CADTH

Discussion Paper for Engaging With Stakeholders

Building Toward a Potential Pan-Canadian Formulary

January 2022

CADTH

Acknowledgements: CADTH would like to acknowledge the Canadian Institute for Health Information, Non-Insured Health Benefits, and the Patented Medicine Prices Review Board for their contribution in providing data to support this work.

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 representing those with lived and living experience, persons working with Indigenous and other communities often made vulnerable through a combination of social and economic policy, and individuals with backgrounds in ethics, health policy, and drug plan leadership.

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Abbreviations

AHFS American Hospital Formulary Service

ATC Anatomical Therapeutic Chemical

CIHI Canadian Institute for Health Information

CPG clinical practice guideline

FPT federal, provincial, and territorial

HTA health technology assessment

HTR health technology reassessment

MCDA multicriteria decision analysis

NIHB Non-Insured Health Benefits

pCPA pan-Canadian Pharmaceutical Alliance

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About the Consultation

On behalf of a multidisciplinary advisory panel (the panel), CADTH invites stakeholders to provide input on a proposed framework for a potential pan-Canadian formulary. Your input is both needed and highly valuable. Your comments will be used to inform the final report that will be submitted to Health Canada, shared with provincial and territorial governments, and made publicly available. The panel prepared this discussion paper to contribute to the dialogue around this work.

A potential pan-Canadian formulary could address issues that would support all people in Canada — regardless of age, disability, gender, geography, race, or socioeconomic status, among other characteristics — to have access to prescription drugs and select related products. The term *related products* refers to devices that assist with the delivery or administration of and/or are necessary for the optimal use of drugs (e.g., spacer devices for metered dose inhalers or diabetic test strips). This discussion paper presents a roadmap for the development of a potential pan-Canadian formulary including proposed principles, values, and criteria to guide its development. Also included is a summary of the panel's work on a process for selecting 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, which could include reassessments or therapeutic reviews) and how this work could be incorporated into existing health system processes. Questions for stakeholders are included in the relevant sections.

Please submit your responses and comments using CADTH's **online form.**

You are welcome to respond to all or some of the questions. The consultation period will close by end of business day on **February 25, 2022**. If you have any questions about this consultation, please email us at requests@cadth.ca.

Public Posting of Stakeholder Input

To encourage conversation on these topics and ensure transparency, CADTH will publish the comments received through this consultation. **By submitting your written comments to CADTH, you or the organization you represent (if you are submitting on behalf of an organization) agree to the full disclosure of this information.** CADTH will not edit or validate your feedback or any references or links you include. CADTH will also not publish your personal contact information.

You will be asked to provide CADTH with certain personal information, including your name, contact information, and affiliation, at the time of submission. Although CADTH encourages respondents to self-identify in their submission, you are not required to do so. However, if you choose to make an anonymous submission, CADTH will not be able to follow up with you on any issues you raise.

CADTH reserves the right to refuse to post feedback, in whole or in part and at its sole discretion, deemed to be unrelated to the issue under consultation; contain complaints and/or compliments about identifiable individuals; contain personal identifiers and/or other information that may identify a third party; be abusive, obscene, harassing or threatening, or otherwise inappropriate; potentially include defamatory or libelous comments; or not comply with CADTH's Terms of Use and/or Privacy Policy.

Setting the Context

A formulary typically contains a list of prescription drugs and other products that could be covered by 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.[1] The general purpose of a formulary is to ensure that the treatments that are used are safe, effective, affordable, and cost-effective (i.e., how well a drug or technology works in relation to how much it costs).

The goal of 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 Canada's diverse population. Of note, the term "related products" refers to devices that assist with the delivery or administration of and/or are necessary for the optimal use of drugs (e.g., spacer devices for metered dose inhalers or diabetic test strips). Only a select handful of products were discussed by the panel as a test case.

In developing a potential pan-Canadian formulary, the following elements should be addressed:

- 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 so it is based on the best available evidence)
- 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).

For more detail, see the report by the Advisory Council on the Implementation of National Pharmacare[2] entitled A Prescription for Canada: Achieving Pharmacare for All (the council report).[3]

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**. A time-limited, multidisciplinary advisory panel was established 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 federal, provincial, and territorial (FPT) governments; patients; clinicians; industry; and other interested parties.

The exercise of developing a potential pan-Canadian formulary is complex, and the mandate of the panel was limited. The **panel's work did not include:**

- 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
- the identification of governance structures to implement a potential pan-Canadian formulary (i.e., which organization or entity should oversee implementation of a potential pan-Canadian formulary or make funding decisions)
- a 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
- a consideration of the interplay between public and private insurance plans (i.e., coverage as first and second payor)
- other ongoing pharmaceutical initiatives (e.g., Health Canada's Drugs for Rare Diseases Strategy); although out-of-scope of the panel's mandate, it is anticipated that the recommendations in this draft report could be used to inform the discussion on a decision-making framework for drugs for rare diseases.

Background

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 noted in the literature, including the council report. For example, the council report[3] reported that:

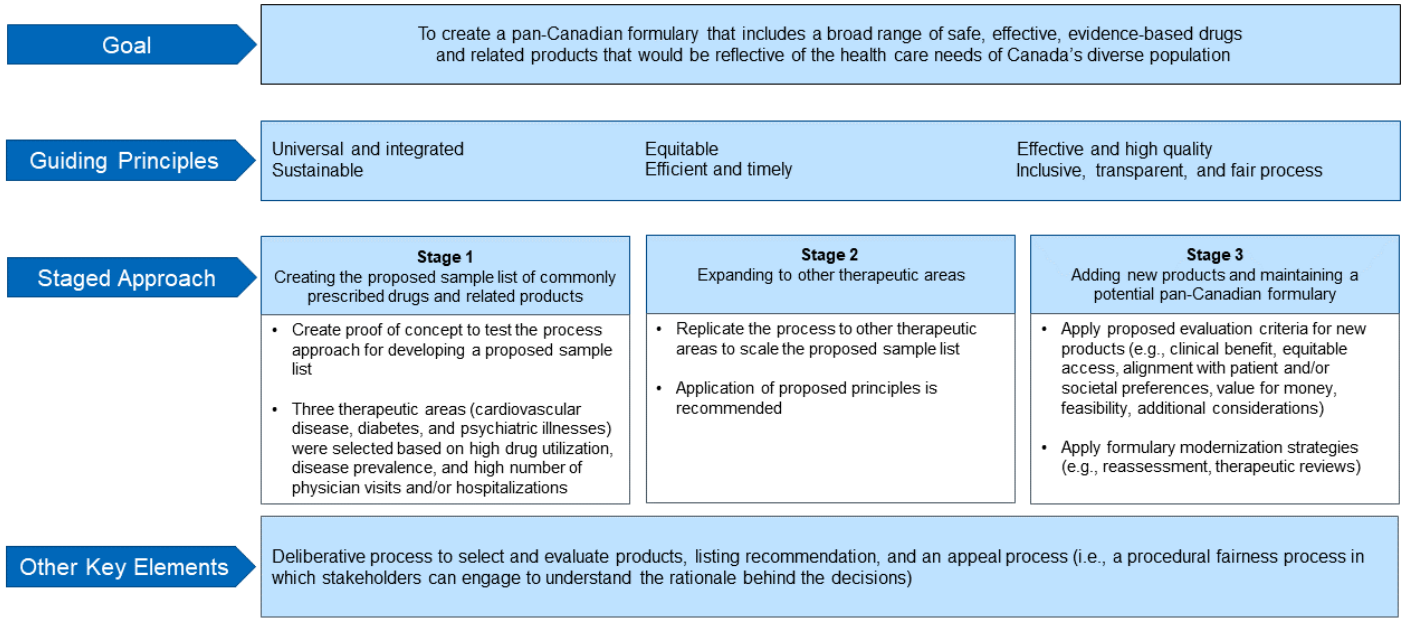
- Nearly 3 million Canadians said they were not able to afford 1 or more of their prescription drugs.
- Almost 1 million Canadians cut back on food or home heating to pay for their prescription drugs or borrowed money to pay for them.
- The nature of work is changing. More people are part-time workers, self-employed, or contract workers. Only 27% of part-time employees have health benefits. For part-time workers, employment can be precarious and may have no 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 type of work they do.

