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A Tool or a Rule? The Use of HTA in Drug Pricing in Canada

Policy Roundtable Highlights

March 2019

Contents

Acknowledgements

This report was prepared by the following Conference Board staff: Cameron MacLaine, Isabelle Gagnon-Arpin, Chantal Edwards, and Monika Slovinec D'Angelo.

The authors thank William (Bill) Dempster for his external review. The authors also thank Fred Horne and Tanya Potashnik for their guidance and input.

This research was funded by AbbVie Corporation and Novo Nordisk Canada Inc.

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Introduction

Health Canada is currently pursuing regulatory reform to the Patented Medicine Prices Review Board (PMPRB), the agency responsible for regulating patented drug pricing.[1] The proposed changes are designed to help modernize the PMPRB and assist it in delivering on its mandate.[2] Two of these changes include (1) the inclusion of pharmacoeconomic value as a new and additional factor to assess whether a drug's price is excessive;[3] and (2) revisions to the list used by the PMPRB to determine whether drug prices are excessive.[4] In response to these and other proposed changes, public and private stakeholders and patient organizations are assessing how the changes will improve the access and affordability of medicines in Canada.

The impacts of implementing HTA factors in pricing regulations remain uncertain. While public health systems across the world use HTA tools to assess drug prices and to make reimbursement decisions, Canada would be the first country to use HTA to set statutory price ceilings. Doing so would provide the PMPRB with an additional tool to protect Canadians against excessive patented drug pricing. It would also allow the PMPRB to compare the price of a drug with a unit of measurement common to all drugs, regardless of their therapeutic class. However, several health sector stakeholders are concerned that the broad and strict use of HTA to develop statutory price ceilings could decrease patient access to medications if they lead to price reductions that reduce incentives for investments in innovative treatments in Canada.

On October 30, 2018, The Conference Board of Canada, in partnership with AbbVie Corporation and Novo Nordisk Canada Inc., convened a policy roundtable of health care stakeholders to learn about and discuss the role of HTA in pharmaceutical pricing. The roundtable included government departments, regulators, industry, and patient groups. Specifically, the objectives of the roundtable were to:

- engage in a collaborative, balanced, and multi-stakeholder discussion on the implications of using HTA in regulating pharmaceutical pricing;
- discuss the most effective policy options for the future.

The half-day roundtable, hosted in Ottawa, featured two keynote presentations followed by an expert panel discussion and a facilitated question and answer session. This briefing:

- outlines several key themes that arose during the day's discussions, including perspectives on the challenges and opportunities associated with drug pricing reform;
- summarizes the key points from the two keynote presentations;
- provides a set of four lessons learned.

The roundtable was chaired by Fred Horne, a Canadian health policy consultant and former Alberta Minister of Health.

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[1] Government of Canada, *Regulations Amending the Patented Medicines Regulations*.

[2] The PMPRB's mandate is to "ensure that prices charged by patentees for patented medicines sold in Canada are not excessive," and "report on pharmaceutical trends of all medicines and on R&D spending by pharmaceutical patentees." See Patented Medicine Prices Review Board, *Mandate and Jurisdiction*.

[3] The new factors to be introduced are pharmacoeconomic value, market size, GDP, and GDP per capita. See Government of Canada, *Regulations Amending the Patented Medicines Regulations*. The HTA tool will be used to help determine a drug's pharmacoeconomic value.

[4] See Government of Canada, *Regulations Amending the Patented Medicines Regulations*.

Key Discussion Themes

This section presents some key themes that arose from a panel discussion on the challenges and opportunities associated with the proposed changes to pharmaceutical pricing policy.

Potential Impacts of HTA

The use of HTA in pricing decisions could lead to several unintended consequences. For instance, the immediate use of HTA could create high uncertainty and unpredictability surrounding drug prices—both in terms of process and if evidence of patient outcomes is not available until several years into the future. There is also concern that the use of HTA could prolong reimbursement decisions and that mandatory rebates through the Maximum Rebated Price mechanism would make drug prices unsustainable. This could discourage pharmaceutical companies from launching drugs in Canada. And, in turn, this could limit the number of innovative treatments available in Canada. Using HTA to set prices below those of international comparator countries could also reduce rebates that can be negotiated with the pan-Canadian Pharmaceutical Alliance (pCPA) and reduce cost savings for public payers.

