those drugs if they were included (e.g., drugs used to treat attention-deficit or hyperactivity disorder in children or drugs used to treat substance use disorders). There may be some population groups, such as pediatric patients, whose needs may not be fully met by the drugs on the proposed sample list. By not fully addressing the drug needs of these groups, inequities could be deepened or introduced. To account for this, additional steps would be needed so that drugs can be added to the proposed list, particularly those drugs that have been flagged for further consideration. The panel emphasized that equitable considerations for a specific drug or related product used in a subpopulation should be factored in when the sample list undergoes further review or refinement.

There were some products that the panel felt needed additional reviews before deciding whether they should be included or excluded from the proposed list. For example, products were flagged for further consideration if there were questions about its potential therapeutic use or value, or any potential safety issues. When recommending drugs for exclusion, the panel tried to clearly state the rationale for the decision, such as the drug had not been reviewed, or had received a negative recommendation from a

Canadian HTA body, or was removed from the market by Health Canada (at the time of the panel discussions).

Related Products

Related products are typically devices that directly support the delivery or administration of and/or are necessary for the optimal use of drugs. In many Canadian jurisdictions, related products may be covered through different programs within the health system, which makes navigating and accessing coverage difficult for patients and prescribers. As such, a potential pan-Canadian formulary could be an opportunity to streamline processes, provide simplified points of access, and ultimately help patients, caregivers, and health care providers access these types of products. Concurring with the comments from the respondents, the panel supports including related product in the same list as drug products in a potential pan-Canadian formulary because this could help improve patient access and potentially improve adherence and optimal use of a drug treatment, all leading to better health outcomes. The panel recognized that the definition for "related products" should neither be so prescriptive that it impedes equity, nor too broad that it limits the sustainability of a formulary. As such, the panel recommended that the definition for related products be directly tied with the drugs that are eligible for listing in a potential pan-Canadian formulary. In addition, inclusion of "safety" in the definition of related products was also suggested by respondents; that is, including products that support the safe use of drugs and safety of drug administration. It is therefore proposed that related products be defined as "devices that directly support the delivery, administration, and optimal use of drugs to assist in the safe use of a drug or are dose management tools to improve patient care."

The panel noted the importance of having a standard set of criteria to determine which related products should be eligible for potential inclusion on the proposed sample list. This standardization will be particularly important when assessing new or emerging technologies that could be numerous, costly, and, depending on size, could impact sustainability of a pharamcare program substantially. However, such assessment should be balanced with a patient-oriented approach and allow for a continued focus on equity. The process to identify which related product could be included in a potential pan-Canadian formulary could replicate the process followed for drug products. As such, related products funded under provincial programs and those that fit the definition (i.e., supported by evidence to directly foster the delivery, administration, and optimal use of a drug to assist in the safe use of the drug, or are dose management tools to improve patient care) could be eligible for consideration. The panel agreed that the criterion should be flexible to allow due consideration to the needs of those who are underserved by the current system, as well as the needs of other therapeutic areas that the panel has not yet considered for the proposed sample list. However, the panel recommends a conservative approach at the initial stage to test and evaluate the criteria, before opening it up to allow for a wider selection of related products. As an example, diagnostic tools and tests and wrap-around services (e.g., counselling) should be excluded in the initial stage of implementation. As a part of future work, the panel suggested exploring if it might be appropriate to ensure a specific related product be listed if it is used to support optimal use of a listed drug and meets the prescribed criteria. This would allow patients

to potentially be automatically eligible for a related product if a drug is accepted for listing, allowing for optimal use of the treatment and also avoid potential administrative hurdles.

The panel considered related products in 3 main therapeutic areas. For instance, related products relevant to diabetes are listed to varying degrees in public drug plan formularies; these were assessed by the panel for potential inclusion on the proposed sample list. Although public drug plan listing for home blood pressure monitors seemed rare, if it existed at all, some panel members suggested considering home blood pressure monitors for potential inclusion in the pan-Canadian formulary, given the importance of blood pressure control in long-term disease management. After deliberation, however, the panel flagged home blood pressure monitors in the proposed sample list. The panel acknowledged that further assessment of the therapeutic value of home blood pressure monitors and a comparison of the different models that are available on the market would be necessary to make a decision on their potential inclusion or exclusion.

Table 2: Proposed Assessment Criteria for the Proposed Sample List

Assessment criteria[a]	Panel recommendation	Reasons considered by the panel and corresponding key principles
• Product is listed by most of the identified public drug plans (as an open and/or restricted benefit) • Product addresses equitable access (e.g., used by different age groups, including pediatrics) • Consideration given to the impact of the drug, if included, on system-wide resource • Other available information (e.g., utilization, biosimilar, or generic product availability)	**Include in the proposed sample list**	• Will address drug coverage gaps because the drug is currently available to a subset of Canadians with limited or no restriction, this leaves some people unfairly without access: **equitable; universal and integrated** • Will remove barriers or meets the needs of people made vulnerable by systemic inequities (e.g., drugs for treating substance use disorder): **equitable** • Will allow more adequate options for clinicians and patients (considering subpopulations, including children, women of reproductive age, patients with comorbidities such as renal impairment, among others): **universal and integrated** • Will remove barriers to access (e.g., availability in different formulations that would allow easier access for those in rural, remote, and Indigenous communities): **equitable** • Will support greater drug adherence and reduce burden of administration or provide unique advantage (e.g., route or frequency of administration): **effective, safe, and high quality; efficient and timely**

Assessment criteria[a]	Panel recommendation	Reasons considered by the panel and corresponding key principles
		• Will potentially offset health care costs in other areas of the system where a condition could be managed or a decline be prevented by a drug (e.g., prevent frequent hospital or redundant physician visits); this could also provide less variation in health status across social groups and geography: **sustainable; equitable**
• Product is listed by 1 or more of the identified public drug plans (as an open benefit and/or restricted benefit) • Requires further review or broader consultation with clinical community before a decision • No longer best practice or standard of care for this therapeutic area	**Flag for further consideration by experts**	• Assessment of potential safety issues required: **effective, safe, and high quality** • Assessment of therapeutic use or value required: **effective, safe, and high quality** • Role of the drug in current practice for this therapeutic area is unknown or uncertain: **effective, safe, and high quality** • Low utilization in conjunction with uncertainty of therapeutic value or availability of more tolerable or effective alternatives: **effective, safe, and high quality** • Comparative assessment is recommended when it would add decision-making value: **effective, safe, and high quality**
• Product is not listed on any of the identified public drug plans at the time of the assessment • Major safety issues identified by Health Canada	**Exclude from the proposed sample list**	• Product may not have been reviewed or may have received a negative recommendation from a Canadian HTA body: **effective, safe, and high quality** • Product removed from market by Health Canada (at the time of the panel discussions): **effective, safe, and high quality**

HTA = health technology assessment.

[a]The assessment included a review of all the following information: listing status; utilization data (claims and claimants, including breakdown by age and sex, if available); availability of generic or biosimilar for the drug molecule; information about safe use in those who are pregnant or breastfeeding; whether it was included on the WHO, FDA, or CLEAN Meds lists; clinical opinion; and references from RxFiles.

Summary of Results for 3 Therapeutic Areas

Figure 7 represents a high-level summary of the results based on the previously outlined assessment criteria. For detailed information about each drug and related product recommendation, please refer to Appendix 3.

Figure 7: Summary of Results for 3 Therapeutic Areas

Included on proposed sample list (Total = 204 products)	Flagged for further consideration (Total = 54 products)	Excluded from proposed sample list (Total = 29 products)
Cardiovascular diseases •108 drugs	**Cardiovascular diseases** •18 drugs and 1 related product	**Cardiovascular diseases** •14 drugs
Diabetes •28 drugs and 8 related products	**Diabetes** •9 drugs	**Diabetes** •7 drugs and 1 related product
Psychiatric illnesses •60 drugs	**Psychiatric illnesses** •26 drugs	**Psychiatric illnesses** •7 drugs

Discussion Highlights

The following summarizes key discussion points from the panel's deliberation.

Products With Restricted Listing Status

Many products have restricted listing status on the FPT formularies. However, for the purposes of the proposed sample list, these products were accepted as being covered by a public drug plan without conducting further analysis on the types of listing restrictions. The panel acknowledge that having restrictions (e.g., who can prescribe or clinical criteria) to access select drugs or related products may be needed to ensure appropriate use and for optimal patient care. However, the panel noted that listing restrictions could be a barrier to access.

The panel recommended that, in future, such listing restrictions should be based on an assessment of the type of listing restrictions across jurisdictions. Panel members also highlighted that the existing variation in listing restrictions on a given drug across FPT formularies leads to inequity. Because of such considerable jurisdictional variations in the way "restrictions" was defined and applied, the panel recommended that harmonization of the eligibility criteria should be considered in the future to ensure equitable access across Canada. The criteria should also be regularly revisited as evidence evolves. The following are examples of drugs and related products for which the panel recommended the use of restrictions based on an assessment of clinical value and cost-effectiveness to ensure appropriate use; these examples include, eplerenone, ivabradine, evolocumab, alirocumab, tadalafil, sildenafil, insulin pump, and continuous or flash glucose monitor.

Although outside the scope of their mandate, panel members also recognize that there are opportunities to improve and streamline the workflow for clinicians in navigating these restrictions, which would help reduce the amount of unnecessary, time-intensive,

and costly administrative barriers for clinicians and their patients. This result would align with the panel's recommended principles of universal and integrated, as well as efficient and timely. The panel would welcome the opportunity for further dialogue to explore the issues that remain underdeveloped and were identified in this report, including an assessment of restricted listings across jurisdictions for specific classes of drugs and related products.

Combination Products

Combination products were included if each component of the combination was also included on the proposed sample list (e.g., metformin and linagliptin). For combination products, if 1 of the components had been flagged for further review (e.g., if alogliptin was flagged in the combination metformin and alogliptin), the combination itself was also flagged on the proposed sample list. Similar to the general process followed for flagged drugs, any component of the combination that is flagged should be further assessed, and the combination product itself may require additional review. The panel discussed that combination products may support patient access and adherence to treatment by reducing the burden of administration. However, it was felt that, assuming clinical effectiveness, the inclusion of combination products should be contingent on the general principle that the cost of the combination drug should be no higher than the summed price of the individual components if listed. There may be further important considerations, such as other costs (e.g., system costs of prescribing or dispensing), dosing or administration convenience, and comparative efficacy or safety relative to separate administration or monotherapy (e.g., synergistic effect or reduced toxicity due to lower doses). Overall, any additional cost of the combination product (compared to monotherapies) should be justified by evidence of improved patient outcomes. However, the panel acknowledged that price negotiation remains outside the scope of the panel's work; as such, further review and expert consultation would be needed for these other cost considerations. It is also important to acknowledge that value assessment of combination drugs may need to vary for other therapeutic areas (e.g., oncology drugs).

Non-Prescription Drugs

A limited number of nonprescription (e.g., over-the-counter) products were discussed. The panel used the same process as the one used for prescription drugs to determine whether to include these products on the proposed sample list. The panel considered the assessment of over-the-counter products that are part of usual treatment for specific indications or disease conditions (e.g., acetylsalicylic acid as a preventive therapy for cardiovascular disease) to be an important aspect of reducing barriers to access, but also recognized the frequent absence of robust data to support assessments. However, the panel discussed the potential widespread use of over-the-counter medications and the impact this may have on public funds if such medications are listed on formularies. Therefore, the panel noted that restrictions (e.g., the requirement of a prescription) might be needed to ensure appropriate and judicious use.

List Refinement

The panel acknowledged that patient perspectives, experience, outcomes, and diversity should be included as fundamental aspects of the refinement process. It is also important to ensure multi-stakeholder involvement.

The proposed sample list of drugs and related products should be further refined, with a particular focus on drugs and related products that have been flagged for additional consideration. This refinement could take the form of clinical expert consultations or reviews on therapeutic use, safety, or relative clinical and/or cost-effectiveness. Additionally, a MCDA could be explored as part of refining the list; refer to the Deliberative Process section for additional information about the MCDA process.

As part of the principle of sustainability, cost-effectiveness is acknowledged as an important contributor to fiscal sustainability and should be part of the process for ultimately determining what is included or not included on a potential pan-Canadian formulary. Due to time and resource constraints, the panel did not conduct cost-effectiveness analyses for each product in the original sample list and relied on available information when deliberating the development of the proposed list. However, the panel recognized that the economic dimension of cost-effectiveness is important to ensure a sustainable system and should be conducted as part of the refinement process because the panel's deliberation was done at a specific point in time and newer evidence may have evolved since its discussion or new products may have become available. For example, if 2 drugs have the same effects in all respects (the same effectiveness over the same duration of treatment, and with the same side effects), the more cost-effective drug is the one that costs less (cost-minimization analysis). Priority setting is necessary as resources are never unlimited. The panel welcomed the guidance from CADTH's Health Economics Advisory Council (HEAC) on how the proposed sample list might be further refined using health economic principles and from a cost-effectiveness lens. The panel felt that insights from the HEAC would complement the panel's expertise and experience. A high-level summary of an exploratory proposal from the HEAC was presented to the panel and is included in Appendix 4. The panel felt that this would encourage further dialogue and due consideration as part of developing a potentially innovative and important framework for incorporating pharmacoeconomic considerations into a potential pan-Canadian formulary.

The panel felt that additional review may be warranted when there are multiple drugs that belong to the same pharmacological class, and/or have similar indications and places in therapy. As such, the proposed sample list overall would need to be reviewed periodically as part of the formulary refinement and modernization process, particularly when there is a new drug that could be added into a therapeutic class with several similar drugs, or when a drug's listing status changes from *not listed* to *listed*.

While it is not known how the pan-Canadian formulary, if implemented, will fit into the current public and private drug reimbursement system, the panel emphasized that continuity of care would be critical, regardless. Should any change occur in how drugs are reimbursed, the panel supports putting measures in place so that patients would be

safely transitioned to another (included) drug when appropriate. The panel also discussed having possible exceptions (e.g., criteria) for patients whose conditions could significantly deteriorate if a drug or possible alternatives may not be available on the proposed sample list.

Stage 2: Expanding to Other Therapeutic Areas

The next stage of creating a potential pan-Canadian formulary involves scaling the process to add other drugs and select related products for other health conditions to the proposed sample list. The panel acknowledged that experts, patients, and organizations that serve groups that are traditionally underrepresented should be involved as part of the expansion to other therapeutic areas.

The panel reflected on comments from respondents and felt that the value of the work to expand to other therapeutic areas could be diminished in the absence of clarity about the out-of-scope issues and this clarity would ideally be addressed before further work is undertaken or done in parallel for it to be meaningful. This includes assessing the impact of other pharmaceutical initiatives (e.g., the drugs for rare diseases strategy) in an ongoing way to ensure alignment, where feasible, in terms of design and application of principles, as well as reduced duplication of effort upon implementation. Moreover, the landscape of pharmacotherapy is rapidly changing, and the impact of novel therapies, such as precision medicines, is still unclear. Therefore, it was recommended that the processes for formulary review and expansion should evolve as more information becomes available. In addition, the needs of subpopulations would require giving careful thought to ensure that gaps are not created.

The panel deliberated on different ways to expand to other therapeutic areas and felt that the approach taken to generate the proposed sample list allowed the panel to consider the patient impact and need in a structured way while meeting the purpose of a potential pan-Canadian formulary. As the ATC classification system identifies 14 main pharmacological groups,[21] the process would need to be replicated for the other 11 therapeutic areas.

The panel recommends that the 6 principles (e.g., universal and integrated, equitable) be applied in the assessment of other therapeutic areas. The proposed approach would follow the review steps described previously by considering the available information from different sources (e.g., listing status from existing FPT formularies; utilization data; availability of other information, such as if a molecule has a generic or biosimilar product; information about safe use in those who are pregnant or breastfeeding; and references summarizing available drugs and use in Canada, among others). These considerations should be supplemented with literature reviews of pharmacotherapeutic areas that have been shown to improve health outcomes in people made vulnerable by systemic inequities (if available). This would be particularly helpful when there are research findings that could address drug access issues in disadvantaged communities. For example, an article by Keeys et al. (2021)[22] concluded that formulary management and drug utilization review processes provide an opportunity to consider disparities in the representation of sex, race, and ethnicity in clinical trial data. Further, these authors

mention that if available, information on prevalence or proportion of underrepresented groups within the population and/or condition under study should be considered. Identifying the known or potential significance of these disparities can also increase awareness and help address inequities in health care.[22]

Respondents to the consultation reflected on publicly shared national health priorities as a possible approach to prioritizing the expansion to other therapeutic areas. Given that setting such priorities is not within the scope of the panel, the panel recommended that assessment of the remaining 11 therapeutic areas should be completed in a systematic manner. As the intent is for all therapeutic areas to be reviewed and included in a potential pan-Canadian formulary before implementation, the order of review is likely to be less important.

If it is decided to expand the prototype pan-Canadian formulary to other therapeutic areas, the panel proposed that a working group be formed. Members with a mix of expertise should be included to conduct reviews within the therapeutic areas to identify drugs and related products to be included on the potential pan-Canadian formulary. The working group could be composed of key members with rotating experts for each specific area (e.g., oncology, respirology), as well as members of this panel to establish knowledge continuity. It is important to involve interested parties in the decision-making process. Once all therapeutic areas have been considered, the panel recommended proposed criteria on how to add new drugs and related products, as well as strategies to maintain the proposed list over time.

Stage 3: Adding to and Maintaining a Potential Pan-Canadian Formulary

Process for Identifying and Reviewing New Products

The panel recognized that adding new products and new indications for existing products to the potential pan-Canadian formulary could have a significant impact on the health and wellness of individuals and on the health care system as a whole. Therefore, carefully considered policies and procedures would need to be followed when reviewing these products. The panel expressed reservations about the current process for reviewing drug products. For a new drug product to be considered for inclusion in a public drug plan, the manufacturer must complete 3 steps, (1) approval by Health Canada that the drug may be sold in Canada, (2) HTA review (typically through CADTH or INESSS), and (3) pricing agreement via the pCPA and/or FPT payer. The sponsor (i.e., the submitter of the file) decides when the initial application is made. HTA assessments are currently conducted using a "first-in, first-out" process based on when submissions are filed. This process is typically used by the regulatory and HTA bodies to manage the submission and review processes. Because of the potentially high volume of submissions and limited available resources, this method does not sufficiently allow for priority setting, which is important for intentional, values-based resource allocation.