According to results from a 2016 survey, the unaffordability of drugs prevented 5.5% of Canadians from taking 1 or more medications as prescribed.[4] Of the treatments not adhered to because of cost, most were drugs for treating psychiatric health conditions. The survey report also stated 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.[4]

Overview of the Proposed Framework

Figure 1 provides an overview of the proposed framework for a potential pan-Canadian formulary the panel has developed. 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 the 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 select and evaluate products, formulary modernization strategies (i.e., an approach to align formularies with current evidence), a listing recommendation, and an appeal process. The panel acknowledged that, to enhance transparency, it is important to have clear, publicly accessible, and easy-to-understand communications about each listing recommendation as well as the reason for each recommendation. Robust policies for appeal or reconsideration of decisions are also an integral part of the framework.

Figure 1: Proposed Framework for a Potential Pan-Canadian Formulary



Developing a Framework for a Potential Pan-Canadian Formulary

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

As a starting point for meeting preparation and orientation, the panel was provided with a set of principles and definitions from the published literature. These were varied in theme and touched on areas related to disease prevalence and evidence of efficacy, safety, comparative cost-effectiveness, and health system feasibility. The principles were sourced from key Canadian documents such as the *Canada Health Act*[5] as well as a limited literature search. This information was supplemented by a focused internet search for relevant grey literature and publications on principles regarding prescription drug access in the Canadian context. Examples of the identified literature include policy statements or recommendations from Canadian professional[6] or patient advocacy associations,[7] policy research papers,[8] and published health technology assessment (HTA) deliberation principles.[9]

The panel acknowledged that the framework and process must allow for a strong focus on universal access — access for all people in Canada across geographic and cultural contexts. The panel noted that applying a population health perspective might put already disadvantaged populations further behind and not allow the needs of individual patients or communities to be adequately identified or addressed.

The panel felt that access to prescription drugs should be a priority to help address equity issues. Specifically, the panel noted concerns about situations that could risk patients having reduced access or no access to safe and effective drugs that address the needs of a particular patient population. This includes, but is not limited to, situations in which there are barriers regarding access to existing treatment and health care service plans or the broader social determinants of health.

The process of selecting drugs and related products for a potential pan-Canadian formulary would, ideally, consider not only clinical effectiveness and cost-effectiveness but also 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 significant cost to reach an IV clinic. As such, the framework should be flexible and take into account the impact on and needs of diverse patient populations (e.g., considering treatments that require less testing or that are easier to administer and use). This may require cost-effectiveness models that incorporate a broader perspective that would include health care costs and implications in remote locations, not just populated areas.

A potential pan-Canadian formulary that lists drugs available to people living in Canada could help make prescription drugs more accessible, especially to those who currently do not have access for reasons beyond their control, including both historic and contemporary inequities. This work should not widen the gap between communities and groups. The panel deemed it important to incorporate evidence that considers diverse populations, perspectives, and experiences, and to assess value in a way that captures the experiences of a wide range of populations.

Proposed Principles

The panel recommended 6 guiding principles (Table 1). The proposed principles are not ranked in order of importance nor are they independent from one another. Each influences, balances, supports, and, in some cases, builds on the others. For each principle, the panel has identified *content values* to guide decisions such as which drugs to include in a formulary and *process values* to guide how systems should function and decisions should be made. At times, the proposed principles may be in tension; for example, equity and timeliness may be in opposition with sustainability. In these cases, careful balancing will be required, accompanied by transparent justification for any trade-offs that are made.

The panel acknowledged that it has attempted to speak on behalf of Canadians. However, despite careful deliberations and diverse composition, the perspectives offered by the panel were inevitably limited. Therefore, the proposed principles require thoughtful and inclusive public engagement.

Question 1: Do you agree with the proposed principles and definitions? Please provide the reason(s) and suggested changes, if any.

Table 1: Proposed Principles and Definitions

Framing the principles	Draft principles and definitions		Values to support principles
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	Content or process values[a]
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 they need regardless of their diversity characteristics (which include, but are not limited to, socioeconomic status, age, sex, gender, genetic characteristics, disability, geography, and membership in a cultural group).	**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	**Content values** • **Equal outcomes:** Structures and processes should improve equality of outcomes for the

Framing the principles	Draft principles and definitions		Values to support principles
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	Content or process values[a]
		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.	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** • **Diversity data–driven:** 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.
What standard of effectiveness will be acceptable?	**Effective and high quality**	A potential pan-Canadian formulary should strive to provide access to Canadians 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, by incidence and prevalence; benefits should sufficiently outweigh harms; should meet unmet health needs in the intended patient population and provide sufficient improvement to patient and caregiver quality of life. **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.

Framing the principles	Draft principles and definitions		Values to support principles
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	Content or process values[a]
Who should benefit from the potential pan-Canadian formulary?	**Sustainable**	The people of Canada should benefit from a formulary management system that **maintains its own viability** and **supports long-term development and vision.**	**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. • **Value for money:** Formulary decisions should consider the cost-effectiveness of drugs to maximize benefit for unit of expenditure.
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 drug access to meet relevant patient health goals.
Whose perspectives should be considered in system design and decision-making?	**Inclusive, transparent, and fair process**	A potential pan-Canadian formulary should be developed and managed in **collaboration with stakeholders**, 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. • **Reason driven:** Deliberation about a formulary listing should be based on reasons that are articulated in language understood by all stakeholders, with openness to different ways of knowing

Framing the principles	Draft principles and definitions		Values to support principles
	Principles (important commitments the system must live up to)	Definition (in the context of a potential pan-Canadian formulary)	Content or process values[a]
			and sensitivity 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. • **Transparency**: The overall process of creating and managing a formulary should be explicit, clear, and accountable to all people in Canada.