In addition, the introduction of HTA, combined with other changes to the PMPRB's decision-making process, will provide the PMPRB with significant administrative power. This would contrast with its current role as an advisory agency and could negatively impact its relationship with the private sector if the private sector's negotiating power is reduced. Concerns have also been expressed about the real or perceived conflicts of interest that may arise as the result of PMPRB's involvement in regulation and policy roles.

The Patient Experience

One concern shared by roundtable participants was the need to protect patients' access to innovative treatments. Some participants indicated that new pricing regulations by the PMPRB could reduce patient access to medicines if manufacturers chose not to seek approval for new drugs in Canada or not to reduce their investments in research and development. This contrasts with the PMPRB's belief that the removal of outliers, such as the United States, from the basket of comparator countries would lower drug prices and improve patient access to new and innovative drugs in the long run. Some participants added that discussions on drug pricing should focus on the number of lives saved and improved, instead of on price ceilings and rebate maximums. To alleviate some of the uncertainty around how the use of HTA will affect patients, it was strongly recommended that the PMPRB seriously consider patients' feedback and interests in its pricing decisions.

Understanding the PMPRB's Decision-Making Process

Roundtable participants expressed the need to better understand the specific methodology that will be used in the application of the new factors proposed by the PMPRB pricing decisions. They suggested that the PMPRB's intention to adjust price ceilings based on the new factors could be important in larger markets. These markets are where public payers with limited resources may have difficulty affording drugs that would otherwise be considered cost-effective.

The PMPRB is currently consulting with sector stakeholders on how these adjustments will be made.

Participants also asked for more clarity on how changes to cost-effectiveness thresholds are linked to value. The proposed changes to the PMPRB guidelines have increased the threshold from $30,000 per QALY (Quality of Adjusted Life Year) to $60,000 per QALY.[5] Other participants acknowledged that while a precise threshold cannot be established for all drugs, further consideration of pharmaceutical cost and value is needed.

Improving Collaboration and Consistency

Roundtable participants acknowledged the need for improved collaboration between organizations involved in setting pharmaceutical prices. For example, it was suggested that collaboration and deliberation between stakeholders (such as CADTH as well as patient groups) in the development of the PMPRB's guidelines could lead to better long-term outcomes for all of those affected by pharmaceutical pricing.

Keynote Presentations

This section summarizes the content of presentations from the day's two keynote speakers. Michael Drummond spoke about how organizations in the U.K. use HTA tools to make pricing and reimbursement decisions. In her presentation, Tanya Potashnik spoke about how the PMPRB's new framework and guidelines will help Canada respond to changes in the pharmaceutical market.

A U.K. Perspective on HTA in Drug Pricing: Implications on Access and Implementation

Presenter: Michael Drummond, Professor, University of York, United Kingdom

Quality Adjusted Life Year (QALY)

In health economics, evaluations of health and health care services are based on principles of opportunity cost and trade-offs. In Canada, where resource scarcity and system uncertainty underscore the need to develop efficient policy, Health Canada is determining whether to allow the PMPRB to use these principles in its decision-making. This echoes the approach taken in the U.K., where the National Institute for Health and Health Care Excellence (NICE) and the Scottish Medicines Consortium (SMC) base reimbursement decisions, in part, on the incremental cost per QALY gained. The QALY metric uses a sliding scale in which a patient's quality of life begins at 1.0 (representing perfect health) and decreases for each condition associated with worsened health. Death is ascribed a value of 0. For public reimbursement planning and administration, QALYs have historically offered a reliable and accurate process for reviews of patented drugs.

[5] For an explanation of the QALY metric, see the summary of the keynote presentation titled, "A U.K. Perspective on HTA in Drug Pricing: Implications on Access and Implementation."