The panel explored alternative approaches to the first-in, first-out process for reviewing new products and indications for inclusion on a potential pan-Canadian formulary. The following options were explored:

Option 1: A prioritization model could be developed to align with Health Canada's priority reviews.[23] This would allow for a predictable process for identifying drugs that represent a significant therapeutic advancement. Although this approach could support a seamless integration between regulatory and HTA processes, it does not address the inability to control when a submission is initiated.

Option 2: A clear and transparent scoring system that would prioritize new drug submissions could be created and applied (e.g., new innovative products that address unmet needs of a population could score higher and be prioritized on a review agenda).

Option 3: Opportunities to work together at an international level to review and prioritize products collectively could be explored. There have been international collaborations in several areas of regulatory and HTA processes. This could potentially save on resources and accelerate access for Canadians and international partners.

In reflecting on the comments from respondents, the panel felt that a hybrid submission review model was well supported and would be a reasonable option. As such, the submission review model should allow for 2 pathways to drug reimbursement review — a standard process to review drugs (based on a first-in, first-out model), and a provision to fast track assessment of select drugs that meet an unmet need or have exceptional benefits. Drugs should meet a set of established criteria to be eligible for a priority review or fast track review (i.e., shorter timeline for reimbursement review). Multifactorial criteria, potentially including a scoring system, combined with process to allow patients, clinicians, and other interested parties to be involved should be established. The proposed criteria could include: product that addresses unmet need or treats people and populations that live in underresourced communities, novelty of treatment, demonstrates impact on population health and quality of life, impact on health care system, and so forth. The panel emphasized that not all innovative therapies offer significant benefit over current therapies. Noting the limited data to demonstrate the impact (e.g., on adherence or quality of life) of different routes of administration or less frequent dosing, the panel recommended that any change in formulation should not warrant consideration for a priority review. Further, inclusion of a drug in a clinical practice guideline (CPG) alone should not be sufficient to be considered for a priority review because of the variability in, and limitations of, CPGs. The prioritization framework could also consider incentivizing drugs that have been studied and are approved for underrepresented population (e.g., pediatric, as well as those who are pregnant or breastfeeding) to encourage submission of data on underrepresented population.

Overall, in developing a prioritization framework, the panel emphasized that the patient voice and those in underrepresented communities should be included. Abelson and colleagues described 6 principles to guide patient and public involvement in HTA: their involvement should be purposeful, pragmatic, fair and equitable, proportional, evidence-informed, and transparent. Depending on the stage of the HTA process, the form of

involvement of patients and the public will vary.[24] The panel encouraged continued strong engagement and collaboration with all key health partners (e.g., patients, clinicians, industry, government, and HTA bodies) through all steps in the process.

Conceptually, the panel recognized that transparency of process, and consistency in application will be important to ensure the submission review process is fair and predictable. Additionally, the submission review process should be agile, efficient (in terms of use of resources and improved efficiency of the system), and timely. The process should also consider impact from an equity perspective (i.e., the impact of prioritizing — or not — certain drugs for review on underrepresented populations). The criteria for prioritization should also remain flexible to accommodate the needs of other therapeutic areas that may have yet to be considered, and the operational practicality may be different than the 3 therapeutic areas that the panel has considered for the proposed sample list. Before any implementation, the panel also noted the need for an analysis to understand the impact of this potential new hybrid submission review process on the current systems (e.g., CADTH or INESSS reimbursement review).

The panel agreed with respondents that, where possible, national and international collaborations should be leveraged and applied in the review of pharmaceutical and related products. As an example, there have been ongoing collaborations between Health Canada, CADTH, and INESSS in terms of conducting aligned or concurrent reviews to expedite drug reviews, and subsequent access to drugs. Given the demonstrated reductions in overall completion time for these reviews, the panel recommends that concurrent reviews become the norm. Enhanced cooperation with international HTA bodies, or other parties, such as private insurers, as applicable, could help reduce potential duplication of effort, and promote sharing of best practices.

Selecting New Products for a Potential Pan-Canadian Formulary

Proposed Criteria

Policies and procedures should be followed routinely and accurately each time an evaluation is needed. To guide the evaluation of new drugs and new indications for a potential pan-Canadian formulary, it was recommended in the council report[2] that the following proposed criteria be considered: alignment with patient and societal values, clinical benefit, feasibility of adoption into health systems, and economic implications (e.g., value for money).

These proposed criteria are aligned with current Canadian deliberative frameworks, which include factors that are typically contemplated in an explicit manner by committees that make recommendations for drugs and related products.[25] As an example, INESSS adopted the methodological framework for evaluating drugs for listing purposes that the Conseil du médicament had developed to conduct evaluations.[17] INESSS must first assess the therapeutic value of a medication. If this is not established to its satisfaction, the institute sends a notice to that effect to the minister. If it considers that the therapeutic value of a medication has been established, it sends its recommendation to the minister after assessing: the reasonableness of the price charged; the cost-effectiveness ratio of the medication; the impact that entering the

medication on the list will have on the health of the general public and on the other components of the health and social services system; and the advisability of entering the medication on the list, given the purpose of the basic prescription drug insurance plan.[26] In contrast, CADTH's drug expert committees apply the 4 criteria noted in the council report. Each element is important to the review, and it is the sum consideration of all elements that the expert committee uses to formulate a reimbursement recommendation.[27] It is important to note that CADTH's Health Technology Expert Review Panel uses a multicriteria framework that considers the strength and quality of available clinical evidence; the strength and quality of available economic information; current practices and resource utilization patterns; and other factors, including, but not limited to, patient input and practical, ethical, environmental, and psychosocial considerations.[28] Based on a review of these frameworks, the panel considered the following 2 additional criteria — equitable access and additional considerations or long-term thinking — to enhance the deliberative process. Table 3 outlines the proposed evaluation criteria. The panel also provided additional guidance on how each criterion could be applied and the elements that would need to be taken into consideration when evaluating a new product. The components of the proposed criteria should not be considered separately. Instead, they must be deliberated together during the evaluation to ensure that safe, effective, cost-effective, and affordable treatments are considered for listing. Similar to the proposed guiding principles outlined in Table 1, these proposed criteria are not presented in any particular order of priority.

The proposed criteria are linked with the guiding principles and provide the basis for decision-making with respect to the evaluation and selection of drugs and related products for a potential pan-Canadian formulary. For example, the principle of health system sustainability is integrated into the proposed evaluation criteria of new drugs by considering the needs of Canadians over time. This is done by taking a long-term view and looking at the broader impact of a drug on the health system and Canadian society, examining the feasibility of adding the drug, and recognizing the value society gains for the financial investment in the drug. By adopting the criteria proposed by the panel, future HTA processes will be sensitive to the guiding principles.

Discussion Highlights

Alignment with patient and societal values: As patient and societal values may vary by condition, the panel felt there should be emphasis on disease-specific stakeholder consultation being conducted during the gathering of information phase of the review process and included in the deliberations. Importantly, values of Canadian society that are relevant to informing drug reimbursement decisions should be identified and balanced with values of patients and caregivers who are directly impacted by the decisions. Measures of societal value should reflect the diversity of Canada and provide an informed understanding, to allow for a democratic method to address difficult ethical and moral dilemmas. Integrating values prioritized by those living in Canada — for example, treatment-related factors (efficacy, safety) and disease-related factors (severity, quality of life) — into reimbursement recommendations will help decision-makers optimize distribution of limited public funds.[29] In addition to considering patient and societal values, it remains important to continue multi-stakeholder engagement with

each review such that it includes perspectives from different experts, including those with lived or living experiences and clinicians who have specialized knowledge, expertise, and experience in treating patients with the condition under discussion.

Clinical benefit: The panel discussed various aspects of what the term *clinical benefit* entails. In addition to traditional considerations such as efficacy and effectiveness on clinically meaningful outcomes, emphasis was placed on accounting for unmet need. Specifically, unmet health needs in the intended patient population, including the level of need and availability of treatment, were thought to be important considerations to guide the evaluation of new products and/or indications. The panel also discussed how the term *clinical benefit* has specific meaning in the context of a clinical trial. However, it could potentially be considered too restrictive when trying to identify the true value of the treatment. The potential pan-Canadian formulary could be an opportunity to consider a broader concept of benefit, outside the context of a conventional clinical trial (e.g., range of patient-reported outcomes and impacts, benefits outside the health care system, or societal benefit). For example, INESSS considers the impact of the drug under review on the population health and review submissions may include information on "the anticipated benefits associated with the drug from a societal or public health perspective (e.g., impact on caregivers, harm reduction, spread of the disease in the population)."[30] Exploring clinical benefit from a different perspective with a pan-Canadian formulary could be considered as a path for access to a wider range of therapies than currently available. To some degree, whether this approach should be taken will depend on the broader, out-of-scope vision of the plan; however, the benefit to patients, including populations made vulnerable by social and/or economic policies, could be significant.

Equitable access: The addition of this proposed criterion is to help close gaps in access to drugs between communities and groups. The panel emphasized that no individual or group should be further disadvantaged because of their health status or resulting health needs. Consideration of equitable access is generally not part of current deliberative processes, in particular for drug reviews; however, it was felt that inclusion of this proposed criterion should be inherent to the construction and application of the evaluation process. As an example, the panel suggested that the deliberations include a consideration of the gaps in existing treatment that affect subpopulations with unique needs. This would be particularly important for populations made vulnerable by systemic inequities, and where access to opportunities for health care are limited by factors beyond their control.

Feasibility of adoption into health systems: Considering the impact — including financial feasibility — of including a drug on a potential pan-Canadian formulary is crucial because there are some drugs that can have a substantial budget impact. It will be an important consideration for those who fund and administer the formulary to ensure the sustainability of the program. Key considerations in this domain may include taking into account resourcing requirements involved with the treatment, if covered; practical considerations such as capacity to implement the recommendation (e.g., requirement for case-by-case review by experts, availability of clinics, or logistics of administering specialty drugs); and others.

Economic implications: Similar to clinical benefit, the value of the drug should be viewed from the perspective of its impact on the population as well as individuals (achieving and maintaining physical and mental health), and on other components of the health system. As value-based decision-making can take a broader perspective in defining "value," the considerations for evaluating value could also include opportunity costs outside the public payer perspective. For example, INESSS also incorporates the burden of disease by looking at the cost of the disease to society, or to the health and social services system. Furthermore, the pharmacoeconomic analysis used in the review of drugs by INESSS are presented from a societal perspective, as well as a public health and social services system perspective.[30]

Additional considerations or long-term thinking: The panel discussed opportunities to be forward thinking and to consider other elements that could address future issues that are not contemplated in the current Canadian drug evaluation processes. In particular, the role of different types of evidence and how they could be incorporated into the evaluation of new drugs was discussed. For example, the panel considered the role of real-world evidence (RWE) and real-world data (RWD) in evaluating new drugs and re-evaluating older drugs. RWE is defined as "evidence about the use, safety, and effectiveness of a medical product, technology, or drug that is based on or derived from analysis of data generated in a real-world health care setting." Whereas RWD "includes information about the health of individuals or the delivery and/or outcomes of health care that is collected outside of traditional clinical trials and thus reflects results within the context of the particular health care system."[31] RWD could provide valuable information by complementing randomized controlled trial data and reducing uncertainties with evidence that cannot or have not been addressed by an appropriately constructed, funded, and monitored clinical trial. Efforts will be required to encourage development of RWD and incorporate this more broadly into drug evaluations. Although improving processes for evaluation and/or generation of RWE and RWD was out of scope, the panel recognized that much work in this area is ongoing nationally and internationally.

The current HTA processes involve engagement and input from patient groups, clinician organizations, drug plans, and other experts, all specific to individual therapies or class reviews. These are well regarded throughout the world and are continuously evolving and adapting to the ever-evolving scientific and medical communities. Although individual patient-reported experiences are viewed together with available scientific evidence data during HTA reviews, the current system may be perceived not to give equal weight to patient perspective and experiences relative to evidence generated from clinical trials. Key areas for improvement could include enhancing the rigour in the data collection, with emphasis placed on high-quality data. Overcoming barriers with incorporating and weighing individual patient-reported experiences into HTA reviews require a commitment to rigorous, high-quality RWD collection and appraisal. Standardization of RWD methodologies internationally would significantly improve its adoption and usefulness. As new methodologies to assess the quality of RWE are developed, these could be incorporated into the criteria to enhance decision-making.

Additionally, the panel discussed the nature of evidence-informed decision-making, and that the term *evidence-informed* "reflects the multifactorial nature of health system decision-making, in which the best available information is a key, but not sole, consideration."[32] As an example, using tacit (colloquial) evidence, which includes knowledge and opinions gained from experience, to complement and help contextualize the scientific (codified) evidence for a drug or related product. The panel reflected on the importance of incorporating the lived and living experiences of people who would be impacted by the drug under review. The panel felt that it would be important to consider different ways of knowing to create space for interaction among diverse groups and individuals impacted by the decision. In light of our commitment to engage respectfully and humbly with First Nations, Inuit, and Métis peoples, communities, organizations, and governments, this may be an opportunity to bring together Western and Indigenous ways of knowing to help shape the potential pan-Canadian formulary and its decision-making processes. How this could be co-developed should be explored more in-depth as part of future work.

Table 3: Proposed Assessment Criteria for Evaluating New Products

Proposed criteria	Considerations
Alignment with patient and societal values	• Based on disease-specific, multi-stakeholder consultation • Benefits and reduction of burdens to persons living with the condition and their caregivers • Reduction of harms to patient health
Clinical benefit	• Efficacy and effectiveness of the drug on clinically meaningful outcomes • Incidence and prevalence in Canada of the relevant health condition • Unmet health needs in the intended patient population (including level of this need, and the existence and availability of other treatments to address this need) • Benefit measured outside of the context of a conventional clinical trial (e.g., societal benefit) • Safety • Health-related quality of life • Novelty of therapy (e.g., dosing frequency or mode of administration)
Equitable access	• Gaps in existing treatment that affect subpopulations with unique needs • Impact on health determinants and opportunities to achieve equal health outcomes across the population • Potential to address particular disadvantages of individuals and groups of persons who will be directly affected by the recommendation • Ease of access to health care services by the intended population • Impact on populations' access to health care opportunities; individuals or populations could be at risk if their access to the opportunity for health and wellbeing are limited by factors beyond their control and exacerbated by unintended consequences of social policy (decisions), difficult procedures (steps required to access resources), and/or behaviour (stigma)

Proposed criteria	Considerations
Feasibility of adoption into health systems	• Costs and resources involved in the treatment, if covered (e.g., drug costs, dispensing costs, costs of human and/or infrastructure resources for treatment administration, and costs of managing toxicities and/or side effects) • Complexity of implementing conditions for assessment or follow-up associated with a listing recommendation • Future health care challenges that might be created or impacted by the drug • Level of burden on the system's budget
Economic implications	• Impact that adding the drug on the pan-Canadian formulary will have on the health of the population, including the ability to remain physically and mentally healthy, and on the other components of the health system, both now and in the future • Reasonableness of the cost charged and its cost-effectiveness (how well a drug or technology works in relation to how much it costs) • If appropriate, costs unique to relevant subpopulations • Measured from a comprehensive, broader system-level view (e.g., societal perspective, where applicable)
Additional considerations or long-term thinking	• Standardizing the evidence and controlling for variability in data quality found in clinical trials and real-world evidence • Opportunities to incorporate other ways of knowing (e.g., Indigenous ways of knowing) • Uncertainty of long-term benefits and harms • Ethics, including questions about ownership and consent (e.g., for genetic materials) • Other competing values that deserve consideration

Related Products

The panel agreed with the respondents' comments that each of the 6 evaluation criteria (Table 3) used for assessment of drug products was applicable to new related products, while recognizing appropriate use and clinical benefit as important considerations. However, it is important to note that related products may not have the same level of high-quality evidence and have a different regulatory review framework and process from drug products; therefore, adaptation or modification of the evaluation criteria may be necessary. As a part of future work, additional evaluation criteria for related products may need to be developed and such additional criteria should be assessed for their alignment with the principles established by the panel.

Deliberative Process

It would be critical to leverage existing systems to reduce duplication of processes, particularly when deciding whether to add or re-evaluate a product on public formularies. The panel provided recommendations on an approach to enhance current deliberative processes by using the proposed criteria and applying them in practice. The panel proposed that adding and evaluating products for a potential pan-Canadian formulary should leverage existing expert committees (e.g., CADTH Canadian Drug Expert Committee, CADTH pan-Canadian Oncology Drug Review Expert Review Committee, Comité scientifique d'évaluation des médicaments aux fins d'inscription, Comité de

l'évolution des pratiques en oncologie). These expert committees would typically make a conclusion to recommend a product (i.e., reimburse), to recommend a product with conditions or criteria (i.e., reimburse with conditions and/or criteria), or to not recommend a product (i.e., do not reimburse). Of particular interest, the panel explored ways to structure the deliberative process so that decisions are informed by evidence from multiple disciplines and perspectives in an objective manner.