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

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

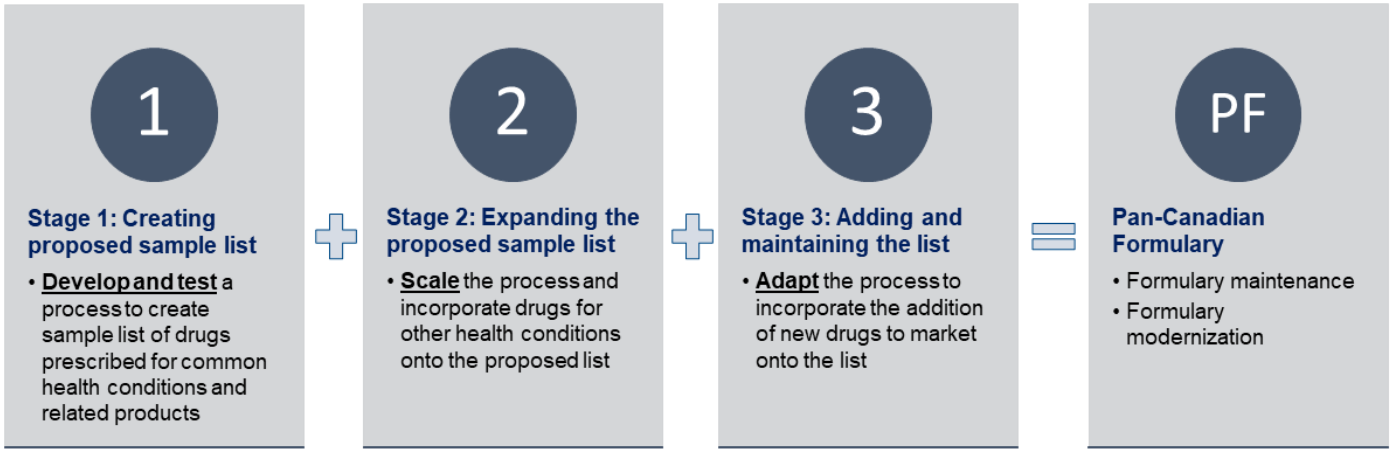
The panel explored several potential approaches for creating a proposed list of commonly prescribed drugs and related products. One approach involved a comprehensive assessment that compares products for the same indications and applies the criteria typically considered by committees that make listing recommendations (e.g., clinical benefit, equitable access, feasibility, value for money, among others) (see Table 1). Although thorough, this type of comparative assessment would require more time and more resources than were available to the panel to complete its work. Furthermore, the data needed to evaluate each drug against the criteria may not be easily available or available at all. This would be a particular challenge with the “equitable access” criterion. 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 proposed a sample list of prescription drugs and related products as a starting point. The panel acknowledged the limitations associated with creating a proposed sample list. For example, comprehensive HTA methodologies could not be followed; therefore, the panel used available information when deliberating the development of the proposed sample list.

The panel undertook a 3-stage approach (see Figure 2) in its deliberations:

- **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 system.

Figure 2: Staged Approach to the Creation of a Pan-Canadian Formulary



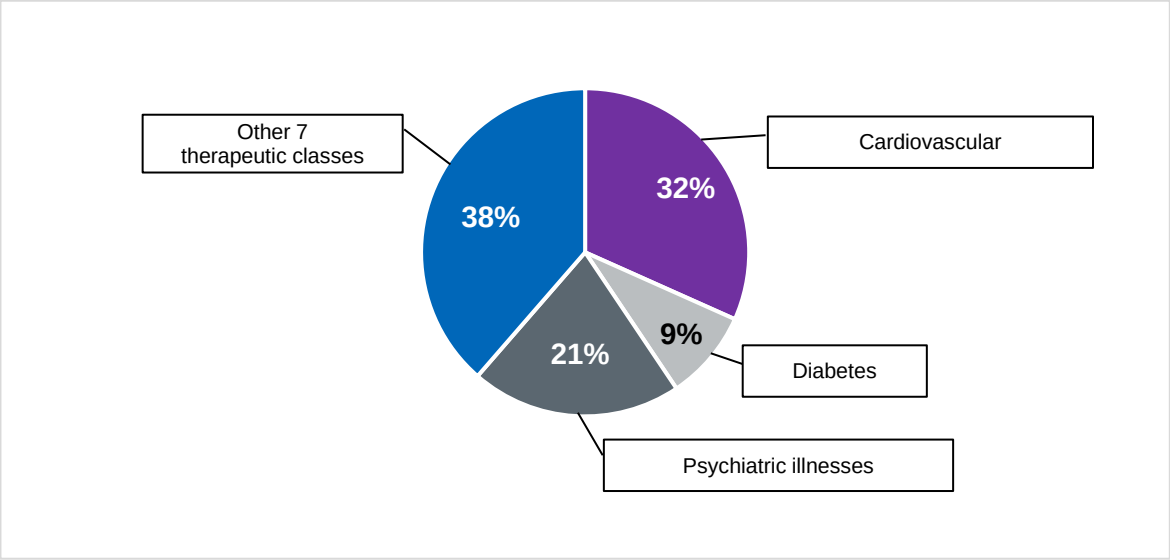
Stage 1: Approach to Creating the Proposed Sample List of Commonly Prescribed Drugs and Related Products

The Process

To develop the proposed sample list of commonly prescribed drugs and related products, the panel first identified therapeutic areas on which to focus. Consideration included those 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. 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. According to IQVIA Pharmaceutical Trends for 2020, these 3 therapeutic areas coincide with those included in the top 10 therapeutic classes of prescriptions dispensed in Canadian retail pharmacies. Specifically, prescriptions for cardiovascular drugs (including antihyperlipidemics), diabetes drugs, and psychotherapeutic drugs together represent approximately 62% of those dispensed for the top 10 therapeutic classes presented (IQVIA is a global provider of health care–related data and analytics) (see Figure 3).[10] The panel reviewed drugs and related products that fell within these therapeutic areas, and compared the listing status of each product on the existing public drug plan formularies to identify gaps in access. By applying the proposed principles to 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 for additional expert consultation, or excluded from the proposed sample list. This method was effective for prioritizing the principle of equity as well as universality and integration.