A provincial model using MCDA, integrated within a values-based deliberative process, was presented as a case example.[33] The traditional form of MCDA involves 3 steps: defining the decision problem, selecting criteria that reflect relevant values, and constructing the performance matrix.[34] The MCDA method aims to enhance consistency and transparency by identifying, collecting, and structuring information to support decision analysis. Values-based deliberative methods create the culture within which analysis tools are used and specify how discussion will take place, who will get to speak when, and how the power for making and contesting arguments and resolving disagreements will be allocated. These methods influence and potentially allow a structured way to include different societal values.[34]

The provincial model case example included 6 criteria: clinical effectiveness, quality of life, safety, severity, unmet clinical need, and equity.[33] A point allocation method was used to weight the criteria, and a formal scoring tool was also developed using a 4-point rating scale. An overall benefit score for a given drug was calculated by multiplying the weight by the score for each criterion, and then summing across the criteria. When deliberating the overall benefit score, the cost per patient and overall budget impact would also be discussed. The provincial model case example also considered the opportunity cost of the total amount spent for the given drug. This allowed for considerations such as the value placed on the drug being reviewed relative to other priority areas of spending.[33]

The panel recognized that there is no perfect approach to assist decision-making. MCDA processes are limited by challenges such as how criteria are defined (i.e., by whom, if the criteria are fixed) and weighted (based on whose preferences), how to consider opportunity costs, and how to address uncertainty.[34] Quantitative weighting of criteria has been found to require substantial investment and may not always have appropriate societal representation.[34] Based on the comments received, the panel acknowledged that moving to an MCDA model would be a substantial shift from the current HTA decision-making process, with a steep learning curve, and risk a potential loss of consistency with past HTA reviews. Therefore, a thorough research into MCDA systems and their potential impact on the existing system should be conducted before any decision to proceed with implementing a MCDA model. This research should involve consultation with all interested parties and experts. The development and design of any deliberative framework should be cognizant to not create or further exacerbate inequities and continue to support patient-oriented care. Whichever deliberative methods are used, the panel felt strongly that the process underpinning the decision-making, as well as the principles guiding formulary decisions and processes, be made transparent to all stakeholders.

Ensuring Transparency Through Clear Communication

The review and evaluation of new prescription drugs is a very complex area requiring expertise from many scientific and technical disciplines, as well as invaluable insights from people with lived or living experiences. As such, it is recognized that the reports that are produced may not be in plain language. The currently published HTA recommendations and reasons for those recommendations are important for ensuring transparency. However, the panel felt that transparency efforts could be enhanced by fostering and maintaining dialogues between those affected by the recommendation and those making the recommendation. This dialogue could include producing clear, publicly accessible, easy-to-understand communications. Additionally, a robust appeal process could be implemented to ensure procedural fairness by providing the applicant with an opportunity to appeal the recommendation. It is important to note that procedural fairness is not concerned with whether the outcome of the decision was fair, but rather whether the process was fair.

Maintaining a Potential Pan-Canadian Formulary

Developing and maintaining a formulary is essential to ensuring that drugs are used in a safe, appropriate, and cost-effective manner. As evidence evolves and new therapies become available, it would be important to reassess if drugs already listed in the formulary continue to offer the same value. Re-evaluation of a listed product could result in no change in the listing status or the criteria for a drug, removal of the drug from the formulary, or modification of the criteria associated with the drug. As with any standard formulary management processes, the panel strongly supports that a potential pan-Canadian formulary should also undergo regular re-evaluation. This would ensure that the formulary continues to be informed by up-to-date evidence, and is sustainable, effective, and of high quality.

Formulary modernization is a way to align formularies with current evidence, but it is also a resource-intensive process. As a result, the panel highlighted that judicious resource allocation should be applied into formulary modernization to derive true benefits, and that certain criteria be developed to determine which of the drugs or drug classes listed in the formulary should be prioritized for re-evaluation. Some of the criteria suggested by respondents were related to clinical or economic benefit or uncertainty, unmet need, gaps in equitable access, availability of new evidence, or availability of alternative therapy with practice-changing evidence.

The panel noted that there is a lack of consistent data to assist with prioritization or to conduct re-evaluation of a given drug or related product. The value of RWD was emphasized in this context, as it can provide valuable information on how a drug is being used in practice versus how it was intended to be used when initially listed in the formulary. As such, existing research networks such as the CADTH Post-Marketing Drug Evaluation (PMDE) program may provide a platform to answer questions from decision-makers on post-marketing drug safety and effectiveness.

Re-evaluation can include reassessments of single drugs, therapeutic reviews (or drug class reviews), and consideration of prescribing guidance resources. Concurring with the

respondents, the panel encourages meaningful and transparent engagement, and collaboration with health partners (e.g., patients, clinicians, industry, government, and HTA bodies) throughout the prioritization and evaluation processes.

Reassessment

A life cycle approach or a reassessment is defined as "a structured evidence-based assessment of the clinical, social, ethical, and economic effects of a technology, currently used in the health care system, to inform the optimal use of that technology in comparison with alternatives."[35] The goal of taking a life cycle approach is to re-evaluate listed products to ensure resources are properly allocated — that is, to improve system efficiency by informing the reallocation of resources away from low-value care to higher-value care.

A reassessment is an ongoing process to inform the optimal use of a health technology throughout its life cycle. It can result in recommendations for more open or restrictive criteria, or no change to the criteria, leading to decreasing, increasing, or maintaining current levels of use, and in rare cases, recommendations for discontinuing the use of a technology (obsolescence). A reassessment can include clinical evaluation (systematic reviews), economic evaluation, current utilization analysis, current practice analysis, identification of practice and knowledge gaps, and identification of barriers to optimal use. In current practice, reassessments are conducted on an ad hoc basis or through a standard process. The process can be initiated by relevant health authorities, formulary management entities, and in some cases by drug manufacturers. Reasons for a reassessment could be informed by:

- new evidence (through post-market reviews for safety and efficacy, or utilization reviews)
- ongoing concerns with high utilization potentially due to inappropriate use
- a process to identify potentially low-value care at regular intervals
- a requirement to re-evaluate a new technology within a certain number of years after its entry into the formulary.[35]

The panel acknowledged that reassessments should be a holistic process. In conducting a reassessment, diverse perspectives of current users must be considered while applying the principles and methods of HTA. Active engagement with patients, caregivers, clinicians, industry, and formulary administrators is considered key to ensuring that the most appropriate technologies are identified for a reassessment. The panel recommended that sufficient guidelines be established for a process to identify appropriate drugs for a reassessment. Topic identification, selection, and prioritization for a reassessment should consider the resource requirements, as well as current health care priorities and the comparative impact of the technology being considered. While recognizing the resource-intensive nature of conducting reassessments, the panel noted that the process must be efficient, timely, and able to meet the quality standards. The panel also emphasized that the principles of equity must be upheld through formulary management strategies because some "low-value" technologies may still be appropriate for specific (albeit, a small number) patients. The panel also noted that drugs that are

currently excluded from the proposed sample list may be included based on a reassessment in future if the evidence supports its inclusion, or a reassessment could result in adding, removing, or modifying restrictions such as clinical criteria on drugs currently listed in the proposed sample list.

A potential pan-Canadian formulary should be a dynamic and living system. Given how evidence continues to evolve with new research, the process for reimbursement of drugs and related products should be iterative, responsive, evidence-driven, and patient-centred. The panel emphasized that the potential pan-Canadian formulary should take a learning health system approach (i.e., leverage advancements in science, technology, and practice to improve health system performance at a lower cost).[36]

The panel recognizes that formularies are challenged with the everyday need to assess new technologies, and reassessment of existing technologies often cannot be prioritized. However, the panel strongly believes that taking a life cycle approach, along with other formulary modernization strategies, should be an integral part of the formulary management system to ensure an equitable, sustainable, effective, and high-quality formulary.

Therapeutic Reviews

Therapeutic reviews are conducted to support drug reimbursement or policy decisions, and they may be useful in situations where there is uncertainty about the comparative clinical or cost-effectiveness within a particular therapeutic category or class of drugs.[37] These are large-scale reviews of multiple drugs as opposed to reassessments of single drugs. One goal of therapeutic reviews can be to provide policy recommendations for modernizing the formulary.[38] These reviews may be initiated in response to requests from policy-makers or as part of regular formulary management processes.

The therapeutic review process involves numerous steps and can vary in approach, scope, areas of focus, and stakeholder involvement.[37,39,40] Drugs are reviewed in a systematic manner for relative efficacy and safety, as well as use, cost, cost-effectiveness, and uniqueness.[40,41] Inclusion of direct and/or indirect costs should also be considered. Patient preferences and input from clinical experts are also important considerations.[37] Panel members also noted that security of supply may be an important consideration given the potential impact on patient care when significant drug shortages occur. Because the review process can involve consultation and opportunities for feedback from various stakeholders (e.g., patient groups, health care providers, policy-makers, health institutions or regions, and industry), the length of reviews can vary depending on the complexity of the topic, and can often take more than a year.[37-40] There may be cases where a streamlined approach would be appropriate to efficiently deliver evidence and analysis; for example, by leveraging existing robust published evidence when de novo meta-analyses or economic analyses are not required.

Prioritization of review areas also may occur based on various factors, including relevance (e.g., to patient and policy-makers, or based on drug utilization), timeliness, feasibility (e.g., amount of available evidence), and potential impact or value. These considerations may be in response to changes in utilization patterns, product additions,

changes in available evidence, or safety concerns (e.g., misuse).[38,39] As such, these broader reviews may be an important part of regular, ongoing formulary maintenance process; this will ensure that the formulary and any associated clinical criteria are reflective of current evidence.[39,41] Furthermore, regular reviews provide an opportunity to improve efficiency in the health care system, including procurement and inventory management.[41] A review of a particular therapeutic area may also provide opportunity to identify the place in therapy for new drugs that are introduced into a class or therapeutic area, as well as for existing drugs. Such a process involves the review of current evidence of all relevant (i.e., approved in Canada) drugs that fall under a class (e.g., angiotensin-converting enzyme [ACE] inhibitors) or a therapeutic category (e.g., antihypertensive drugs).[37]

During the development of the proposed sample list, the panel expressed a need for further review of certain classes of drugs within the created list; for example, via a therapeutic review process. There can be a variety of reasons for conducting a therapeutic review. For the purposes of creating and refining the proposed sample list, the panel felt that revisiting some classes of drugs through a therapeutic review could ensure the safe, appropriate, and cost-effective use of the drugs included in the list. The panel recognized the need for a sustainable formulary to ensure appropriate, continued access for all people living in Canada, while balancing considerations for equity (e.g., having treatment options to meet needs of subpopulations). There was consensus that if multiple options with a similar therapeutic profile (and same indication[s]) are available, a review is recommended to identify the optimal number of options based on clinical benefits and cost-effectiveness, as well as alignment with the principles of equitable and sustainable.

The panel emphasized that the therapeutic reviews should be conducted as part of an iterative process of formulary management and performed in line with the principles identified within the framework (refer to Table 1). Table 4 lists classes of drugs or therapeutic areas in the proposed sample list that the panel felt could benefit from further review. Recommendations for further review were made for drug classes that include numerous options with the same mechanism of action or similar therapeutic use (e.g., ACE inhibitors, 3-hydroxy-3-methylglutaryl-coenzyme A [HMG-CoA] reductase inhibitors [statins]). Some drug classes were also identified as a result of emerging evidence (e.g., potential cardiac benefit of dipeptidyl peptidase-4 inhibitors), use in a highly specialized disease area requiring further expertise (e.g., pulmonary arterial hypertension), or safety issues requiring further consideration (e.g., benzodiazepines). The panel also noted that these therapeutic reviews should consider usage in subpopulations, including pediatric patients. Lastly, the panel felt strongly that conducting therapeutic class or drug class reviews must be balanced with ensuring that no additional barriers are inadvertently imposed on patients while awaiting the results of such work (i.e., ensuring continued timely access and optimal transition).

Table 4: Examples of Specific Drug Classes That May Benefit From Therapeutic Reviews

Therapeutic area	Drug class
Cardiovascular diseases	Angiotensin-converting enzyme inhibitors
	Angiotensin II receptor antagonists
	Beta-adrenergic blocking drugs (cardio-selective and non-selective)
	HMG-CoA reductase inhibitors
	Low molecular weight heparins
	Miscellaneous vasodilating drugs[a]
	Phosphodiesterase type 5 inhibitors[a]
Diabetes	Dipeptidyl peptidase-4 (DPP-4) inhibitors
	Incretin mimetics (glucagon-like peptide-1 [GLP1] agonists)
	Sodium-glucose cotransporter-2 (SGLT2) inhibitors
Psychiatric illnesses	Benzodiazepines
	First-generation (typical) antipsychotic drugs
	Selective serotonin-reuptake inhibitors

[a] For the treatment of pulmonary arterial hypertension. Because pulmonary arterial hypertension is a highly specialized disease area and multiple options are available with a similar therapeutic profile, the panel recommended further review by clinicians with expertise in this area to identify the optimal number of therapeutic options based on clinical benefits and cost-effectiveness, as well as alignment with the principles of equitable and sustainable.

Prescribing Guidance Resources

Alignment between a formulary and prescribing guidance resources can have a positive impact on patient care and can support appropriate clinical decision-making. Therefore, the panel noted that a potential pan-Canadian formulary should take into account recommendations from prescribing guidance resources. Conversely, the panel encourages the clinician community to consider listings in a formulary when developing prescribing guidance resources. As such, the ongoing work to implement a potential pan-Canadian formulary should include establishing appropriate channels of regular communication with the clinician community and other interested parties.

Unbiased, up-to-date, and evidence-based prescribing guidance resources are essential for appropriate prescribing. Creators of prescribing guidance resources must be transparent about any conflicts of interest. Examples of prescribing guidance resources identified by the panel include: CPGs, Choosing Wisely Canada resources, prescribing guidance documents from academic detailing groups, drug stewardship (e.g., opioid stewardship documents), deprescribing resources, and best practices. The panel considered best practices as guidance where recommendation or decisions are systematically developed and evidence-informed based on the highest quality evidence; it was considered in a broader context to accommodate commitment to different forms of evidence, as well as commitment to cultural sensitivity (including Indigenous ways of knowing and patient experiences, among others). The panel supports the notion that

prescribing decisions should be made by a health care provider with their patient, and that a potential pan-Canadian formulary is not meant to be a mechanism for implementing prescribing guidance resources.

To support a learning health system approach, the panel noted that there are organizations and networks available to support reviewing the appropriateness of drug prescribing. These organizations often provide resources, such as practice guidelines, summary documents, practice support tools, and academic detailing support. Some example groups with whom collaboration may be sought were highlighted (e.g., Choosing Wisely Canada, the Canadian Deprescribing Network). For instance, the Canadian Deprescribing Network promotes the reduction or stopping of prescription drugs that may no longer provide benefit or may be causing harm. The group raises awareness and shares knowledge by bringing together health care leaders, clinicians, decision-makers, academic researchers, and patient advocates.[42]

Formulary Management Practices

The panel noted that it would be important to include detailed assessments and discussions of formulary management best practices as part of the broader implementation plan. One such example was on biosimilar and generic products. If biosimilar and generic products are available for a particular drug molecule, the panel felt that the least costly product could be selected and prioritized for listing. The panel reviewed the comments received and continues to support the recommendation in the council report[2] that encouraged both generic and biosimilar use, including generic and biosimilar substitution. The panel also supports expedited reviews of these products. As an example, as of 2019, CADTH no longer reviews biosimilars; INESSS uses an expedited process so as not to create any delays.[43,44]

As part of formulary management, proactive strategies will be required to prevent, minimize, and/or manage the impact of drug shortages. Drug shortages have been an ongoing issue both within the Canadian health care system and globally. According to Drug Shortages Canada, a drug shortage is defined as a situation "in which the manufacturer…that sets out the drug identification number assigned for a drug is unable to meet the demand for the drug."[45] The panel noted that there should ideally be more than 1 choice of drug molecule within each class or category and, if possible, more than 1 supplier. The intent of providing options is to mitigate issues caused by drug supply shortages, allow for patient and clinician preference, and address medical need. To prevent and mitigate drug shortages, as well as address this issue at the national level, the Multi-Stakeholder Steering Committee on Drug Shortages was established in Canada in 2012.[46] This committee brings together representatives from various groups, including industry associations, FPT governments, and health care professional associations. Under the committee's work, the impact of drug shortages is minimized and/or mitigated as much as possible through the collaborative efforts of governments, supply chain players, and health care providers.[46] As such, it is critical to ensure that when operationalizing a potential pan-Canadian formulary, linkages be made with this network and other similar networks to manage potential drug shortages.

Future Scope

The panel recognizes that this is a unique opportunity to improve access to drugs and related products for people living in Canada. As part of building this process together, it is important to ensure meaningful and early engagement with all interested parties (e.g., patients, clinicians, industry, governments, associations, pharmacy, private insurers, employers, labour groups) throughout each step of the process to achieve success. It is important to meaningful engage with First Nations (status and non-status), Inuit, and Métis peoples, in urban, rural, or remote communities. Indigenous-specific considerations should be interwoven throughout the design and implementation of a potential pan-Canadian formulary, so that Indigenous governance, Indigenous data sovereignty, and Indigenous ways of knowing, being, and doing (which would include approaches to healing, and health and wellness) are appropriately reflected.

Many of the feedback responses were related to areas that were beyond the scope of the panel's mandate. Although these elements are out of scope of the panel's mandate, the panel acknowledges that they are important to address as part of the design and implementation of a potential pan-Canadian formulary, and should be taken into account as part of future work. Specifically, the panel felt it would be important to highlight the following:

Addressing out-of-scope topics: As noted in the introduction of this report, several topics were beyond the scope of the panel's mandate. These included but are not limited to: an assessment of current drug plan processes or expectations about whether or how coverage on existing drug plans might be impacted by a potential pan-Canadian formulary; consideration of financing issues (e.g., funding allocation; financial contributions; funding models; budget scope, size, and amount; or individual drug plan budgets or projected estimates for those budgets); the terms for coverage (e.g., patient contributions, such as copayments or deductibles) and patient eligibility, including status; and consideration of the interplay between public and private insurance plans. These issues should be clarified for the work to be meaningful. The panel's recommendations are based on its interpretation of the council report,[2] review of the comments shared by respondents to the consultation, and other assumptions noted in this report. Further clarity of these elements could result in the recommendations being refined or enhanced.

Follow-on work: The work that has been completed to date reflects testing of 1 potential approach, and is a preliminary step in developing a potential pan-Canadian formulary. Further steps are required to build on the process to scale and expand the proposed sample list. Additionally, this approach must also consider existing interprovincial and territorial differences. In this regard, a more complex ecosystem view is required to construct a pan-Canadian formulary.

Transparency regarding governance: This work has been focused on the principles, values, and criteria to make decisions on the selection and evaluation of prescription drugs and related products, as well as the process by which these criteria would apply.

Although out of scope, the panel emphasized that it is important to also identify and be transparent about the parties that will be making these decisions.

Leverage and enhance existing processes to reduce duplication of processes: If it is intended to be an add-on or overlaying model, it is important to ensure that a potential pan-Canadian formulary would work with existing structures and systems, and be synchronized with existing drug programs across the country. A risk-benefit analysis should be conducted to make this determination. While reflecting on the principle of universal and integrated, the panel felt that leveraging existing systems would reduce duplication of processes, as well as provide opportunities to enhance existing processes. For example, decisions to add or re-evaluate a product on public formularies are often guided by committees and processes; therefore, it would be critical to leverage infrastructures from existing systems (e.g., HTA processes such as CADTH and INESSS) to reduce duplication of processes, particularly when deciding whether to add or re-evaluate a product on public formularies. As part of future work, it might be helpful to conduct a scan of the different provincial and territorial reimbursement models to inform the possible gaps. There may also be opportunities for current HTA expert committees to assess whether and how to adapt the proposed criteria and considerations set out in Table 3 as part of current deliberative processes. An important consideration when streamlining and integrating processes is that the process(es) chosen should result in minimal duplication to prevent delays in drug access and be seamless for patients.

Ensuring continuity of care: There could be an opportunity to improve continuity of care for patients transitioning from hospital to community settings or vice versa. This transition often creates gaps in patient access to therapies or inadvertently creates scenarios in which drug wastage can occur. There have been efforts to collaborate and share resources within health authorities and/or hospitals; for example, a National Hospital Formulary Collaborative,[47] with representatives from the drugs and therapeutics or pharmacy and therapeutics committees for various health authorities (10 provinces with CADTH as a liaison), has been created to explore opportunities for collaboration and sharing information on best practices. The panel recognizes the importance of seamless transitions between community and hospital settings to improve continuity of care. If moving forward with a potential pan-Canadian formulary, the panel recommends a more centralized approach in reviewing prescription drugs that could be used in both community and hospital settings, as well as other settings (e.g., prisons, military) to support improved patient care. In addition, the panel encourages future synchronization and harmonization of hospital formulary drug lists and a potential pan-Canadian formulary.

Centralizing data systems: The panel identified a need for more effective and integrated data systems in Canada. Data infrastructure and system linkages need to be in place to monitor and evaluate appropriate use and patient outcomes. Current cross–provincial and territorial data linkages are limited in some situations, and may need to be enhanced. It is recognized that there is a need for better data to support decision-making; for example, there is a lack of data collected on subpopulations or data to address inequities in drug access to demonstrate the impact on equity for select populations made vulnerable by systemic inequities.

Supporting appropriate use: In developing a potential pan-Canadian formulary, it would be important to explore approaches that could examine the listing criteria to encourage appropriate use and meet patient needs; as well as how this might create a platform to meaningfully engage with patients, medical professionals, researchers, payers, regulatory colleges, and others to drive optimal use of medications.

Change management for implementation and performance measurement frameworks: Program implementation considerations should be explored to conduct a detailed impact analysis of the proposed framework and the proposed sample lists. As well, a change management strategy should accompany any transition to a potential pan-Canadian formulary. This may include incorporating conditions that would prevent treatment gaps (e.g., a legacy clause that would allow patients to maintain their current treatments). Performance measurement frameworks should be developed and deployed as part of the implementation of a potential pan-Canadian formulary. The panel noted the importance of evaluating its impact, and determining if the desired results are achieved. This will also provide opportunity to review processes and make necessary adjustments to improve both efficiency and effectiveness.

Creating synergies with other pharmaceutical initiatives: The panel recognizes that there is ongoing work with other pharmaceutical initiatives. One such initiative is the National Strategy for Drugs for Rare Disease.[48] As such, it is critical that the pan-Canadian formulary work be complimentary to these initiatives. There could be opportunities to create a platform for multi-stakeholder engagement to ensure that there are no inadvertent gaps or inconsistencies in policy objectives.

Conclusion

Developing a framework for the design and implementation of a potential pan-Canadian formulary is complex.

The panel considered what would serve all people living in what has become known as Canada today and years into the future. The panel strongly feels that, while policies need to respond to the issues of today, a lasting framework must be resilient, agile, sustainable, and adaptable to the unforeseen but inescapable changes of tomorrow. It is our belief that the recommendations shared within this report will provide decision-makers with the framework and tools necessary to initiate the steps necessary for creating and implementing a pan-Canadian formulary.

The single most important message to convey on behalf of people living in Canada is one of timeliness. We encourage decision-makers to consider our recommendations, and to meaningfully engage all interested parties to explore the changes necessary for ensuring that all people living in Canada have access to a broad range of safe, effective, evidence-based drugs and related products.

As an independent panel making non-binding recommendations in support of a broader discussion about a potential pan-Canadian formulary, we are grateful to CADTH and the government for this opportunity to be part of the process and this discussion.

Appendix 1: Proposed Sample List Methodology, Assumptions, and Limitations

Methodology

To develop the proposed sample list of commonly prescribed drugs and related products, the panel first identified therapeutic areas on which to focus. Several factors were considered when making the selection. For example, the panel explored which therapeutic areas involve drugs with the highest utilization, which diseases are the most significant and growing in prevalence, and which conditions account for high numbers of clinician visits and/or hospitalizations in Canada. Based on these considerations, the panel selected 3 therapeutic areas: cardiovascular diseases, diabetes, and psychiatric illnesses.

The first step in developing the sample list was to identify drugs and related products for the 3 therapeutic areas (cardiovascular diseases, diabetes, and psychiatric illnesses) to generate an initial list. This initial list of drugs and related products was then further refined by the panel through discussion. The panel used predefined assessment criteria that it developed to review each drug and related product on the initial list to determine if it would be included or excluded from the sample list, or flagged for further consideration by experts.

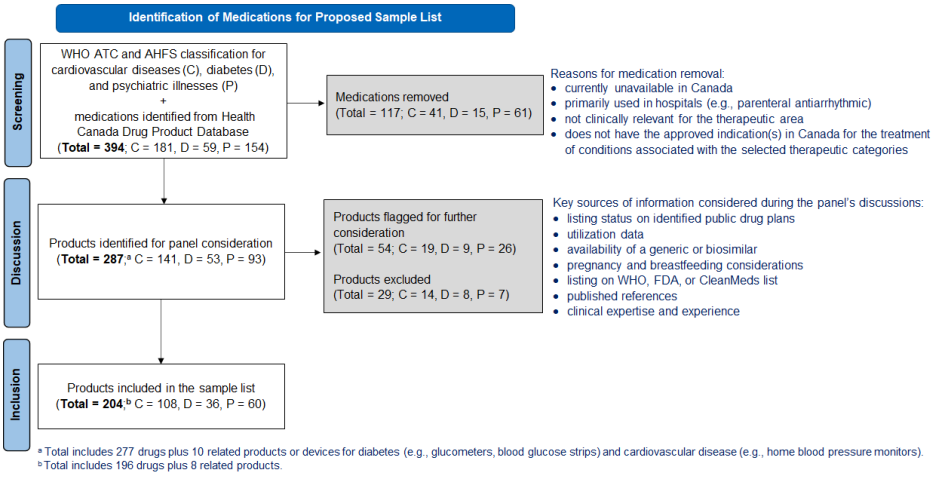
Figure 8 outlines a summary of how the proposed sample list was created, with further information provided in the following text. Details on the predefined assessment criteria used by the panel are presented in Table 2.

Drug Products

- To generate the initial list of drugs for the panel to discuss, information was sourced from the WHO ATC classification system and the American Hospital Formulary Service (AHFS) for drugs. This was done to capture drugs that fall under the corresponding therapeutic classes identified in the IQVIA Pharmaceutical Trends for 2020.[20]
- Each drug was searched on the Health Canada Drug Product Database to determine if the drug is currently available in Canada. If the status of the drug was "marketed," it was included on the list. If the drug was not listed in the Drug Product Database, or if the status of the drug was "dormant," "cancelled," or "approved" (but not "marketed"), it was removed from the list because these drugs are currently unavailable in Canada. Drugs that do not have approved indication(s) in Canada for the treatment of conditions associated with the selected therapeutic areas were also removed.
- Drugs that are primarily used in hospitals were also removed as part of the screening (e.g., the parenteral antiarrhythmic lidocaine was removed from the list).

- For each drug on this initial list, the following information was provided to the panel, if available, to help with deliberations:
- formulary listing status for each provincial and territorial public plan (the Non-Insured Health Benefits [NIHB] program formulary was used for Northwest Territories and Nunavut; Yukon was reported separately as its own formulary)
- whether a generic or biosimilar exists for each drug molecule
- considerations during pregnancy and breastfeeding, as gathered from *Briggs Drugs in Pregnancy and Lactation Twelfth Edition*[49]
- utilization data (both claimant and claim) from 3 main sources (IQVIA, Canadian Institute for Health Information [CIHI], and NIHB) and, when possible, broken down by age group and sex (note that there was no single source for utilization data)
- inclusion on an EML (WHO, FDA, or CLEAN Meds).

Figure 8: Identification of Drugs for 3 Therapeutic Areas



AHFS = American Hospital Formulary Service; ATC = Anatomical Therapeutic Chemical; C = cardiovascular diseases; D = diabetes; P = psychiatric illnesses.

Related Products

- Related products are typically devices that directly support the delivery or administration of and/or are necessary for the optimal use of drugs. A number of sources of information were used to identify related products, including Canadian Pharmacists Association *Minor Ailments* (Diabetes Care Devices chapter),[50] Diabetes Canada,[51] and Hypertension Canada.[52]
- When available, listing status and utilization data were recorded for each provincial and territorial public plan.
- For utilization data on related products for diabetes, ATC classification as per methodology developed by CIHI was used if available.

Assumptions

- If a potential pan-Canadian formulary is intended to be an add-on or overlaying model, it is important to ensure that it would work with existing structures and systems, and be synchronized with existing drug programs across the country. If it is decided that a potential pan-Canadian formulary will be implemented in the future, all therapies included in current drug plans that are not included in the potential pan-Canadian formulary could continue to remain available through those plans. The funding options (e.g., payer of last resort) need broader discussion and consultation; however, this is out of scope of the panel's work.
- The recommendations are based on the best available information and expert opinion at the time of discussion and are subject to change as new information becomes available.
- Because there is a fixed amount of time in which to perform the analysis and make recommendations, the panel decided to take a pragmatic approach and propose a sample list of prescription drugs and related products. The panel acknowledged the limitations associated with creating a proposed sample list. For example, when a comprehensive HTA methodology could not be used, whether because of resourcing or time constraints, the panel used available information when deliberating the development of the proposed list. It was not the mandate of the panel to conduct reassessments or drug class reviews for the purpose of this work. The panel assumed that there would be future refinements of the proposed sample list that would include a review of clinical effectiveness and cost-effectiveness evaluations.
- Listing status was based on the molecule and identified irrespective of formulation or route of administration (as long as it was administered in a community setting). For the purpose of creating a sample list, the panel took a liberal approach and assumed that the listing status for a molecule was the same for all available formulations (including different salts). That is, if 1 formulation of a particular molecule was an open benefit, listing status was indicated as such. For jurisdictions with multiple drug plans, if a molecule was an open benefit in at least 1 public plan (e.g., Nursing Home Program or Institutional Pharmacy Program in Prince Edward Island), it was accepted as such.
- Each existing drug plan includes both "unrestricted benefit" therapies (also called *open benefit* or *general benefit*) and "restricted benefit" therapies (e.g., limited to certain prescribers, require meeting specific clinical criteria). There were considerable jurisdictional variations in the definitions; therefore, for the purposes of this work, anything categorized as "restricted" was simply noted as restricted regardless of definition and without further analysis. The panel assumed steps will be taken in the future to revisit any restrictions and harmonize any necessary eligibility criteria.

Limitations

- The WHO ATC Classification System and AHFS Pharmacologic-Therapeutic Classification System do not specify exact indications. Drugs with different therapeutic uses may also be assigned several ATC codes or AHFS categorizations or be classified under their primary use, which could fall outside of the 3 therapeutic categories explored for the list of drugs. In some cases, several ATC codes could be assigned to various strengths or routes of administration with different therapeutic

uses. However, care was taken to capture relevant drugs and under the appropriate categories.

- Drugs that do not have approved indication(s) in Canada for the treatment of conditions associated with the selected therapeutic areas were excluded; they are anticipated to be captured when other therapeutic areas are reviewed in the future (e.g., levodopa and decarboxylase inhibitor for Parkinson disease was excluded from this list but would be considered in the future when neurologic conditions are reviewed). However, before finalizing the potential pan-Canadian formulary, a review process is suggested to ensure all clinically relevant drugs and related products commonly used in clinical practice are included.
- Although other ongoing pharmaceutical initiatives (e.g., Health Canada's Drugs for Rare Diseases Strategy) were out of scope of the panel's mandate, some drugs that may fall under these initiatives (e.g., drugs that could be used for rare conditions such as pulmonary arterial hypertension) were included on the list of drugs. These drugs fell within the WHO ATC Classification System and AHFS Pharmacologic-Therapeutic Classification System categories used to generate the list of drugs for the 3 therapeutic classes used as part of the test case. However, a clear definition of the term *rare disease* was unknown at the time of the panel's deliberations, and no drugs were removed based on the rarity of the condition. Further refinement of the list will be required once definitions and specific parameters of such initiatives are established.
- It is recognized that drug costs are publicly available, although they are likely not reflective of the final price because of negotiation, bundling, and other strategies confidentially agreed to between the manufacturer and drug plan. As a result, drug cost was not factored into the assessment of the proposed sample list and that the panel relied on the public plan listing status as a factor for consideration. Many of these products also have generic or biosimilar versions, which would have different pricing. To ensure that the proposed list is sustainable, negotiations for these products could be conducted. Issues related to the negotiation of drug pricing and budgets remain outside the scope of the panel's work.
- Listing status was searched using the publicly accessible main e-formularies for each of the identified public drug plans. Therefore, the proposed sample list does not include drugs or related products that may be covered under specialized programs for well-defined groups of patients, such as disease-specific funding programs. Public drug plans may also have separate pathways for reimbursing drugs for patients who meet specific criteria or through case-by-case assessments (e.g., special or compassionate access programs).
- The search for listing status of each drug on the identified public drug plans was done only at 1 point in time and reflects results recorded in August 2021. The listing status does not reflect any updates made to the formularies thereafter. This means the change in status for drugs or related products that became listed on the formularies after this time would not have been captured. As such, the proposed list would need to be reviewed periodically as part of the formulary refinement process.
- Information regarding drug utilization was obtained from the IQVIA PharmaStat dataset for the 2020 calendar year. The IQVIA PharmaStat dataset includes private and public claims for drugs dispensed from community pharmacies in all provinces of Canada except Prince Edward Island. In addition, the dataset does not include territorial or federal drug plans. Moreover, the age of the patient is not available in the dataset; as a result, claims could not be reported based on patient age.

- NIHB drug utilization data are claims data for the 2020 calendar year. Not all drugs or related products have claims data available or reported because the information was suppressed (i.e., not disclosed due to low numbers that may compromise confidentiality).
- CIHI data represent the number of patients and not the number of claims. Only public payer data are captured, excluding Quebec and NIHB. Individuals with unknown age (0.0002%) or sex (0.03%) were excluded from the analysis. Due to the design of public drug programs in Canada (i.e., adults 65 years of age and older and low-income families or individuals are the only populations covered in all public drug plans), there are limited data on claims made by younger populations. As a result, it is not a population-based system that captures all Canadians.
- Related products (e.g., supplies for patients with diabetes) have an assigned ATC code based on the methodology developed by CIHI. Data on utilization of non-drug products for patients with diabetes in New Brunswick were not included in the CIHI data.
- In accordance with CIHI and NIHB privacy policies, if the number of beneficiaries was fewer than 5 (but greater than 0), the number was suppressed to ensure confidentiality.
- Utilization data were only obtained for 1 calendar year, and may have been affected by extraneous factors that occurred during that year (e.g., global pandemic). However, the data were meant to provide a general snapshot on usage, which is 1 of many factors in the decision-making process. For future processes, identifying trends in utilization over several years should be considered.
- Some assumptions made, as previously listed (e.g., listing status for a molecule was the same for all available formulations), may not be reflective of current formularies; however, for the purpose of the panel's work, some steps were simplified so the focus could be on testing the process within the available time frame.
- Other limitations include the extremely short timelines and the difficulties accounting for variation in health care infrastructure and access to care across Canada.

Appendix 2: Classification System Used to Identify Drugs

Both WHO's ATC classification system and the AHFS classification system were used to identify drugs from the following categories:

Cardiovascular Diseases

AHFS 20:12 Antithrombotic Agents

AHFS 24:00 Cardiovascular Drugs

AHFS 88:24 Vitamin K

ATC B01 Antithrombotic Agents

ATC B02BA01 Phytomenadione (Vitamin K)

ATC C01 Cardiac Therapy

ATC C02 Antihypertensives

ATC C03 Diuretics

ATC C04 Peripheral Vasodilators

ATC C07 Beta Blocking Agents

ATC C08 Calcium Channel Blockers

ATC C09 Agents Acting on the Renin-Angiotensin System

ATC C10 Lipid Modifying Agents

Diabetes

AHFS 68:20 Antidiabetic Agents

AHFS 68:22 Antihypoglycemic Agents

ATC A10 Drugs Used in Diabetes

ATC H04AA01 Glucagon

Devices for diabetes

Psychiatric Illnesses

AHFS 28:16 Psychotherapeutic Agents

AHFS 28:20 Anorexigenic Agents and Respiratory and Cerebral Stimulants

AHFS 28:24 Anxiolytics, Sedatives, and Hypnotics

AHFS 28:28 Antimanic Agents

AHFS 28:36:08 Anticholinergic Agents

ATC N03AF01 Carbamazepine

ATC N03AG01 Valproic Acid/Divalproex

ATC N04AA Tertiary Amines

ATC N04AC01 Benztropine

ATC N05 Psycholeptics

ATC N06A Antidepressants

ATC N06B Psychostimulants, Agents Used for ADHD and Nootropics

ATC N07B Drugs Used in Addictive Disorders

Appendix 3: Proposed Sample Lists of Drugs and Related Products

The panel made the following recommendations for the 277 drugs and 10 related products presented for cardiovascular diseases, diabetes, and psychiatric illnesses. Drugs and related products that were included, flagged for further review, or excluded are listed in Table 5, Table 6, and Table 7, respectively.