Figure 3: Prescription Usage in Canada (Based on Top 10 Therapeutic Classes in 2020)



Source: Adapted from IQVIA, Top 10 Therapeutic Classes in Canada, 2020.[10]

The 3 selected therapeutic areas include a set of drugs that are commonly or universally included in the identified FPT drug formularies because these drugs were presumed to have demonstrated sufficient clinical benefit. It was also presumed that a proportion of Canadians do not have adequate access to these drugs. If the resulting panel recommendations are followed, a starting point would be to ensure that the most commonly prescribed drugs and related products currently available to some Canadians would be made available to all people living in Canada.

A key limitation to this approach is that there might be drugs selected according to the panel's recommended principles for inclusion in the proposed sample list that are not included on some of the FPT formularies. That is, the various 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. In addition, 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. As an example, the panel noted that the use of a specific drug or related product in a subpopulation should be considered in greater detail when the sample list undergoes further review or refinement. Furthermore, steps for scaling the process and for expanding the proposed sample list (as noted in Figure 2) would also be important for developing a potential pan-Canadian formulary.

Assessment Criteria for the Proposed Sample List of Commonly Prescribed Drugs

The panel was provided with an Excel spreadsheet including 277 drugs (cardiovascular diseases = 140; diabetes = 44; psychiatric illnesses = 93) and 10 related products (e.g., blood glucose test strips), along with their listing status, related utilization data (claims and claimants by age and sex, if available), whether there is a generic or biosimilar available for

the drug molecule, the pregnancy and lactation recommendations, and references summarizing available drugs and their use in Canada (if information could be publicly sourced). The panel members received this spreadsheet before the 3 teleconference meetings dedicated to this review for review of the proposed sample list in advance. Table 2 outlines the predefined assessment criteria used by the panel to determine if a drug or related product should be included, flagged for additional expert consultation, or excluded from the proposed sample list.

When selecting drugs for the proposed sample list, the panel was mindful not to widen access gaps that already exist for other drugs from the same class. That is, the panel tried to make consistent recommendations for drugs that have a similar listing status across jurisdictions. 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/hyperactivity disorder in children or drugs used to treat substance use disorders). There were some products that the panel felt needed additional reviews before deciding whether it should be included on 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, 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). The panel emphasized the importance of continuity of care and of putting measures in place so that patients would be transitioned to another drug when appropriate, including possible exceptions for patients whose conditions are currently well-controlled with drugs that are excluded from the proposed sample list.

Question 2: Do you agree with the proposed assessment criteria? Please provide the reason(s) and suggested changes, if any.

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 all or most of the identified public drug plans (as open and/or restricted benefit) • Addresses equitable access (e.g., used by different age groups, including pediatrics) • Biosimilar or generic product available • Other available information (e.g., references)	**Include in the proposed sample list**	• Will address drug coverage gaps because drug is currently available to a subset of Canadians with limited or no restriction, this leaves some people unfairly without access: **equity, universality, and integration** • Will remove barriers or meets needs of people made vulnerable by systemic inequities (e.g., drugs for treating substance use disorder): **equity** • 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): **universality and integration** • Will remove barriers to access (e.g., availability in different formulations that would allow easier access for those in rural, remote, and Indigenous peoples communities): **equity**

Assessment criteria[a]	Panel recommendation	Reasons considered by the panel and corresponding key principles
		• Will support greater drug adherence and reduces burden of administration or provides unique advantage (e.g., route or frequency of administration): **effectiveness, efficiency, quality**
• Product is listed by 1 or more of the identified public drug plans (as open benefit and/or restricted benefit) • Requires further review or broader consultation with clinical community prior to 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: **effectiveness** • Assessment of therapeutic use or value required: **effectiveness** • Role of the drug in current practice for this therapeutic area is unknown or uncertain: **effectiveness** • Low utilization in conjunction with uncertainty of therapeutic value or availability of more tolerable or effective alternatives: **effectiveness** • Comparative assessment is recommended when it would add decision-making value: **effectiveness**
• Product is not listed on any of the identified public drug plans • 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: **effectiveness** • Product removed from market by Health Canada (at the time of the panel discussions): **effectiveness**

HTA = health technology assessment.

[a] The assessment included a review of all the following information: clinical opinion; 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 pregnant and lactating women; whether it was included on the WHO, FDA, or CleanMeds lists; and references from Rx Files.

Summary of Results for 3 Therapeutic Areas

Figure 4 represents a high-level summary of the results based on the above assessment criteria. For detailed information about each drug and related product recommendation, please refer to Appendix 2.

Figure 4: Summary Results

The panel highlighted the following key discussion points as part of the deliberation.

List Refinement

The proposed sample list of drugs should be further refined, with a particular focus on drugs that have been flagged for additional consideration. This refinement could take the form of clinical expert consultations or reviews of the safety, relative clinical and/or cost-effectiveness, particularly where there may be multiple drugs available belonging to the same class (e.g., “me-too” drugs), as appropriate. In addition, the proposed list overall would need to be reviewed periodically as part of the formulary modernization process, particularly when there is a new drug that could be included into a therapeutic class or when a drug’s listing status changes from *not listed* to *listed*.

Formulary Management Practices

Two examples to support the identification of formulary management practices were discussed by the panel. One such example was on biosimilar and generic products. If biosimilars and generics are available for a particular drug molecule, the panel felt that the least costly product could be selected and prioritized for listing. The panel supported the recommendation in the council report that encouraged both generic and biosimilar use, including generic and biosimilar substitution. Moreover, the panel considered that mechanisms such as reference-based reimbursement (e.g., limiting reimbursement to the lowest-priced drug in a category) could be used to ensure sustainability when the evidence shows that drugs within a given category treating the same condition (such as hypertension) are equally safe and effective. The panel noted that it would be helpful to include detailed assessments and discussions of formulary management best practices as part of the broader implementation plan.

Products With Restricted Listing Status

Many products have restricted listing status, and these were accepted as being covered by a public drug plan without conducting further analysis on the types of restrictions that were imposed on the product. Although, it was outside the scope of the panel, members did recognize that current mechanisms of tiered restriction may work well for some of these drugs, but the workflow for clinicians could be considerably improved and streamlined. The following are examples of drugs and related products for which the panel recommended including restrictions (e.g., clinical criteria) based on therapeutic benefit and potential cost-effectiveness for select patient groups: eplerenone, ivabradine, evolocumab, alirocumab, tadalafil, sildenafil, insulin pump, and continuous or flash glucose monitors. Recommendations for restricted listing status should be based on an assessment of the type of restrictions across jurisdictions for specific classes of drugs and related products, which the panel noted would be valuable to conduct in the future.

Combination Products

Combination products were included if each component of the combination (e.g., metformin and linagliptin) was also included on the proposed sample list. For combinations in which 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. The flagged component will need to be further assessed and may require additional review of the combination product itself.