For decisions (particularly exclusions) made mainly based on formulary listing status, the panel noted the importance of reviewing the drug list regularly. The search for the listing status of each drug on the identified public drug plans was done only at 1 point in time and reflects results recorded in August 2021. The listing status does not reflect any updates made to the formularies thereafter.

Table 5: Proposed Sample List of Drugs and Related Products to Include

Drug class	Name of drug or related product
Cardiovascular diseases	
Thiazide-like diuretics	Chlorthalidone Hydrochlorothiazide Indapamide Metolazone
Loop diuretics	Ethacrynic Acid Furosemide
Potassium-sparing diuretics (mineralocorticoid [aldosterone] receptor antagonists)	Amiloride Eplerenone Spironolactone Amiloride and hydrochlorothiazide Spironolactone and hydrochlorothiazide Triamterene and hydrochlorothiazide
Angiotensin-converting enzyme inhibitors	Benazepril Captopril Cilazapril Enalapril Fosinopril Lisinopril Perindopril Quinapril Ramipril Trandolapril Cilazapril and hydrochlorothiazide Enalapril and hydrochlorothiazide

Drug class	Name of drug or related product
	Lisinopril and hydrochlorothiazide Perindopril and indapamide Quinapril and hydrochlorothiazide Ramipril and hydrochlorothiazide
Angiotensin II receptor antagonists	Candesartan Eprosartan Irbesartan Losartan Olmesartan medoxomil Telmisartan Valsartan Candesartan and hydrochlorothiazide Eprosartan and hydrochlorothiazide Irbesartan and hydrochlorothiazide Losartan and hydrochlorothiazide Olmesartan medoxomil and hydrochlorothiazide Telmisartan and hydrochlorothiazide Valsartan and hydrochlorothiazide Telmisartan and amlodipine Valsartan and sacubitril
Dihydropyridine calcium-channel blocking agents	Amlodipine Felodipine Nifedipine
Non-dihydropyridine calcium-channel blocking agents	Diltiazem Verapamil
Nitrates	Glyceryl trinitrate (nitroglycerin) Isosorbide dinitrate Isosorbide mononitrate
Direct vasodilators	Hydralazine Minoxidil
Alpha-adrenergic blocking agents	Doxazosin Prazosin Terazosin
Alpha-adrenergic agonists	Clonidine Methyldopa Midodrine
Cardio-selective beta-adrenergic blocking agents	Acebutolol Atenolol Bisoprolol Metoprolol Atenolol and chlorthalidone

Drug class	Name of drug or related product
Non-selective beta-adrenergic blocking agents	Nadolol Pindolol Propranolol Sotalol Timolol Pindolol and hydrochlorothiazide
Non-selective beta and alpha-adrenergic blocking agents	Carvedilol Labetalol
Miscellaneous cardiac drugs	Ivabradine
Class I antiarrhythmic agents	Disopyramide Flecainide Mexiletine Propafenone
Class III antiarrhythmic agents	Amiodarone
Miscellaneous antiarrhythmics	Digoxin
HMG-CoA reductase inhibitors	Atorvastatin Fluvastatin Lovastatin Pravastatin Rosuvastatin Simvastatin Atorvastatin and amlodipine
Cholesterol absorption inhibitors	Ezetimibe
Bile acid sequestrants	Cholestyramine Colesevelam
Fibric acid derivatives	Fenofibrate Gemfibrozil
Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors	Alirocumab Evolocumab
Miscellaneous antilipemic agents	Niacin and nicotinic acid
Platelet-aggregation inhibitors (oral antiplatelets)	Acetylsalicylic acid Clopidogrel Ticagrelor
Coumarin derivatives	Warfarin
Direct thrombin inhibitors	Dabigatran
Factor Xa inhibitors	Apixaban Rivaroxaban Edoxaban
Low molecular weight heparins	Dalteparin Enoxaparin

Drug class	Name of drug or related product
	Tinzaparin
Hemorrheologic agents	Pentoxifylline
Vitamin K activity	Vitamin K1 (phytonadione)
Diabetes	
Biguanides	Metformin Metformin and dapagliflozin Metformin and empagliflozin Metformin and linagliptin Metformin and saxagliptin Metformin and sitagliptin
Sulfonylureas	Gliclazide Glyburide
Dipeptidyl peptidase-4 inhibitors	Linagliptin Saxagliptin Sitagliptin Linagliptin and empagliflozin
Incretin mimetics (glucagon-like peptide-1 agonists)	Semaglutide
Sodium-glucose cotransporter-2 inhibitors	Canagliflozin Dapagliflozin Empagliflozin
Meglitinides	Repaglinide
Alpha-glucosidase inhibitors	Acarbose
Insulins Rapid-acting insulin analogues Short-acting Intermediate-acting Long-acting insulin analogues Premixed insulin	 Insulin aspart Insulin glulisine Insulin lispro Insulin regular (Toronto; human) Insulin isophane (NPH; human) Insulin degludec Insulin glargine Insulin (human) combination regular and isophane (NPH) Insulin combination lispro and lispro protamine
Antihypoglycemic (glycogenolytic) agent	Glucagon
Related products: Diabetes supplies	Blood glucose meter Blood glucose strips Blood-letting lancet Continuous or flash glucose monitor Insulin pen needles Insulin pump Insulin syringes

Drug class	Name of drug or related product
	Urine strips
Psychiatric illnesses	
Selective serotonin-reuptake inhibitors	Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline
Selective serotonin and norepinephrine reuptake inhibitors	Duloxetine Venlafaxine
Serotonin modulators	Trazodone
Tricyclics and other norepinephrine reuptake inhibitors	Amitriptyline Clomipramine Desipramine Doxepin Imipramine Nortriptyline Trimipramine
Miscellaneous antidepressants	Bupropion Mirtazapine
First-generation (typical) antipsychotic drugs	Chlorpromazine Flupentixol (flupenthixol) Fluphenazine Haloperidol Levomepromazine (methotrimeprazine) Loxapine Periciazine (pericyazine) Perphenazine Pimozide Prochlorperazine Trifluoperazine Zuclopenthixol
Second-generation (atypical) antipsychotic drugs	Aripiprazole Clozapine Lurasidone Olanzapine Paliperidone Quetiapine Risperidone Ziprasidone
Mood stabilizers	Carbamazepine

Drug class	Name of drug or related product
	Lithium Valproic acid (including divalproex)
Barbiturates	Phenobarbital
Miscellaneous anxiolytics, sedatives, and hypnotics	Buspirone Diphenhydramine
Wakefulness-promoting agents	Modafinil
Anticholinergic agents and N-methyl-D-aspartate (NMDA) receptor antagonist (for drug-induced extrapyramidal symptoms)	Benztropine
Psychostimulants	Amphetamine (mixed salt) Dexamphetamine (dextroamphetamine) Lisdexamfetamine Methylphenidate
Non-stimulant agents for attention-deficit/hyperactivity disorder	Atomoxetine Guanfacine
Treatment of addiction and substance use disorder (alcohol, opioid, nicotine)	Acamprosate Buprenorphine Buprenorphine, combinations Methadone Naloxone Naltrexone Nicotine Varenicline

Table 6: Proposed Sample List of Drugs and Related Products to Flag for Future Review

Drug class	Name of drug or related product
Cardiovascular diseases	
Loop diuretics	Bumetanide
Dihydropyridine calcium-channel blocking agents	Nimodipine
Miscellaneous vasodilating agents	Ambrisentan Bosentan Epoprostenol Macitentan Riociguat Selexipag Treprostinil
Phosphodiesterase type 5 inhibitors	Sildenafil Tadalafil

Drug class	Name of drug or related product
Bile acid sequestrants	Colestipol
Fibric acid derivatives	Bezafibrate
Platelet-aggregation inhibitors (oral antiplatelets)	Dipyridamole Dipyridamole and acetylsalicylic acid Prasugrel
Factor Xa inhibitors	Fondaparinux
Low molecular weight heparins	Nadroparin
Related products: Medical device	Home blood pressure monitors
Diabetes	
Biguanides	Metformin and alogliptin
Dipeptidyl peptidase-4 inhibitors	Alogliptin
Incretin mimetics (glucagon-like peptide-1 agonists)	Dulaglutide Liraglutide Lixisenatide
Thiazolidinediones	Pioglitazone
Insulins Long-acting insulin analogues Premixed insulin	 Insulin detemir Insulin glargine and lixisenatide Insulin combination aspart and aspart protamine
Psychiatric illnesses	
Selective serotonin and norepinephrine reuptake inhibitors	Desvenlafaxine
Serotonin modulators	Vortioxetine
Monoamine oxidase inhibitors	Moclobemide Phenelzine Tranylcypromine
Miscellaneous antidepressants	Tryptophan
First-generation (typical) antipsychotic drugs	Promethazine
Second-generation (atypical) antipsychotic drugs	Asenapine Brexpiprazole
Benzodiazepines	Alprazolam Bromazepam Chlordiazepoxide Diazepam Flurazepam Lorazepam Nitrazepam Oxazepam Potassium clorazepate (clorazepate dipotassium) Temazepam

Drug class	Name of drug or related product
	Triazolam
Miscellaneous anxiolytics, sedatives, and hypnotics	Chloral hydrate Hydroxyzine Zolpidem Zopiclone
Anticholinergic agents and N-methyl-D-aspartate (NMDA) receptor antagonist (for drug-induced extrapyramidal symptoms)	Amantadine Trihexyphenidyl

Table 7: Proposed Sample List of Drugs and Related Products to Exclude

Drug class	Name of drug or related product
Cardiovascular diseases	
Vasopressin antagonists	Tolvaptan
Angiotensin-converting enzyme inhibitors	Perindopril and amlodipine
Angiotensin II receptor antagonists	Azilsartan medoxomil Azilsartan medoxomil and chlorthalidone
Renin inhibitors	Aliskiren
Cardio-selective beta-adrenergic blocking agents	Nebivolol
Miscellaneous cardiac drugs	Ranolazine
Class III antiarrhythmic agents	Dronedarone
Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors	Inclisiran
Miscellaneous antilipemic agents	Icosapent ethyl Lomitapide Omega-3-triglycerides including other esters and acids
Antithrombotic agents, miscellaneous	Caplacizumab
Other nutritional agents	Ubidecarenone (coenzyme Q10 or ubiquinone)
Diabetes	
Biguanides	Metformin and canagliflozin
Sulfonylureas	Glimepiride
Incretin mimetics (glucagon-like peptide-1 agonists)	Exenatide
Thiazolidinediones	Rosiglitazone
Insulins Short-acting Intermediate-acting Long-acting insulin analogues	 Insulin regular (pork) Insulin isophane (NPH; pork) Insulin degludec and liraglutide
Related products: Diabetes supplies	Alcohol swabs

Drug class	Name of drug or related product
Psychiatric illnesses	
Selective serotonin and norepinephrine reuptake inhibitors	Levomilnacipran
Serotonin modulators	Vilazodone
Miscellaneous antidepressants	Esketamine
Miscellaneous anxiolytics, sedatives, and hypnotics	Eszopiclone Lemborexant
Wakefulness-promoting agents	Solriamfetol
Anticholinergic agents and N-methyl-D-aspartate (NMDA) receptor antagonist (for drug-induced extrapyramidal symptoms)	Profenamine (ethopropazine hydrochloride)

Appendix 4: Exploratory Proposal to Support List Refinement

The panel recognized that the demand for health care will be greater than the public health care system's resources (or ability to meet demand). Therefore, difficult choices will need to be made to create a pan-Canadian formulary, which could have significant implications both in terms of what access is provided and consequently what cannot be funded. The panel welcomed guidance from HEAC on how the proposed sample list might be further refined in consideration of health economic principles and from a cost-effectiveness lens to ensure that population health would be improved by each drug's listing on a potential pan-Canadian formulary. It is important to note that this simplified summary is but 1 possible model and is intended to be an illustrative example to guide future work with regards to refining the proposed sample list.

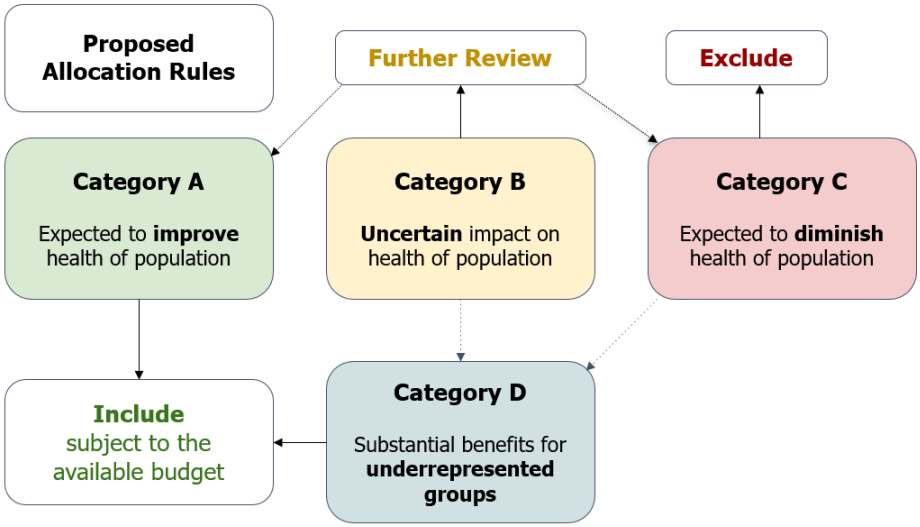
Example Adapted From Discussion With HEAC:

The following approach could be taken to refine the sample list by applying 4 key categories and criteria to determine if a product should be included or excluded, subject to the available budget. Refer to Figure 9 for an illustration of the approach.

- Category A (products that are expected to improve the health of the population): Products in this category should be included if they meet the following:
  - These products are found to be cost-effective at list prices (e.g., a prespecified dollar threshold per quality-adjusted life-year that reflects health opportunity cost). It is important to note that if an explicit threshold is set in the future, it should be aligned with HTA systems in Canada..
  - The product is not cost-effective at its list price, but would be cost-effective with a discount of less than 30%. It is recognized that discounts negotiated by the pCPA are confidential. However, the Auditor General of Ontario found that, "For 2016/17, the total rebate received is close to 30% of the total expenditures for brand-name drugs." As such, 30% is used as a starting point for discussion.
  - The product is generic and reimbursed by most public drug plans.
- Category B (products that have an uncertain impact on the health of the population): Products in this category should undergo further review to determine if they meet the following:
  - The product is not cost-effective at the list price even with a discount between 30% and 50%. This percentage is only a placeholder. The maximum amount negotiated by the pCPA is unknown, as is the maximum discount that a government could feasibly negotiate under a potential pan-Canadian formulary. This should be updated with a more accurate figure, if possible. In this case, additional review and/or negotiations may be needed for the drug to be eligible for category A; otherwise, it will fall under category C, unless it can meet category D requirements.

- Category C (products that are expected to diminish the health of the population): Products in this category should be excluded if they meet the following:
  - The product is not cost-effective at the list price, even with a discount of more than 50%. As previously noted, this percentage is only a placeholder, and should be updated with a more accurate figure, if possible.
- Category D (products that provide substantial benefits for underrepresented groups): Products in this category should be included in exceptional cases if there could be substantial benefits demonstrated for populations made vulnerable by social and/or economic policies. This category would apply to products that fall into categories B and C. Additional criteria would need to be formulated by a group of experts and broadly consulted on with interested parties.

Figure 9: Cost-Effectiveness Considerations When Refining the Proposed Sample List



Note: A solid line refers to the intended pathway, while a dotted line refers to a potential pathway.

Appendix 5: Feedback From Respondents to the Consultation Process

The panel would like to thank all respondents who took the time to submit feedback through the online questionnaire or participated in the focus group. Input from respondents is valuable in shaping this important work, and the panel has carefully considered all the comments and taken every effort to incorporate what was heard through this consultation process.

Background

The panel recognized that stakeholder engagement is a key aspect of its work, and consulted widely to ensure that a rich and comprehensive foundation of knowledge and perspectives were incorporated into its recommendations.

The main component of stakeholder engagement was an online questionnaire, made available in English and French, to solicit feedback on specific aspects of the panel's work. This online consultation was held between January 11 and February 25, 2022. The questionnaire consisted of 9 questions, 3 of which had 2 parts (i.e., split as parts a and b). It was not mandatory for submitters to respond to every question. In addition, an online information session was held for any interested parties on January 18, 2022.

A focus group was also held in late February to ensure the perspectives of populations made vulnerable by social and/or economic policies are included in developing a potential pan-Canadian formulary. The panel felt that understanding and accounting for the possible impacts of a potential pan-Canadian formulary on populations made vulnerable through a combination of social and economic policy, particularly Indigenous people and those who have experienced historic and ongoing impacts of colonization, is a critical part of its responsibility. On behalf of the panel, CADTH purposefully reached out to organizations that serve these populations for their input. The discussion that took place among representatives of the organizations that agreed to participate allowed for a shared experience and for the panel and CADTH to seek deep and meaningful input from groups that CADTH typically would not have the opportunity to engage with or that may have specific insights that would not typically be captured by CADTH's existing stakeholder network. Invitations were sent to 15 organizations that serve communities at a national level and have a mandate or program that supports health-related initiatives, such as access to medications.