Nonprescription Drugs

A limited number of nonprescription (i.e., over the counter) products were identified. The panel used the same process as used for prescription drugs to assess whether to include these products in the proposed sample list. The panel considered the assessment of over-the-counter products that are part of usual treatment (e.g., acetylsalicylic acid) to be an important aspect of reducing barriers to these products. 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. As such, the panel noted that restrictions (e.g., the requirement of a prescription) might be needed to ensure appropriate and judicious use.

Related Products

Question 3a: Do you have suggestion(s) on a definition and/or criteria to determine the eligibility of related products that could be included on a pan-Canadian formulary? Please provide details.

Question 3b: Should related products be listed in the same list for drugs and have the same evaluation criteria applied to them (see Table 3)? Please provide the reason(s). Note that this question pertains only to evaluation of related products; there will be an opportunity to comment on the proposed criteria for evaluation of new drugs in question 6.

Related products (devices that assist with the delivery or administration of and/or are necessary for the optimal use of drugs), primarily those for patients with diabetes, were also assessed by the panel for inclusion on the proposed sample list. The panel felt strongly that the inclusion of related products on a potential pan-Canadian formulary should be explored because this could help improve patient access and could potentially improve adherence with drug treatment. In many cases, these related products are covered through different programs within the health system, which makes accessing coverage difficult for patients. As such, a potential pan-Canadian formulary could be an opportunity to streamline the process, provide simplified point of access, and ultimately help patients access these types of products. However, the panel noted the importance of having a standard set of criteria to help determine which related products should be eligible for inclusion on the potential pan-Canadian formulary. This standardization will be particularly important when assessing new or emerging technologies that could be numerous and costly and might impact sustainability.

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. To do this, the process would need to be replicated for other therapeutic areas. The WHO Anatomic Therapeutic Chemical (ATC) Classification System identifies 14 main pharmacological groups.[11]

Question 4a: Do you support the proposed approach to expand to other therapeutic areas? Please provide the reason(s).

Question 4b: Should the remaining therapeutic areas be prioritized based on national health priorities? Please provide the reason(s).

The proposed approach would follow the review steps described previously by considering the listing status from existing FPT formularies, utilization data, availability of a generic or biosimilar for the drug molecule, information about safe use in pregnant and lactating women, and references summarizing available drugs and use in Canada. These considerations would 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, Keeys et al. (2021)[12] found that considering disparities in the representation of sex, race, and ethnicity in evidence-based formulary management and drug utilization review processes could help address inequities. If this information is available, the prevalence or proportion of underrepresented populations within the population and/or disease or condition under study, along with the known or potential significance, should also be considered.[12]

The panel recommends that the proposed principles (e.g., universal and integrated) be applied. As part of the refinement, the panel suggests that products listed under specialized programs (e.g., cancer and special drug programs) be included. This is because product listing and eligibility, among other aspects, may differ across the country and a gap could inadvertently be created. In considering which therapeutic area to expand next, the panel also suggested that therapeutic areas could be prioritized based on national health priorities.

In terms of expanding future work to other therapeutic areas, the panel proposed that a working group be formed, including members with a mix of expertise, to conduct the reviews to identify drugs 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, respiratory).

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

Selecting New Products to Be Considered on a Potential Pan-Canadian Formulary

The panel recognizes 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 selecting 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, a pharmaceutical manufacturer typically must file a complete submission in accordance with the prescribed requirements (e.g., clinical and economic information) to the regulatory body (e.g., Health Canada), HTA bodies (e.g., CADTH and/or Institut national d'excellence en santé et en services sociaux [INESSS] for Quebec), the pan-Canadian Pharmaceutical Alliance, and the FPT payor. Assessments are currently conducted using a "first-in, first-out" process based on when submissions are filed. These regulatory bodies typically use this process 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 an important for intentional, values-based resource allocation.

Question 5a: Which option could be adopted as an alternative to a first-in, first-out submission review process? Please provide the reason(s) for your choice.

Question 5b: What criteria could be used to identify priority products?

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.[13] This would allow for a predictable process for identifying products 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.

The panel encourages strong engagement and collaboration with all key stakeholders (e.g., patients, clinicians, industry, government, and HTA bodies) through all steps in the process and recommends the use of a transparent process.

Proposing Evaluation Criteria for New Products on 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[3] that the following proposed criteria be considered:

- alignment with patient and societal values

- clinical benefit
- feasibility of adoption into health systems
- 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 drug (and related products) recommendations.[14] The panel also considered 2 additional criteria — equitable access and additional considerations or long-term thinking — to enhance the deliberative process. The proposed criteria are linked with the guiding principles and provide the basis for decision-making with respect to the selection and evaluation of drugs 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.

The proposed criteria should not be considered separately. Instead, they must be deliberated together during the evaluation to ensure that safe, effective, and the most affordable treatments are considered for listing. Table 3 contains the proposed 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.

Question 6: Do you agree with the proposed evaluation criteria and the considerations for new products? Please provide the reason(s) and suggested changes, if any.

Table 3: Proposed Evaluation Criteria for New Products to Be Considered on a Potential Pan-Canadian Formulary

Proposed criteria	Considerations
Alignment with patient and societal preferences	• Benefits and reduction of burdens to persons living with the condition and their caregivers • Benefit and reduction of harms to patient health • Maximization of flexibility for access to prescription drugs that meet the principles and criteria of the formulary
Clinical benefit	• Relevant health condition and its corresponding incidence and prevalence • Efficacy and effectiveness of clinically meaningful outcomes for the drug • Unmet health needs in the intended patient population (including level of this need, i.e., the existence of other treatments for the underlying condition for the specific population targeted by the drug) • Safety • Health-related quality of life • Frequency and mode of administration
Equitable access	• Access to health care services of the intended population • Subpopulations with unique needs or who fall into gaps between existing therapies • Health determinants to ensure equitable health outcomes for the population

Proposed criteria	Considerations
	• Particular disadvantages of individuals and groups of persons who will be directly affected by the recommendation • Impact on populations' access to the opportunity for health; 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 social policy (decisions), procedures (steps required to access resources), and/or behaviour (stigma)
Feasibility of adoption into health systems	• Availability of resources for the therapy, if covered (such as drug-only costs and costs of human and/or infrastructure resources for therapy administration and management of toxicities and/or side effects) • Future health care challenges that might be created or impacted by the drug • Level of burden on the system's budget
Value for money	• Impact that adding the drug on the list will have on the health of the population and on the other components of the health system both now and in the future • Reasonableness of the cost charged and its cost-effectiveness (a measure of the net cost or efficiency of the drug and companion technology compared with other drug and non-drug alternatives) • If appropriate, costs unique to relevant subpopulations, including those outside the public health system
Additional considerations (long-term thinking)	• Explore standardizing the evidence and controlling for variability in data quality found in clinical trials and real-world evidence, which could incorporate other ways of knowing (e.g., Indigenous ways of knowing) • Novelty of the therapy • Uncertainty of long-term benefits and harms • Potential questions about ownership and consent (e.g., genetic materials) • Other competing values that deserve consideration

Deliberative Process

Question 7: Should the deliberative process include weighting of the evidence or a score for each criterion? If yes, how should weight be distributed among the proposed criteria?

The panel provided recommendations on a deliberative process for using the proposed criteria and applying them in practice. The panel proposed that evaluating and selecting products for a potential pan-Canadian formulary should involve an expert committee. The expert committee would make a recommendation or conclusion to approve a product (i.e., reimburse), to approve a product with conditions or criteria (i.e., reimburse with conditions and/or criteria), or to not approve a product (i.e., not reimburse). Of particular interest, the panel explored ways to structure the deliberative process so that evidence from multiple disciplines and perspectives could be weighted.

A provincial model using multicriteria decision analysis (MCDA), integrated within a values-based deliberative process, was presented as a case example.[15] The traditional form of MCDA involves 3 steps: defining the decision problem, selecting criteria that reflect relevant values, and constructing the performance matrix.[16] 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.[16]

The provincial model case example includes 6 criteria: clinical effectiveness, quality of life, safety, severity, unmet clinical need, and equity.[15] A formal scoring tool was developed using a 4-point rating scale.[15] An overall benefit score for a given drug is 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.[15] The provincial model case example also considers the opportunity cost of the total amount spent for the given drug, which further contributes to the assessment and value placed on the drug under review relative to other spending priorities.

The panel recognized that there is no perfect approach to 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.[16] Quantitative weighting of criteria has been found to require substantial investment and may not always have appropriate societal representation.[16] Whichever deliberative methods are used, the panel felt strongly that the process underpinning the decision-making, as well as the rationale underlying specific formulary decisions, be made transparent to all stakeholders.

Maintaining a Potential Pan-Canadian Formulary

Developing and maintaining a formulary is essential to ensure that drugs are used in a safe, appropriate, and cost-effective manner. Once a product is evaluated or re-evaluated, it can be listed on a formulary. Products that are already listed can be removed or any associated criteria with a product can be modified. In addition, standard formulary management processes often include periodic or even regular updates, which the panel felt would be an appropriate expectation for a potential pan-Canadian formulary. This would ensure the formulary is sustainable (1 of the outlined key principles) as well as evidence-based, effective, and of high quality.

Formulary modernization is a way to align formularies with current evidence. This can include reassessments, therapeutic reviews, and assessments of prescribing guidelines. The panel encourages strong and transparent engagement and collaboration with all key stakeholders (e.g., patients, clinicians, industry, government, and HTA bodies) through all such processes.

Current Canadian drug review processes generally focus on the assessment of new products. There is a desire to ramp up formulary modernization strategies (e.g., reassessments, therapeutic reviews) and to re-evaluate existing listed products with emerging new evidence on a regular cycle (e.g., every 3 years to 5 years). This would likely increase the workload of stakeholders throughout the health system (e.g., clinicians, patients and patient groups, researchers, industry, regulators, and plan administrators).

Question 8: What measures could be put in place to ensure operational sustainability, with limited resources and time, including the ability of

stakeholders to participate meaningfully in multiple processes (e.g., should there be a prioritization system for listed products to be re-evaluated or other criteria to determine eligibility for reassessment or therapeutic reviews)?

Reassessment

Health technology reassessment (HTR) is defined in *Health Technology Reassessment: An Overview of Canadian and International Processes* 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."[17] The goal of HTR is to re-evaluate listed products to ensure resources are properly allocated — that is, moving resources away from low-value care to higher-value care.

HTR is an ongoing process to inform the optimal use of a health technology throughout its life cycle. HTR can result in recommendations for decreasing, increasing, or maintaining current levels of use and, in rare cases, recommendations for discontinuing the use of a technology (obsolescence). HTR can include clinical evaluation (systematic reviews), economic evaluation (cost-effectiveness, cost-utility, and cost consequence analyses), current utilization analysis, current practice analysis, identification of practice and knowledge gaps, and identification of barriers to optimal use.

Given how evidence continues to evolve with new research, the process of drug (and related product) reimbursement should be iterative, responsive, evidence-driven, and patient-centred. HTR is a life-cycle approach to the use of drugs that ensures system efficiency by supporting alignment with current evidence and reallocating resources to higher-value care, which ensures optimal patient care and improves patient outcomes.

The panel acknowledged that HTR should be a holistic process. In conducting an HTR, diverse perspectives of current users must be considered, while applying the principles and methods of HTA. Active engagement with patients, providers, and formulary administrators is considered key to ensuring that the most appropriate technologies are identified for HTR.

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.[18] One goal of therapeutic reviews can be to provide policy recommendations for modernizing the formulary.[19] 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.[18,20,21] Drugs are reviewed in a systematic manner for relative efficacy and safety, as well as use, cost, cost-effectiveness, and uniqueness.[21,22] Inclusion of direct and/or indirect costs should also be considered, as should patient preferences and input from clinical experts.[18] 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 1 year.[18-21]

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 an evidence-based therapeutic review could ensure the safe, appropriate, and cost-effective use of the drugs included in the list. If there are a number of drugs with the same indication, a therapeutic review could also help shorten the list, if required, by informing which drugs could be removed. 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.

Appendix 3 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, 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.

Prescribing Guidelines

Unbiased, up-to-date, and evidence-based clinical practice guidelines (CPGs) are essential for appropriate prescribing. Authors of CPGs must be transparent about any conflicts of interest and be representative of the diverse population demographics of Canada. The panel recognized that prescribing decisions should be made by a patient and their health care provider, and that the formulary is not meant to be a mechanism for implementing CPGs. However, alignment between the formulary and CPGs can have a positive impact on patient care and can support appropriate clinical decision-making. Therefore, a potential pan-Canadian formulary should consider CPG recommendations. The panel encourages the clinician community to consider the formulary in developing prescribing guidelines. Therefore, the ongoing work to implement a potential pan-Canadian formulary must establish appropriate channels of regular communication with the clinician community.

Part 3: Exploring Opportunities to Leverage and Enhance Existing Processes

While reflecting on the “universal and integrated” principle, the panel concluded that it is important to ensure that a potential pan-Canadian formulary would work with existing structures and systems. The panel felt that leveraging existing systems would reduce duplication of processes as well as provide opportunities to enhance existing processes as described below.