Additionally, careful thought and effort were made to invite representatives from the Assembly of First Nations, Inuit Tapiriit Kanatami, and Métis National Council. The invitation remains open and CADTH is committed to engaging respectfully and humbly with First Nations, Inuit, and Métis peoples, communities, organizations, and governments — first to continue our initial efforts to listen and learn, and then to offer a role in supporting Indigenous health and wellness.

To encourage conversation on these topics and enhance transparency, comments received through the consultation have been posted on the CADTH website. Table 8 summarizes the key highlights of the feedback received through the online questionnaire and focus group. The entirety of this broad consultation informed this final report.

Respondents

CADTH received 92 responses through the online questionnaire, reflecting feedback from a wide range of perspectives (e.g., patient groups, health care professionals, individuals from clinical societies, government and related agencies, associations, pharmaceutical companies, device companies, private insurance companies, researchers, consultants, and others).

The pharmaceutical industry (n = 26) and patient groups (n = 21) represented a majority of the responses; 2 of the 21 patient group responses were on behalf of multiple organizations and represented a total 22 patient organizations. The majority of responses (n = 62) were received from respondents in Ontario, largely due to the geographical location of the headquarters for industry, patient groups, clinical societies, and professional associations. Eleven responses were received from Quebec and 9 were received from respondents in British Columbia. Fewer than 5 responses were received each from Alberta, Saskatchewan, Manitoba, Nova Scotia, and New Brunswick. No responses were received from Newfoundland and Labrador, Prince Edward Island, Yukon, Northwest Territories, and Nunavut.

The focus group welcomed representatives from 6 organizations. Diverse perspectives were heard from the following organizations that work with and advocate on behalf of people made vulnerable by social and/or economic policies:

1. Canadian Centre on Substance Use and Addiction (CCSA)
2. Canadian Mental Health Association (CMHA)
3. Canadian Network for the Health and Housing of People Experiencing Homelessness (CNH3)
4. CanAge
5. Council of Canadians with Disabilities (CCD)
6. Federation of Black Canadians (FBC).

Feedback Discussion Process

A summary of feedback was shared with the panel. The panel also had access to all 92 individual submissions. The panel members carefully reviewed all feedback received, and discussed key themes to collectively identify how the comments and suggestions could further shape their work. The panel discussed the feedback over 3 meetings. Much of the work was done before each meeting to ensure each panel member had an opportunity to review all feedback and was prepared to discuss each key theme and

topic areas. Importantly, the panel felt it was paramount that all feedback received were considered using an approach that ensures proper due diligence in ensuring the voices of all who participated were heard.

To guide their thought process, the panel members followed some overarching questions when reviewing feedback:

7. Do the comments affect their understanding of their work?
    - If so, how?
    - If not, why not?
8. What is the panel's recommendation to address the issue?

Much of the feedback involved out-of-scope topics. For these, the panel members reviewed and provided comments to guide future work for a potential pan-Canadian formulary. The panel felt that the recommendations need to remain high level at this stage rather than getting into procedural specificity and scenario analyses. These details would be part of next steps in the development of a potential pan-Canadian formulary.

All decisions made based on the feedback received have been incorporated into this final report.

Summary of Feedback Received

The following table outlines the key themes of feedback that were received through the online questionnaire and focus groups. The views expressed in Table 8 are those of the submitting organization or individual. As such, they are independent of the panel or CADTH and do not necessarily represent or reflect the view of the panel or CADTH. No endorsement by the panel or CADTH is intended or should be inferred.

Table 8: Summary of Feedback

Theme: Principles and definitions
Topic: Principles and definitions used to guide the development and maintenance of a potential pan-Canadian formulary
Respondents generally expressed agreement with the principles developed by the panel, and noted that the principles would contribute to improving and strengthening the principles under the *Canada Health Act*. However, there were inquiries to further elaborate on the goal of the framework and objectives of the proposal; for example, how following the principles of a pan-Canadian formulary could contribute to continuity of care, and address issues such as disparities, inequities, and unmet patient needs in the Canadian drug reimbursement system. Many respondents also sought clarity on how these principles will be implemented or operationalized (e.g., how the principles will be prioritized, balanced, and reconciled in the formulary decision-making process given inevitable tensions, such as between equitable access and sustainability and cost-effectiveness). Feedback was also received that the panel should consider aligning diversity characteristics presented in the principles with the grounds under the *Canadian Human Rights Act* or other recognized health system principles. There was also encouragement to align and integrate a potential pan-Canadian formulary with the wider Canadian health care system, to minimize duplication of effort by leveraging existing systems, and through a predictable, transparent process and judicious use of industry and government resources in drug reviews. There was also concern that medications are seen as a

"cost driver;" rather, there was suggestion to view them as an investment in the health care system to improve system efficiency. It was also suggested to factor in and elaborate on how "culturally appropriate access" is embedded into the principles, specifically in terms of considerations made for First Nations, Inuit, and Métis peoples' health, as well as to consider differences in needs and level of access to drugs in rural and remote communities versus urban areas. Recommendations to revise statements on applying a population health perspective were also received, as the definition of *population health* has evolved over time, and it is important to ensure that the needs of individuals are identified. Inclusive and transparent public engagement was also recommended, particularly with current and future users of the formulary, to ensure the process is patient-centred. Suggestions on how to refine the definitions of the principles, and how the principles could be applied in practice were received; for example, ensuring a clear, transparent, and accountable process. Additionally, suggestions on replacing current principles, aligning with other principles in the Canadian health system, or adding new ones were received.

Theme: Assessment criteria

Topic: Assessment criteria used to create a sample list of commonly prescribed drugs

About the proposed assessment criteria

Respondents generally agreed with the staged approach proposed by the panel. However, additional suggestions were provided to improve clarity of the process, as well as nuances involved in this complex process. Specifically, several respondents suggested that the panel revisit the proposed assessment criteria to reflect on how the principles are reflected in them, and whether any biases or gaps were inadvertently created by applying them to the sample list.

There were also recommendations to draw from other sources of information in addition to listing status to make decisions (e.g., guidelines, patient registries), as well as to establish a process for meaningful, transparent, and inclusive engagement with the patient community. Requests were also made for clarification of some terminology used, for example *best practice*, were also received.

Some respondents strongly suggested that the assessment criteria should be flexible enough to meet the needs of special populations, and at the same time ensure populations made vulnerable by social and/or economic policies are not further disadvantaged. This work could be an opportunity to ensure no additional gaps in access to drugs are created — including continuity of care when patients are moved from 1 payer to another (hospital to community, public to private plans or vice versa).

Other related issues

There were also requests to further elaborate on the panel's recommendations on over-the-counter medications, combination products, flagged products, and issues related to drug shortages. Although there was general support for prioritizing the use of biosimilars and generics, some did not agree with the substitution policies. A few alternative approaches were suggested; for example, building a separate list solely for over-the-counter medications or low utilization drugs, or following an essential medicines list model.

Theme: Related products

Topic: Definition and/or criteria to determine the eligibility of related products that could be included in a pan-Canadian formulary

Definition of a related product

In general, respondents agreed with the proposed definition of related product, and provided suggestions to further clarify this definition. Those who support the definition shared examples of the types of products that could be included, such as devices related to medically required monitoring when taking a listed drug (e.g., continuous glucose monitoring, blood

pressure monitors) and products that support drug adherence and safety (e.g., pill splitters, dosettes). It was noted that the overall value of a related product could extend beyond simply improving adherence.

Some respondents suggested to either restrict or broaden this definition. Those in support of a "restricted" definition suggested only to include related products that provide optimal use of specific medications for optimal response, and when its use is evidence based. Those who support a broader definition advised that related products should be inclusive of products and/or services that are essential for a patient to either initiate on or continue to receive a treatment and/or are required to ensure optimal treatment benefit. These could include supplies necessary for dose adjustment or safe drug administration (e.g., insulin pens with memory), diagnostic testing to determine appropriate drug choices (e.g., pharmacogenomic testing), digital health technologies or services performed by nurses and pharmacists as part of drug administration and monitoring. Some respondents also suggested inclusion of non-pharmacological products essential to manage daily life, or devices that provide symptomatic relief (e.g., continuous positive airway pressure [CPAP] machines), as well as non-drug products used to maintain health, address stigma, or avoid exacerbating the medical condition, particularly in populations that may face challenges with access to basic products (e.g., wound care supplies, moisturizers, and supplements).

There were some respondents who disagreed entirely with the current definition and advocated for broader consultation first.

Criteria to determine eligibility for assessment

There was general agreement to establish clear eligibility criteria to identify which related product could be further assessed for inclusion on a potential pan-Canadian formulary. Some specific recommendations for criteria to determine eligibility were provided, though they were varying and sometimes conflicting. Some examples of the commonly suggested criteria include "necessity" (i.e., required for effective delivery of medication); "actionability" (i.e., necessary for adjustment of pharmacotherapy, such as dosage or holding a dose); demonstrated evidence of improving outcomes; and successful management or elimination of barriers for patients. Respondents also suggested exploring provincial and territorial public drug benefit programs to identify established criteria to determine the eligibility of related products, or other existing guidelines or policy statements to inform this work. Some respondents cautioned that narrow inclusion criteria could have implications for patients and their health.

Topic: Including related products on the same list of drugs or a separate list

Inclusion on drug list

Respondents generally agreed that related products should be listed on the proposed pan-Canadian formulary (i.e., same list as drugs) or continue to be offered through another benefit program so that patients will have coverage for these items. There was support for the panel's recommendation, and agreement that having the related products on the same list will streamline processes for patients, caregivers, and health care providers and provide a simplified point of access.

Evaluation criteria

Reasons were shared for and against using the same evaluation criteria for both drugs and related products. Given that related products are integral to the optimal use of the drug, and work in tandem with a prescribed drug to achieve intended health outcomes, similar evaluation standards could ensure timeliness and alignment of therapeutic use for both drugs and related products. However, some respondents suggested modification or even a different set of criteria for related products. Some suggested that related products may not have the same level of high-quality evidence and may not go through similar regulatory rigour (efficacy and safety) as drug products. Most importantly, drugs and devices are fundamentally different in terms of their application. Further, respondents noted challenges in applying the criteria for different types of devices.

Some respondents recommended very different approaches for evaluating related products; for example, automatically including related products once a drug is included in a formulary; others suggested a similar approach but with additional evaluation of supportive evidence.

Theme: Expanding to other therapeutic areas

Topic: Proposed approach for expanding to and including other therapeutic areas

Respondents suggested that the proposed approach to the sample list is generally acceptable and a good foundation for the immediate generation of a foundational formulary process. Some suggested that expansion should be a patient-based approach. It is important to serve the medication needs of identified patient populations, particularly those underserved by existing public drug plans. Respondents noted that input from patient organizations that have better visibility of the real needs of people should be involved in the expansion to other therapeutic areas.

Determining which areas to expand to next should involve broad consultation to identify needs of patients and to understand the experiences and complexities of health service requirements of patients. Consideration of pharmacotherapeutic areas that have been shown to improve health outcomes in people made vulnerable by systemic inequities is particularly important to ensure equitable access to drugs for all people living in Canada. Some respondents noted that current advancements in drug innovation are shifting treatment paradigms toward more targeted therapies. Expanding the proposed approach to areas such as oncology and orphan diseases might be too restrictive and create challenges in implementing the complex and individualized treatment algorithms required by these patient populations. There were also suggestions against prioritizing 1 therapeutic area over others, but rather develop a full formulary before implementation. It was also proposed that the panel consider vulnerable groups or unique patient populations with uncommon diseases independently. Although several respondents supported the inclusion of products listed under specialized drug programs (e.g., cancer drug programs), others asked for details on how this process may account for the very specific eligibility criteria for targeted therapies and the unique way these oncology drugs are funded across the jurisdictions.

Some respondents suggested that expansion should be based on medical need, sustainability, patient access, and cost-saving, such as, the availability of generic and biosimilar medicines. There were also suggestions for conducting an impact analysis before expansion, in order to identify the gaps being filled and ensure that the needs of patients are being met. Overall, there was agreement that out-of-scope issues should be addressed in a thoughtful and meaningful way before proceeding with expansion.

Topic: Prioritizing remaining therapeutic areas based on national health priorities

Respondents who supported prioritizing remaining therapeutic areas based on national health priorities noted that it cannot be overly political and should be nimble. Some suggested that priorities should be based on clear health disparities that are common across Canada. Other criteria could include disease prevalence balanced with priorities such as disease severity, limited alternative options, and patient impact.

Other respondents did not support the approach to prioritize based on national health priorities. These respondents noted that priorities may, importantly and to the benefit of patients and patient care, vary by region, by sociodemographic and sociocultural factors, by ethnicity, and many other factors. Some respondents voiced concerns that the focus ought always to be on ensuring high-quality patient care and optimal health outcomes, and that it was unclear how such prioritization schemes might be implemented (e.g., proper governance structures and engagement with stakeholders). They felt that national priorities and the political landscape often reflect societal preferences and decisions. Some offered alternative approaches; for example, based on patient need, impact, and value.

Theme: Submission review initiation process
Topic: Alternative to first-in, first-out process
There was no agreement on any 1 option (of the 3) as an alternative to a first-in, first-out submission review process. In fact, several respondents felt that a first-in, first-out approach is optimal, as it was thought to be the most predictable, transparent, fair, (logistically) feasible, and logical; and as a result, would make the Canadian market more attractive for new drugs. However, other respondents noted that the first-in, first-out process lacks any prioritization, does not consider factors such as (unmet) patient needs, and does not consider the fact that not all new drugs offer substantial health outcomes. Several respondents suggested that a hybrid approach (combining option 1 and option 2, for example) could result in an equitable and efficient review process. Option 1 would align with current regulatory and health technology assessment processes, creating policy consistency, and offer predictable processes and timelines. Option 2 would help address unmet medical needs through a clear, transparent scoring system with opportunities for engagement with patients, clinicians, and other health partners, resulting in a timely, equitable, and flexible process with a level of control. Some respondents supported option 3 (albeit, as a part of combination) as it would reduce duplication of effort, allow sharing of best practices, and possibly accelerate adoption of real-world evidence into health technology assessment reviews. Some felt international collaboration as a concept is worth considering, but more information or details are needed to fully consider this; and this may be more suitable as a very long-term plan. While some respondents did not agree that any of the options were ideal, others suggested entirely different options, often referring to improving existing processes and harmonizing currently used methods rather than adding new elements. Exploring processes used by other countries was also suggested. In other cases, respondents noted that more information and context, particularly on out-of-scope areas, is needed before selecting an option. There was recommendation for further exploration and analysis of the options, focused on how it improves patients' lives, as well as its feasibility of implementation. It was mentioned that numerous factors (e.g., unmet medical needs, innovative activities, disease populations) must be considered to determine the most appropriate approach.
Topic: Criteria to identify priority products for review
Respondents suggested detailed criteria such as those relating to unmet needs or people and populations that live in underresourced communities, novelty of treatment, impact on individual and population health and quality of life, impact on health care system, disease severity, drug adherence, as well as availability of biosimilar and generics. The overarching thoughts that were relayed through the feedback are that patient involvement must remain a key consideration; criteria must be multifactorial and look beyond basic financial considerations; and there should be a process for patients, clinicians, and other health partners to recommend priority products. Some respondents strongly support that all medications proceed through the same process. Others thought that special consideration may need to be given to drugs used in oncology (e.g., priority given to curative treatments and a clear and clinically significant overall survival advantage). It was also noted that because each therapeutic field presents its own unique needs and challenges, flexibility in the weighting of these criteria would be essential to ensure the best possible health outcomes.
Theme: Adding new products and/or indications
Topic: Evaluation criteria to use when adding new products and/or indications to a potential pan-Canadian formulary
The respondents generally agreed or agreed in part with the proposed evaluation criteria and considerations for new products (and new indications). Several suggestions on ways to refine the approach and further strengthen the evaluation criteria were provided for the panel's consideration. For example, the panel was asked to ensure that the decision-making

and criteria are flexible enough to address unique and diverse patient needs, as well as treatments in certain therapeutic areas. The panel was also asked to consider how effectively the principles have or will be applied when making decisions based on these criteria, and how well they will remain patient-centred. Consistent with this, others suggested including mechanisms for meaningful and accessible engagement with patients and (disease-specific) clinical experts, with particular focus on underrepresented patient populations, and often-underresourced patient organizations. The importance of including broad perspectives were also highlighted, as was ensuring the continued inclusion of multiple views and expertise, particularly those of clinicians who have been involved in the journeys of multiple patients. Respondents noted the importance having clear accountability for processes and decisions.

Suggestions on specific aspects of the evaluation criteria were also received. For example, some recommended taking a comprehensive societal or broad system-level view as part of "value-based" (rather than "cost-based") decision-making, and viewing value using a wider societal and long-term perspective. Furthermore, there were suggestions to ensure that criteria can accommodate for future advancements in evidence generation methods and reimbursement mechanisms (e.g., outcomes-based payer models, real-world evidence development, data sharing across all stakeholder platforms to enable the collection of health outcomes), in order to ensure timely access to medical innovations. There was also encouragement to be open to different types of evidence and include other ways of knowing, such as Indigenous ways of knowing.

Respondents had mixed views on which criteria should be prioritized, indicating the potential for tension between the application of these criteria. There were several requests to clarify or revise the panel's current work (e.g., further defining clinical benefit; explaining how "societal values" will be gathered; changing "societal preferences" to "societal values;" adding impact on both physical and mental health under "value for money"). New evaluation criteria were also presented in the feedback; for example, prioritizing vulnerable populations and applying ethical considerations around disorders and life-saving therapeutics. Conversely, there was feedback expressing concern and seeking clarification on the inclusion of some criteria (e.g., feasibility of adoption or value for money), as these were perceived to potentially hinder patients' access to timely treatment.

Topic: Deliberative process used for evaluating and selecting products for a potential pan-Canadian formulary

Among the respondents who commented on this question (only half the respondents), a majority agreed that the deliberative process should include weighting of the evidence (e.g., multicriteria decision analysis [MCDA] model). Only a small number of respondents did not explicitly agree with incorporating an MCDA model into the decision-making process.