Reducing the Duplication of Processes

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. These processes are often guided by committees. CADTH has expert review committees[23] that could support the evaluation of a new drug or device for a potential pan-Canadian formulary. These experts are appointed and have expertise in different medical specialties, drug therapy, drug evaluation, and drug utilization. They also include patient, caregiver, and public members (for a lay perspective). The panel emphasized that there may be

opportunities for these expert committees to adapt the proposed criteria and considerations set out in Table 3 to enhance its current deliberative processes. Deliberation would involve bringing together individuals with multiple perspectives, experiences, and values to critically examine evidence around a health technology, apply the proposed criteria and tools to support decision-making, share reasons and rationales, and reach a decision on a course of action.

Improving Continuity of Care

There could be an opportunity to improve continuity of care for patients transitioning from hospital to the community or vice versa. This transition often creates gaps in patient access to therapies or inadvertently creates scenarios in which drug wastage can occur. There are ongoing efforts to collaborate and share resources with health authorities and/or hospitals within a province, as well as to re-evaluate the committee guiding the processes and/or the processes themselves. As an example, a National Hospital Formulary Collaborative,[24] 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 set up to explore opportunities for collaboration and share information on best practices.

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 recommendations and reasons for HTA recommendations that are currently published are important for ensuring transparency. However, the panel felt that transparency efforts could be improved by fostering and maintaining dialogues between those affected by the recommendation and those making the recommendation. This dialogue could be enhanced by producing clear, publicly accessible, easy-to-understand communications. A robust appeal process could be implemented to ensure procedural fairness by providing individuals with an opportunity to appeal, particularly if there is potential for stakeholders to perceive that a conclusion was reached in error.

Next Steps

Key Questions for Stakeholder Input

1. Do you agree with the proposed principles and definitions? Please provide the reason(s) and suggested changes, if any.

2. Do you agree with the proposed assessment criteria? Please provide the reason(s) and suggested changes, if any.

3. a) Do you have suggestion(s) on a definition and/or criteria to determine the eligibility of related products that could be included on a pan-Canadian formulary? Please provide details.

   b) Should related products be listed in the same list for drugs and have the same evaluation criteria applied to them (see Table 3)? Please provide the reason(s).

4. a) Do you support the proposed approach to expand to other therapeutic areas? Please provide the reason(s).

b) Should the remaining therapeutic areas be prioritized based on national health priorities? Please provide the reason(s).

5. a) Which option could be adopted as an alternative to a first-in, first-out submission review process? Please provide the reason(s) for your choice.

   b) What criteria could be used to identify priority products?

6. Do you agree with the proposed evaluation criteria and the considerations for new products? Please provide the reason(s) and suggested changes, if any.

7. Should the deliberative process include weighting of the evidence or a score for each criterion? If yes, how should weight be distributed among the proposed criteria?

8. What measures could be put in place to ensure operational sustainability, with limited resources and time, including the ability of stakeholders to participate meaningfully in multiple processes (e.g., should there be a prioritization system for listed products to be re-evaluated or other criteria to determine eligibility for reassessment or therapeutic reviews)?

Please submit your responses and comments using CADTH's **online form** by end of business day on **February 25, 2022**.

After the end of the consultation period, the responses submitted by stakeholders will be presented to the panel for deliberation. A second stakeholder session will be organized in spring 2022 to share the comments that will help refine the report and the key changes that will be incorporated. After this, a final report will be submitted to Health Canada, shared with provincial and territorial governments, and made publicly available.

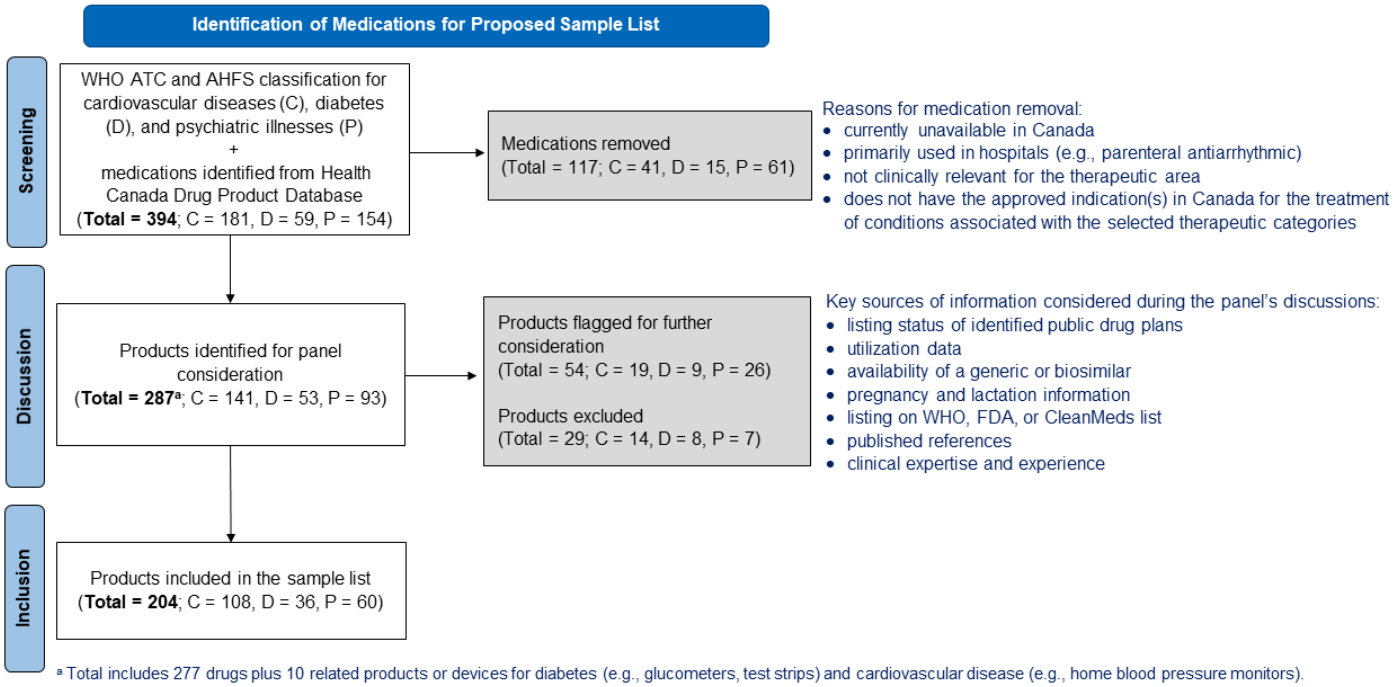
Appendix 1: Methodology, Assumptions, and Limitations

Methodology

Drug Products

- The WHO ATC classification system and the American Hospital Formulary Service (AHFS) classification system were used to identify drugs for the 3 therapeutic areas (see Figure 5). This was done to capture drugs that fall under the therapeutic classes identified in the IQVIA Pharmaceutical Trends for 2020.[10]
- Each drug was searched on the Health Canada Drug Product Database to identify if the drug is currently available in Canada. If the status of the drug was "marketed," it was included in 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 are primarily used in hospitals were removed as part of the screening (e.g., parenteral antiarrhythmic was removed from the list).
- Formulary listing status was recorded 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.)
- Information on whether a generic or biosimilar exists for each drug molecule was recorded.
- Safety in pregnancy and lactation was identified from *Brigg's Drugs in Pregnancy and Lactation* (12th edition).[25]
- Utilization data (both claimant and claim) from 3 main sources (IQVIA, CIHI, and NIHB) were included and, when possible, broken down by age group and sex. Note there was no single source for utilization data.
- Inclusion on an essential medicines list (WHO, FDA, or CleanMeds) was noted.

Figure 5: 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 include device components that function solely as the delivery vehicle and/or are necessary for the management of the drug component

- A number of sources of information were used to identify related products, including Canadian Pharmacists Association *Minor Ailments* (Diabetes Care Devices), Diabetes Canada, and Hypertension Canada.
- When available, listing status and utilization data were recorded for each provincial and territorial public plan (including Yukon and NIHB).
- For utilization data on related products for diabetes, ATC classification as per the methodology developed by CIHI was used if available.

Assumptions

- 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 would continue to remain available through those plans. The funding options (e.g., payor of last resort) need broader discussion and consultation; however, this is out-of-scope of the panel's work.
- 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 serious and growing problem 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."[26]
- 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, they could not follow comprehensive HTA methodologies and, therefore, used available information when deliberating the development of the proposed list. It was not the mandate of the panel to conduct HTRs or class reviews for the purpose of this work. Future refinements of the proposed sample list should include a review of clinical effectiveness and cost-effectiveness evaluations.
- 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 health plan. As a result, drug cost was not factored into the assessment of the proposed sample list. 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 based on the molecule, and identified irrespective of formulation (e.g., oral liquid, sustained release, rapid dissolve). 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 PEI), 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, following less expensive therapies, or with 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 proposed principles, criteria, and process approach will be presented for consultation with interested stakeholders for further refinement.

Limitations

- The 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 under the appropriate categories.
- Drugs that do not have the approved indication or indications in Canada for the treatment of conditions associated with the selected therapeutic areas were excluded; they will likely be captured when other therapeutic areas are reviewed in the future (e.g., levodopa and decarboxylase inhibitor for Parkinson disease would be excluded in this list but would be considered in the future when the therapeutic area for neurologic conditions is 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.
- Listing status was searched using 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. Public drug plans may also have separate programs for well-defined groups of patients (e.g., special drug programs, compassionate access, assistive devices programs).
- The information search on listing status is a point in time (as of August 25, 2021) and does not include any drugs or related products that may subsequently be listed on the formularies after that date.
- 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 in Canada except Prince Edward Island. In addition, the dataset does not include territory 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 that information has been suppressed (i.e., not disclosed due to low numbers which 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., seniors and low-income families or individuals are the only populations covered in all public drug plans), there are limited data on claims made by non-seniors. As a result, it is not a population-based system that captures all Canadians.
- Related products (e.g., diabetic supplies) have an assigned ATC code based on the methodology developed by CIHI. Data on utilization of non-drug products for diabetes in New Brunswick was not included in the CIHI data.
- In accordance with CIHI and NIHB privacy policies, if the number of beneficiaries was less than 5 (but greater than zero), 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 trend 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.
- 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: 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 4, Table 5, and Table 6, respectively.

For decisions (e.g., exclusions) made based on formulary listing status, the information search reflects a point in time and does not include any drugs or related products that may subsequently be listed on the identified public drug plan formularies after that date (i.e., August 25, 2021). As such, the proposed list would need to be reviewed periodically as part of the formulary modernization process, particularly when there is a new drug that could be included into a therapeutic class or when a drug's listing status changes from "not listed" to "listed."

Table 4: 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 Lisinopril and hydrochlorothiazide Perindopril and indapamide Quinapril and hydrochlorothiazide Ramipril and hydrochlorothiazide
Angiotensin II receptor antagonists	Candesartan Eprosartan Irbesartan Losartan Olmesartan medoxomil

Drug class	Name of drug or related product
	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
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

Drug class	Name of drug or related product
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/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 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

Drug class	Name of drug or related product
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 NPH (human) Insulin degludec Insulin glargine Insulin (human) combination regular and NPH Insulin combination lispro/lispro protamine
Antihypoglycemic (glycogenolytic) agent	Glucagon
Related products: Diabetes supplies	Blood glucose meter Blood glucose test strips Blood-letting lancet Continuous/flash glucose monitor Insulin pen needles Insulin pump Insulin syringes Urine test 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

Drug class	Name of drug or related product
	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 Lithium Valproic acid (including divalproex)
Barbiturates	Phenobarbital
Miscellaneous anxiolytics, sedatives, and hypnotics	Buspirone Diphenhydramine
Wakefulness-promoting agents	Modafinil
Anticholinergic agents and 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 5: Proposed Sample List of Drugs and Related Products to Flag for Future Review

Drug class	Drug name
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
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/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

Drug class	Drug name
	Brexpiprazole
Benzodiazepines	Alprazolam Bromazepam Chlordiazepoxide Diazepam Flurazepam Lorazepam Nitrazepam Oxazepam Potassium clorazepate (clorazepate dipotassium) Temazepam Triazolam
Miscellaneous anxiolytics, sedatives, and hypnotics	Chloral hydrate Hydroxyzine Zolpidem Zopiclone
Anticholinergic agents and NMDA receptor antagonist (for drug-induced extrapyramidal symptoms)	Amantadine Trihexyphenidyl

Table 6: Proposed Sample List of Drugs and Related Products to Exclude

Drug class	Drug name
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 / ubiquinone)
Diabetes	
Biguanides	Metformin and canagliflozin
Sulfonylureas	Glimepiride
Incretin mimetics (glucagon-like peptide-1 agonists)	Exenatide
Thiazolidinediones	Rosiglitazone

Drug class	Drug name
Insulins Short-acting Intermediate-acting Long-acting insulin analogues	 Insulin regular (PORK) Insulin NPH (PORK) Insulin degludec and liraglutide
Related products: Diabetes supplies	Alcohol swabs
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 NMDA receptor antagonist (for drug-induced extrapyramidal symptoms)	Profenamine (ethopropazine hydrochloride)

Appendix 3: Examples of Specific Drug Classes That May Benefit From Therapeutic Reviews

Table 7: 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
	Selective serotonin-reuptake inhibitors
	First-generation (typical) antipsychotic drugs

[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 equity and sustainability.

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