While an MCDA process could reduce the subjectivity of a qualitative decision-making process, respondents suggested how the deliberative process (which could incorporate MCDA) could be improvised. Respondents recommended flexibility in the process to account for the specific needs of different therapeutic areas. A rigid decision-making process that does not incorporate multiple perspectives and disciplines could create or exacerbate inequities. While respondents noted that clinical effectiveness and safety should be given greater weight, patient centricity and ensuring inclusion of patient perspectives (i.e., those with lived and living experiences) were also frequently recommended. Several respondents noted that the methodology and weighting should be transparent and fair to all stakeholders (e.g., by ensuring accountability for reasonableness).

Mixed views were expressed on how weights should be distributed among the proposed evaluation criteria, as well as ways to enhance the criteria (e.g., clinical benefit, equitable access, alignment of patient and societal preferences, value for money). Some noted that outcomes-based or other innovative funding agreements, and conditional access contingent on real-world evidence development could be built into the deliberative process. There were recommendations to ensure that the scoring system should be created by those experienced in decision analysis, and that the methodology and weighting should be based on robust methods, through broad consultation, and be made transparent to stakeholders. Respondents

suggested that the scoring system (MCDA) could be used as a starting point for discussion, but emphasis should be on a values-based discussion approach rather than only on quantitative scoring.

Respondents raised a need for reconciliation of the patchwork of separate federal, provincial, and territorial formularies and their respective priorities to address silos. There were also some comments on streamlining and integrating the deliberative processes with other relevant drug review processes in Canada to minimize any duplication of effort, while giving due consideration to gaps in these existing processes.

Theme: Formulary modernization

Topic: Ensuring operational sustainability with multiple processes (i.e., assessments and reassessments)

Respondents were generally in favour of a timely and ongoing formulary modernization process, while many recognized it to be resource intensive. Several respondents support a prioritization system for drug evaluation. There were comments regarding the basis to determine what to prioritize (e.g., clinical or economic benefit or uncertainty, unmet need, gaps in equitable access, availability of new evidence or availability of alternative therapy with practice-changing evidence). Respondents also recommended a transparent and collaborative approach on who's perspective would be considered in determining what should be prioritized.

Some agreed with regular pre-set cycles for review, including having it as a condition for funding in certain circumstances to support accelerated patient access to therapies that show promising benefits (i.e., outcomes-based agreements incorporating real-world evidence). Others suggested developing criteria to trigger reassessments (e.g., when there is new evidence, or a complaint is filed), and a scoring system to prioritize a drug for reassessment. Respondents highlighted the importance of leveraging current formulary modernization initiatives within Canada (e.g., CADTH's therapeutic review process, Choosing Wisely Canada), as well as any international work. Respondents noted that different processes for different categories of therapies and conditions could be established with the potential for expediting reassessment for certain drugs. Considerations for transparency of the process, and equity for the entire population was emphasized.

Conversely, some respondents did not support formulary evaluation and modernization due to the challenges associated with conducting and implementing this process. Some felt that immediate priority should be on the creation of a national formulary, and that identifying new processes for formulary maintenance should be left until after a national formulary is in place. Furthermore, some of the feedback submitted sought clarity on the panel's original recommendations; for example, what is meant by prescribing guidelines (i.e., traditional clinical practice guidelines by health professional societies, or those developed by local jurisdictions). Some respondents stated that more detail on the out-of-scope items were required before providing a response.

Theme: Additional comments

Topic: Additional comments shared by stakeholders

Respondents felt that establishing details of important areas deemed out of scope are a prerequisite to providing meaningful feedback. As such, many of the comments received were on topics beyond the scope of the panel's work. Many stakeholders felt that the issues deemed to be out of scope are the most fundamental matters of importance with respect to a potential pan-Canadian formulary. These key factors include, but are not limited to, financing and impact on existing provincial formularies. For example, many respondents inquired about how a pan-Canadian formulary will fit into an already established private and public model of drug reimbursement in Canada? How will implementation change for the betterment of patients who are not covered by existing drug reimbursement programs? What will be the terms of this reimbursement? What is the expected funding model? Many respondents felt that there should be greater clarity on the government's policy objectives,

and a more coordinated effort to communicate how the many ongoing initiatives related to pharmaceuticals and access are complementing or impacting each other.

Respondents noted that the following should be considered when designing a potential pan-Canadian formulary. Examples include: need for more effective and integrated data systems in Canada; inclusion of hospital formularies; building the system around the most vulnerable (i.e., who is not filling their prescriptions? Who is not accessing care right now? What therapeutic areas have the most patients who cannot afford their medications?); and ensuring meaningful and early engagement with all parties (e.g., government, patients, clinicians, industry, pharmacy, private insurers, employers) throughout each step of the process. Recommendations related to program implementation, such as applying a change management strategy and conducting a detailed impact analysis, were also received. Several respondents also provided suggestions on how a pan-Canadian formulary could be shaped (i.e., policy reform), or other alternatives to the current system; for example, addressing current coverage gaps; considering a mix of public and private system; or conversely, a fully public system. There were suggestions that more emphasis be placed on preventive health measures, as well as allied health and adjunct therapies. A few respondents stated that a strategy for rare diseases needs to be considered as part of the discussion on a potential pan-Canadian formulary, due to overlapping issues and challenges faced by patients with rare diseases. Conversely, some respondents recommended that drugs for oncology and rare disease be excluded from the initiative because these are specialized medicines that require tailored approaches and expert clinical reviewers to help develop appropriate reimbursement recommendations. Many respondents sought more detailed information on the drug plan and program design. Furthermore, there was agreement that the creation of a pan-Canadian formulary could provide an opportunity to strengthen collaboration among all key entities and partners to improve the drug reimbursement ecosystem in Canada. Overall, the feedback agreed on the fundamental need to improve medication access for patients, but recognized the limitations and challenges of current infrastructures, complex funding arrangements, and multitude of drug programs available across the country.

Appendix 6: Sample Essential Medicines List Summary

Introduction

The panel explored several potential approaches for creating a proposed list of commonly prescribed drugs and related products for the potential pan-Canadian formulary. One such option was based on the recommendation made in the council report, that is, "federal, provincial and territorial governments launch national pharmacare by offering universal coverage for a list of essential medicines" and that it "would cover most major conditions and representing about half of all prescriptions."[2] Several stakeholders also made similar recommendations for an "essential medicines" approach as part of the consultation on the *Discussion Paper for Engaging With Stakeholders In Building Toward a Potential Pan-Canadian Formulary*, published by CADTH in January 2022.[53]

WHO defines *essential medicines* as "those that satisfy the priority health care needs of a population." As an alternative to the proposed sample list described in the body of this report, a proposed EML version, hereafter referred to as the Sample EML, was created based on an adaptation of 4 EMLs, chosen for their methodological rigour and alignment with drugs used in the Canadian health care system. Of note, the proposed Sample EML discussed in the following is only at a preliminary stage. The list was generated from screening for potentially relevant drugs. It requires further refinement by experts and in consultation with patients, clinicians, and other health partners. These additional steps are required to ensure the methodology followed and the drugs listed align with the principles and steps that are outlined in this report. The 4 EMLs that were used to create the foundation of the Sample EML are as follows:

WHO Model List of Essential Medicines (WHO Model List), 2021: An evidence-informed guide to help develop a national EML in accordance with local priorities and treatment guidelines. The WHO Model List also includes all drugs listed in the WHO Model List of Essential Medicine for Children.[4,54,55]

- US FDA's List of Essential Medicines, 2020: A list that includes drugs to address immediate medical needs (acute care) likely to occur in a public health emergency.[56]
- CLEAN Meds, 2016: A list of drugs deemed essential and used in the Carefully seLected and Easy Accessible at No Charge Medicines (CLEAN Meds) trial that are relevant to primary care in Canada and used in treatments for both acute and chronic conditions.[57-59]
- Sweden's Wise List, 2015: This list covers 24 therapeutic areas, and recommends essential medicines for diseases that are common in primary and hospital care, as well as complimentary medicines for specialized care.[60,61] Sweden is the only country (other than the US) from the Patented Medicines Prices Review Board (PMPRB)-7 to have an EML.

Methodology

The development of the proposed Sample EML began by combining the drugs listed in at least 1 of the 4 EMLs. The initial screening process removed duplicates, drugs not available in Canada, drugs that do not have a Drug Identification Number, drugs used for non-therapeutic purposes, drugs not used in the community setting, and prophylactic vaccines. Single entity drugs or combination drugs were included in the proposed Sample EML only if they are available in Canada in the exact form listed on the EMLs (i.e., as a single entity drug or a combination drug). Any drug that is available in Canada but does not have a Drug Identification Number (i.e., not listed in the Health Canada's Drug Product Database) were removed; for example, products with a Natural Product Number, which is categorized as a licensed natural health product. Chemicals (e.g., surface disinfectants, transfusion auxiliary products), diagnostic agents, or drugs used for office-use only (i.e., not tied to a specific patient) were considered to be for non-therapeutic use and were removed form the Sample EML. Drugs not used in a community setting were also removed, including those only used in the hospital, infusions requiring specialist care and monitoring in a hospital setting, or when administration is performed as part of a surgery or procedure. Therefore, drugs on the proposed Sample EML are those administered in a community setting, inclusive of outpatient or ambulatory settings, or at home but require the supervision of a health care professional. These also include therapeutic drugs (i.e., not used for diagnostic purposes) administered in a physician's office or other community-based clinical setting, and those that are patient-specific, or dispensed to patients but administered by the physician or other health care provider.

Results

The combination of the 4 EMLs yielded a total of 1,508 drugs. A total of 969 drugs were removed based on the previously mentioned criteria. A total of 539 drugs were listed on the preliminary Sample EML that would require further deliberation. Although drugs listed in some EMLs (WHO Model List and FDA EML) are specific to certain formulations or routes of administration, the drug was added to the Sample EML regardless of formulation or route of administration; that is, as long as the molecule was listed in 1 of the 4 EMLs, it was added to the Sample EML. Table 9 presents information on the ATC classification of the drugs included in the proposed Sample EML. Of note, some drugs fall under more than 1 ATC classification. The proposed steps used in the report to generate the original sample list (e.g., gathering information on public drug plan listing status, utilization data) could be followed to assist in further deliberation to refine the proposed Sample EML.

Table 9: First Level of ATC Classification of the 539 Drugs Listed in the Sample Essential Medicines List

ATC classification	Number of drugs
A - Alimentary Tract and Metabolism	99
B - Blood and Blood Forming Organs	48
C - Cardiovascular System	78
D - Dermatologicals	61
G - Genito-Urinary System & Sex Hormones	38
H - Systemic Hormonal Preparations, Excluding Sex Hormones	18
J - General Antiinfectives, Systemic	92
L - Antineoplastics and Immunomodulating Agents	86
M - Musculo-Skeletal System	12
N - Nervous System	80
P - Antiparasitic Products, Insecticides and Repellents	12
R - Respiratory System	43
S - Sensory Organs	50
V - Various	23

ATC = Anatomical Therapeutic Chemical.

Limitations

The proposed Sample EML is at a preliminary stage. The list was generated from screening for potentially relevant drugs. Should there be a decision to explore this approach further, additional review, assessment, and refinement steps will be required. Given that the determination on which drugs should be removed based on their clinical use (community, hospital-use only, office-use only, prophylactic vaccine) was not validated by clinical experts, a review of the decision by clinical experts familiar with administration in such settings is warranted. Further assessments may include clinical safety, efficacy, cost-effectiveness of the drugs in the EML, as well as unmet patient needs. Based on this assessment, additional review of clinical effectiveness and cost-effectiveness evaluations of the listed drugs may be necessary to ensure it is relevant to the Canadian context. This Sample EML also requires further refinement by experts, after engagement with patients, clinicians, and other health partners. These additional steps are required to ensure the methodology followed and the drugs listed align with the principles and steps that are outlined in the report.

A systematic appraisal of the methodological rigour of the 4 EMLs is also needed to ensure the 4 EMLs were evidence based, transparent, and engaged patients, clinicians, and relevant health partners, and to ensure the safety, efficacy, and cost-effectiveness of the listed drugs. The methodological rigour of some of the EMLs included are recognized; for example, the WHO Model List is evidence based and a comprehensive assessment has been conducted to ensure safety, efficacy, and cost-effectiveness of the

drugs, with the assessment of evidence publicly available. This may potentially eliminate the need to conduct a thorough evaluation (and reduce duplication of effort). However, further assessment and refinement to ensure the Sample EML in its entirety is aligned with the needs of patient in Canada and the health care system is still an important required step. Future refinement of the proposed Sample EML also warrants a distinction between which formulations of each drug are listed, as not all formulations may be deemed to be an essential medicine.

Discussion

The panel considered the limitations and discussed how the principles could apply based on an analysis of advantages and disadvantages with the proposed EML.

A benefit of the proposed Sample EML is that it includes drugs from all 14 therapeutic areas as defined by ATC category. Furthermore, when considering what is marketed in Canada, the proposed Sample EML contains a comparatively smaller number of drugs. A smaller list can support appropriate use of drugs by allowing clinicians to learn more information about fewer drugs. Additionally, a smaller list will have a smaller budget and implementation could potentially be completed in a shorter time frame. Lastly, a smaller list in theory could be easier to manage, monitor, and evaluate. However, this would be offset by potential implementation challenges, depending on details of the pan-Canadian formulary plan, which are out of scope for the panel (e.g., who is covered, what is the role of the current FPT formularies upon implementation of a pan-Canadian formulary). For example, many of the provinces and territories across Canada offer broad-based drug programs that provide relatively comprehensive coverage of drugs; the finalized Sample EML is likely to remain less comprehensive than the existing formularies across Canada. Regardless of whether the potential pan-Canadian formulary will replace, overlay, or underlay existing FPT formularies, if there is a need to transition patients from a comprehensive formulary to (a less comprehensive) one created using an EML approach, there would be several challenges faced by patients, front-line care providers, and plan administrators. Implementing and managing a formulary based on an EML approach that requires transitioning patients to a plan with a smaller formulary would likely result in perpetuating or even exacerbating barriers to equity and sustainability.

There remain several other disadvantages associated with applying an EML approach to the development of a pan-Canadian formulary. While the proposed Sample EML includes drugs used in all 14 ATC categories, it may not be comprehensive enough to include all treatments used in Canada for a given condition. As an example, using the original methodology to generate the sample list, 196 drugs that belonged to the therapeutic areas of diabetes, cardiovascular diseases, and psychiatric illnesses were included; an additional 53 drugs were flagged for further review and could potentially also be included. On the other hand, only 144 out of the 539 drugs were included in the Sample EML fell under these 3 therapeutic areas and overlapped with the drugs included in the sample list created using the original methodology. Additionally, there are concerns that an EML model could limit access to innovative treatments. Furthermore, adopting this approach would result in a list with a small number of drugs within a drug class, which

could potentially limit patient choice, as well as create monopolies in the market (for the listed drugs), and increase the risk of drug supply shortages.

There are also potential disadvantages that are specific to the approach taken to develop this Sample EML. Not all of the 4 EMLs used to develop the Sample EML are fit for our purpose, and each EML has a different set of limitations. The FDA list was created to support public health emergency preparedness and response, and focuses on drugs that can be administered in acute care settings. The drugs meet the definition of a "medical countermeasure" needed to respond to future pandemics, epidemics, and chemical, biological, and radiological or nuclear threats. The FDA EML's application in chronic health conditions is not known. CLEAN Meds was created as part of a trial that looked at change in adherence levels with free and convenient access to a carefully selected list of drugs. It was created and implemented in a carefully controlled academic environment and includes a small list of only 128 drugs. This list excludes drugs prescribed outside the scope of primary care, such as cancer treatments, as well as controlled substances (e.g., opioids, sedatives, and stimulants). The WHO Model List was created for a basic health care system and is meant to be a blueprint to guide the creation of EMLs in individual countries; it generally requires adaptation to meet local priorities and guidelines before adoption.[4] Only further refinement, assessment, contextualization of the WHO Model List could potentially make it relevant to the Canadian context. The Wise List was developed for the Stockholm health care region in Sweden. The resources available to implement the EML, and the health care needs of the region may not be entirely applicable in the Canadian context. Further, not all of the 4 EMLs used to develop the Sample EML consider the economic aspects of the formulary (e.g., cost, cost-effectiveness). Such economic assessment is warranted when developing an EML (or a formulary). The list has not been validated by patients or other relevant stakeholders to ensure all drugs align with the needs of people living in Canada and the Canadian health care system.

The proposed Sample EML only contains drugs and not related products or devices. While the EMLs (except CLEAN Meds) included drugs used in acute care, the process used to develop this proposed Sample EML only included drugs used in community settings. Hence, this Sample EML is not applicable to other health care settings. The current process has not assessed the drugs in the Sample EML to ensure their therapeutic value (for example, identifying whether they are a part of standard of care, and/or whether any potential safety concerns have been raised).

Given the previously mentioned disadvantages, the panel determined that a formulary based on the Sample EML approach would not align with all of the guiding principles recommended by the panel. Table 10 outlines example advantages and disadvantages of the Sample EML approach, and links them to principles that it aligns with (advantages), or those it is incongruent with (disadvantages).

Overall, the advantages do not appear to reflect many of the principles noted in the following and the disadvantages appear to be highly incongruent with the principles of equitable; efficient and timely; and inclusive, transparent, with fair process.

Table 10: Mapping of Principles to Elements of the Sample Essential Medicines List

Content or process values	Alignment	Misalignment
Universal and integrated: **Content values** • **Coherence:** Formulary decisions should align with the broader system for both drug selection and overall health system goals. • **Integrity:** Structures, systems, and formulary decisions should align with the values of users and Canadian society at large (recognizing this will require balancing of competing values). **Process values** • **Comprehensiveness:** Drugs for all types of health care needs should be considered in the overall process. • **Harmonization:** Structures and systems should be synchronized with existing drug programs across the country.	Includes all therapeutic areas	May not be comprehensive — all treatments (part of best practice) used in Canada for a particular condition may not be included
Equitable: **Content values** • **Equal outcomes:** Structures and processes should improve equality of outcomes for the Canadian population, which will improve health equity; diversity competency and non-discriminatory lenses should be applied in system design and evaluation. • **Equitable access:** Listing criteria should include drugs that would (effectively) address health inequities in the system. **Process values** • **Data–driven approach to diversity:** Structures and processes should include the identification of health and health care access data for relevant groups to enable application of the equity criterion in accordance with good data principles and standards of ownership, control, access, and possession.	—	No definition of "essential medicines" in Canada Drugs only (i.e., no related products) Smaller list (fewer drugs within a drug class), which could potentially limit patient choice
Effective, safe, and high quality: **Content values** • **Clinical benefit:** Listed drug products should address relevant health conditions; benefits should sufficiently outweigh harms; listed products should meet unmet health needs in the intended patient population, and provide sufficient improvement to patient and caregiver quality of life. • **Effectiveness:** Considerations should include not only clinical effectiveness and cost-effectiveness,	Smaller list may be easier to implement, manage, monitor, and evaluate The evidence-based and transparent WHO Model List potentially reduces duplication in effort (e.g., drug assessment)	Does not include newer drugs or innovative treatments May not have appropriate comparative treatment in the Canadian context

Content or process values	Alignment	Misalignment
but also effectiveness in equitable access to treatment. **Process values** • **Evidence based:** The process of evaluating drugs for listing should be based on a solid and defensible understanding of acceptable evidence that includes clinical trials and real-world evidence. • **Quality improvement:** The formulary should be continuously reviewed, modernized, evaluated, and improved.		
Sustainable: **Content values** • **Feasibility:** Listing criteria should include the impact of a drug on resources for the therapy, if funded (including drug-only costs and costs of human and/or infrastructure resources for therapy administration and management of toxicities and/or side effects). • **Long-term thinking:** Structure and processes should allow for anticipating and planning for future health care challenges, from new health trends to drug treatments for emerging diseases. • **Economic implications:** Formulary decisions should consider the value for money, cost-effectiveness of drugs to maximize benefit for unit of expenditure, opportunity costs, and overall systems costs.	May have smaller budget (versus original sample list)	Potentially create monopolies in the market (for the listed drugs) Could increase the risk of drug supply shortages
Efficient and timely: **Process values** • **Streamlined:** Decision processes should be efficient and reduce duplication. • **Timeliness:** Decision processes should ensure timely drug access to meet relevant patient health goals.	—	Potential implementation barriers if there is need to transition patients from a broader existing formulary to a less comprehensive formulary Needs further assessment and refinement (including clinical and cost-effectiveness) to ensure it is relevant and aligned with the needs of patients in Canada and the Canadian health care system
Inclusive, transparent, with fair process: **Process values** • **Inclusive:** System operation and evaluation should be undertaken through the various lenses of the multiple stakeholders. • **Open to appeal:** The system should include a procedural fairness process in which stakeholders can engage to understand the rationale behind the decisions. • **Reason driven:** Deliberation about a formulary listing should be based on reasons that are	—	

Content or process values	Alignment	Misalignment
articulated in plain language. Deliberation should be open to different ways of knowing and sensitive to power dynamics that favour some perspectives over others without sufficient justification. • **Respectful:** Deliberation should create space for multiple viewpoints to be heard and engaged, with attention to implicit biases. • **Transparent**: The overall process of creating and managing a formulary should be explicit, clear, and accountable to people living in Canada.		

Conclusion

The panel determined that the pan-Canadian formulary should not be developed based on the proposed Sample EML due to the previously noted limitation and challenges with the approach.

References

1. Government of Canada. Advisory Council on the Implementation of National Pharmacare. Ottawa: Health Canada; 2019: https://www.canada.ca/en/health-canada/corporate/about-health-canada/public-engagement/external-advisory-bodies/implementation-national-pharmacare.html. Accessed 2021 Sep 29.
2. Health Canada. A Prescription for Canada: Achieving Pharmacare for All Final Report of the Advisory Council on the Implementation of National Pharmacare. 2019: https://www.canada.ca/en/health-canada/corporate/about-health-canada/public-engagement/external-advisory-bodies/implementation-national-pharmacare/final-report.html#summ. Accessed 2021 Aug 27.
3. The Conference Board of Canada. Understanding the Gap 2.0. *A Pan-Canadian Analysis of Prescription Drug Insurance Coverage*: https://www.conferenceboard.ca/focus-areas/health/understanding-the-gap. Accessed 2022 May 15.
4. World Health Organization. Selection of essential medicines at country level. Using the WHO model list of essential medicines to update a national essential medicines list. 2020: https://www.who.int/publications/i/item/9789241515443. Accessed 2022 Jun 6.
5. Law MR, Cheng L, Kolhatkar A, et al. The consequences of patient charges for prescription drugs in Canada: a cross-sectional survey. *CMAJ Open.* 2018;6(1):E63.
6. Parrish RH, 2nd. What Is a Formulary, Anyway? Part 2. *Pharmacy (Basel).* 2018;6(3):72.
7. Canadian Institutes of Health Research. Institute of Health Services and Policy Research Strategic Plan 2021-2026. 2021: https://cihr-irsc.gc.ca/e/52481.html. Accessed 2022 May 30.
8. Government of Canada. Canada Health Act. 2020: https://www.canada.ca/en/health-canada/services/health-care-system/canada-health-care-system-medicare/canada-health-act.html. Accessed 2021 Sep 29.
9. Canadian Legal Information Institute. Act respecting prescription drug insurance, CQLR c A-29.01. 2021: https://canlii.ca/t/556nq. Accessed 2022 May 29.
10. Grey matters: a practical tool for searching health-related grey literature. Ottawa (ON): CADTH; 2019: https://www.cadth.ca/grey-matters. Accessed 2021 Jun 14.
11. Canadian Pharmacists Association. A Prescription for a Healthier Canada Rx: PharmAccord. 2017: https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/PharmAccord_Final_Online.pdf. Accessed 2021 Dec 13.
12. Heart and Stroke. Attaining Universal Access to Necessary Prescription Medications in Canada: Improving outcomes in heart disease and stroke. 2019: https://www.heartandstroke.ca/-/media/pdf-files/canada/media-centre/final-en-pharmacare-policy-statement-2019.ashx?rev=f327cd0cf1694c82a9ed4e8796690260. Accessed 2021 Dec 13.
13. Morgan SG, Martin D, Gagnon MA, Mintzes B, Daw JR, Lexchin J. Pharmacare 2020: The future of drug coverage in Canada. Vancouver: Pharmaceutical Policy Research Collaboration, University of British Columbia.; 2015: https://static1.squarespace.com/static/5d4364837cb2650001cd7e1b/t/5d4dc0e3ae5c1700019ae116/1565376740550/2015-Pharmacare2020_MorganEtAl_Report.pdf. Accessed 2021 Dec 13.
14. Bond K, Stiffell R, Ollendorf DA. Principles for deliberative processes in health technology assessment. *Int J Technol Assess Health Care.* 2020;36(4):445-452.
15. Government of Canada. Canadian Human Rights Commission. 2019: https://www.canada.ca/en/human-rights-commission.html. Accessed 2022 May 2.
16. Government of Canada. What is the Population Health Approach? *What is Population Health?*2012: https://www.canada.ca/en/public-health/services/health-promotion/population-health/population-health-approach.html#What. Accessed 2022 May 18.
17. Institut national d'excellence en santé et en services sociaux (INESSS). Evaluation of Drugs for Listing Purposes - A Change of Approach. 2018: https://www.inesss.qc.ca/fileadmin/doc/INESSS/Inscription_medicaments/Processus/Evaluation_of_drugs_a_change_of_approach.pdf. Accessed 2022 Jun 6.
18. The pCODR Expert Review Committee (pERC). Ottawa: CADTH; 2021: https://www.cadth.ca/pcodr-expert-review-committee-perc. Accessed 2022 May 29.

19. Patented Medicine Prices Review Board. Alignment Among Public Formularies in Canada, Part 3: Medicines Assessed by the Common Drug Review. 2022 Feb: https://www.canada.ca/en/patented-medicine-prices-review/services/npduis/analytical-studies/formularies-part3-medicines-assessed.html#limitations. Accessed 2022 May 16.
20. IQVIA. Pharmaceutical Trends. Top 10 Therapeutic Classes in Canada, 2020. 2021: https://www.iqvia.com/-/media/iqvia/pdfs/canada/2020-trends/top10therapeuticclasses_20.pdf?_=1632771870455. Accessed 2021 Sep 29.
21. World Health Organization. Anatomical Therapeutic Chemical (ATC) Classification. 2022: https://www.who.int/tools/atc-ddd-toolkit/atc-classification. Accessed 2021 Sep 29.
22. Keeys CA, Harding BW, Migneco GE, Rahini SS, Coleman HB. New Drug Formulary Management and Utilization: Evidence in Sex, Race, and Ethnicity: 2019-2020. *Ann Pharmacother.* 2021:10600280211019765.
23. Government of Canada. Guidance for Industry - Priority Review of Drug Submissions. Section 2.0: Criteria for Qualification as a Priority Review Submission. 2008: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/priority-review/drug-submissions.html#a2. Accessed 2021 Sep 29.
24. Abelson J, Wagner F, DeJean D, et al. Public and patient involvement in health technology assessment: a framework for action. *Int J Technol Assess Health Care.* 2016;32(4):256-264.
25. Pant S. Overview of Formulary Management Practices of Publicly Funded Provincial and Territorial Drug Plans. *CADTH Health Technology Review.* Ottawa: CADTH; 2021 May: https://www.cadth.ca/sites/default/files/es/es0354-national-formulary-policy-may6.pdf. Accessed 2021 Oct 22.
26. Canadian Legal Information Institute. Act respecting the Institut national d'excellence en santé et en services sociaux, CQLR c I-13.03. 2021: https://canlii.ca/t/554fk. Accessed 2022 Jun 6.
27. Procedures for CADTH Reimbursement Reviews. Ottawa: CADTH; 2022: https://www.cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf. Accessed 2022 Jun 6.
28. Health technology expert review panel deliberative framework. Ottawa: CADTH; 2015: https://www.cadth.ca/sites/default/files/pdf/hterp/HTERP_DFW_e.pdf. Accessed 2022 Jun 6.
29. Rizzardo S, Bansback N, Dragojlovic N, et al. Evaluating Canadians' Values for Drug Coverage Decision Making. *Value Health.* 2019;22(3):362-369.
30. Institut national d'excellence en santé et en services sociaux (INESSS). Guidance Document for Submitting a Request to INESSS. 2018: https://www.inesss.qc.ca/fileadmin/doc/INESSS/Inscription_medicaments/Fiches_inscription/en/Submission_guidance_document.pdf. Accessed 2022 Jun 6.
31. Real-World Evidence: A Primer. Ottawa: CADTH; 2022: https://www.cadth.ca/real-world-evidence-primer. Accessed 2022 May 18.
32. Ahead of the Curve: Shaping Future-Ready Health Systems. *2022–2025 Strategic Plan*. Ottawa: CADTH; 2022: https://strategicplan.cadth.ca/wp-content/uploads/2022/03/cadth_2022_2025_strategic_plan.pdf. Accessed 2022 Jun 6.
33. Laba T-L, Jiwani B, Crossland R, Mitton C. Can multi-criteria decision analysis (MCDA) be implemented into real-world drug decision-making processes? A Canadian provincial experience. *Int J Technol Assess Health Care.* 2020;36(4):434-439.
34. Richardson M, Mittman N, Kaunelis D. Deliberative Appraisal Processes in Health Technology Assessment. *CADTH Health Technology Review*. Ottawa: CADTH; 2021: https://canjhealthtechnol.ca/index.php/cjht/article/view/nm0001/nm0001. Accessed 2021 Oct 22.
35. Pant S, Boucher M, Frey N. Health Technology Reassessment: An Overview of Canadian and International Processes. *Environmental Scan no.85.* . Ottawa: CADTH; 2019: https://www.cadth.ca/sites/default/files/es/es0334-health-technology-reassessment-es.pdf. Accessed 2021 Oct 22.
36. Menear M, Blanchette M-A, Demers-Payette O, Roy D. A framework for value-creating learning health systems. *Health Research Policy and Systems.* 2019;17(1):79.
37. Therapeutic Review Framework and Process. *CADTH Health Technology Review*. Ottawa: CADTH; 2020 Oct: https://www.cadth.ca/sites/default/files/pdf/CADTH_ExternalTherapeuticReviewProcess.pdf. Accessed 2021 Oct 22.

38. Ontario Drug Policy Research Network. Review Process.: https://odprn.ca/research/core-themes/drug-class-reviews/review-process/. Accessed 2021 Oct 22.

39. Tadrous M, Knowles S, Ruddock B, et al. Comprehensive Drug-Class Review Framework for improved evidence-based drug policy and formulary modernization. *Int J Technol Assess Health Care.* 2020;36(1):12-19.

40. Persson EL, Miller KS, Nieman JA, Sgourakis AP, Akkerman SR. Formulary evaluation using a class review approach: experience and results from an academic medical center. *P&T.* 2013;38(4):213-216.

41. Management Sciences for Health, World Health Organization. Drug and Therapeutics Committee Training Course. Session 2. Develping and Maintaining a Formulary. Participants' Guide. Arlington (VA): Management Sciences for Health; 2007: https://docplayer.net/20522174-Drug-and-therapeutics-committee-training-course-participant-s-guide-all-sessions.html. Accessed 2021 Oct 20.

42. The Canadian Deprescribing Network. About The Canadian Deprescribing Network. 2017; https://www.deprescribingnetwork.ca/canadian-deprescribing-network. Accessed 2022 May 19.

43. Pharmaceutical Reviews Update — Issue 8. Ottawa: CADTH; 2019: https://www.cadth.ca/cadth-pharmaceutical-reviews-update-issue-8. Accessed 2022 Jun 6.

44. Tomalin A, Siu E, Wyatt G, West K, S A. An ever-evolving landscape: an update on the rapidly changing regulation and reimbursement of biosimilars in Canada. *Generics and Biosimilars Initiative Journal (GaBI Journal).* 2019;8(3):107-118. http://gabi-journal.net/an-ever-evolving-landscape-an-update-on-the-rapidly-changing-regulation-and-reimbursement-of-biosimilars-in-canada.html. Accessed 2022 Jun 6.

45. Drug Shortages Canada. Drug shortages homepage. 2021: https://www.drugshortagescanada.ca/. Accessed 2021 Sep 29.

46. Government of Canada. Drug Shortages in Canada. 2017: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-shortages.html#a2. Accessed 2022 May 17.

47. Slobodan J. National Hospital Formulary Collaborative. *CADTH Symposium*. Edmonton: Alberta Health Services; 2017 April: https://www.cadth.ca/sites/default/files/symp-2017/presentations/april24-2017/Concurrent-Session-B4-Jeremy-Slobodan.pdf. Accessed 2021 Oct 22.

48. Government of Canada. Building a National Strategy for High-Cost Drugs for Rare Diseases: A Discussion Paper for Engaging Canadians. 2021: https://www.canada.ca/en/health-canada/programs/consultation-national-strategy-high-cost-drugs-rare-diseases-online-engagement/discussion-paper.html. Accessed 2022 May 17.

49. Briggs GG, Freeman RK, Tower CV, et al. Brigg's Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk. 12th ed: Lippincott Williams & Wilkins (LWW); 2021.

50. Silver A. Minor Ailments: Diabetes Care Devices. Ottawa: Canadian Pharmacists Association; 2018.

51. Diabetes Canada. Technology & Devices. https://www.diabetes.ca/about-diabetes/medication-management/tech---devices. Accessed 2021 Sep 10.

52. Hypertension Canada. Blood Pressure Devices. 2022; https://hypertension.ca/hypertension-and-you/managing-hypertension/measuring-blood-pressure/devices2/. Accessed 2022 Jun 6.

53. pan-Canadian Advisory Panel on a Framework for a Prescription Drug List. Building Toward a Potential Pan-Canadian Formulary: Discussion Paper for Engaging With Stakeholders. 2022 Jan: https://www.cadth.ca/sites/default/files/pdf/Pan_canadian_Formulary/CP0026-PanCdnFormulary-Discussion-Paper_FINAL_ForPosting.pdf. Accessed 2022 Jun 6.

54. World Health Organization. WHO Model List of Essential Medicines - 22nd List. 2021: https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02. Accessed 2022 Jun 6.

55. World Health Organization. WHO Model List of Essential Medicines for Children - 8th list. 2021: https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.03. Accessed 2022 Jun 6.

56. U.S. Food & Drug Administration. Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs. https://www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs. Accessed 2021 Jul 27.

57. Taglione MS, Ahmad H, Slater M, et al. Development of a preliminary essential medicines list for Canada. *CMAJ Open.* 2017;5(1):E137-E143.

58. Persaud N, Bedard M, Boozary AS, et al. Effect on Treatment Adherence of Distributing Essential Medicines at No Charge: The CLEAN Meds Randomized Clinical Trial. *JAMA Intern Med.* 2020;180(1):27-34.

59. Persaud N, Lee T, Ahmad H, et al. Protocol for a randomised controlled trial evaluating the effects of providing essential medicines at no charge: the Carefully seLected and Easily Accessible at No Charge Medicines (CLEAN Meds) trial. *BMJ Open.* 2017;7(5):e015686.

60. Eriksen J, Gustafsson LL, Ateva K, et al. High adherence to the 'Wise List' treatment recommendations in Stockholm: a 15-year retrospective review of a multifaceted approach promoting rational use of medicines. *BMJ Open.* 2017;7(4):e014345.

61. Janusinfo. The Wise List 2015 in English. 2022: https://janusinfo.se/inenglish/thewiselist2015inenglish.4.2baa5e3e161e6f22189240.html. Accessed 28 Feb 2022.