There are, however, some challenges associated with QALYs. First, QALYs are calculated using interval scales, and each assessment of an individual's quality of health is ascribed the same value. For example, an increase from 0.3 to 0.4 receives the same value as an increase from 0.8 to 0.9. This is problematic because it gives equal weight to the conditions of seriously ill and very healthy patients. Second, QALYs assume constant proportionality. This means that an individual's valuation of a health state is unaffected by the length of time spent in that state. Thus, spending eight years or eight days in a certain health condition has the same impact on a patient's QALY assessment. Third, QALYs measure health gained from treatment, but not from other issues—such as further factors in the care pathway, convenience, consideration of serious conditions, or incremental innovation—that add important value to health care service delivery.

Incremental Cost Per QALY

QALYs are often combined with medical costs to calculate the cost per QALY, and to assess the cost-effectiveness of a medical intervention. A resulting indicator—the incremental cost-effectiveness ratio (ICER)—is used to summarize the cost-effectiveness of a health care intervention. Once the cost per QALY has been calculated, decision-makers must establish a threshold to determine the maximum amount of funding (per QALY) that a government is willing to pay. This is especially important in public reimbursement settings because government funding is often fixed.

Three common methods are used to establish thresholds:

1. Examining the value displaced (opportunity cost) from introducing a new drug.
2. Determining societal willingness to pay for a QALY.
3. Creating an objective benchmark for the level of spending relative to gross domestic product per capita.

The first approach is the most common, because decision-makers are often unable to determine a threshold independent of public budgets. Indeed, this approach considers the opportunity costs to overall public spending, in which health spending is one of several competing priorities.[6] In the U.K., the National Institute for Health and Care Excellence (NICE) has used a threshold of £20,000 to £30,000 per QALY to determine the cost-effectiveness of a drug therapy. Research on previous decisions for approval of drug therapies by NICE have found that the likelihood of a drug therapy being recommended decreases once the therapy exceeds £20,000 per QALY. However, NICE's thresholds can also vary, depending on the technology under consideration.

Use of Cost Per QALY for Decision-Making in the U.K.

The decision to recommend a drug depends on the indication and patient subgroups. While cost per QALY assessments are used to guide decision-making around new pharmaceuticals, they are applied in a flexible manner (as "a tool not a rule"). This flexibility is important when considering the level of error inherent in estimating specific health indications. Because indicators are calculated differently depending on the methodology used, QALY assessments are best understood as precise estimates within some margin of error.

The following are examples of how NICE uses flexible decision-making for cost per QALYs.

[6] Cameron, Ubels, and Norström, "On What Basis Are Medical Cost-Effectiveness Thresholds Set?"

Patient Access Schemes: In some instances, NICE receives a submission for a drug with an independent cost-effectiveness ratio that is higher than the threshold determined by NICE. In these cases, NICE will encourage the company to enter a patient access scheme. (In Canada, this is referred to as confidential rebate agreements, negotiated by the pan-Canadian Pharmaceutical Alliance (pCPA) to subsidize the cost of the drug.[7])

End of Life Guidance: End of life guidance is defined as a treatment given to a patient who has a prognosis of less than two years to live, and which extends the patient's life for three months or more. Therapies given end of life guidance status can be approved at thresholds of £50,000 per QALY, which is up to 2.5 times the normal threshold.

Modifiers: NICE and the Scottish Medicines Consortium (SMC) consider unique modifiers when opting to approve a drug that exceeds the standard threshold. Modifiers may include increased life expectancy, improvement in QALY, enhanced clinical effectiveness, absence of other therapeutic options, and bridging to other forms of therapy.

Specialized Technologies: Specialized technologies, often referred to as "orphan drugs," are used to treat small segments of the population. In the U.K., an "ultra orphan drug" is defined as a pharmaceutical treatment used for a disease with a prevalence rate of less than 1 per 50,000 people. The threshold for orphan drugs is up to £300,000 per QALY, depending on the number of QALYs gained per lifetime.[8]

Summary

In the U.K., NICE and the SMC partly base reimbursement decisions on the incremental cost per QALY gained. This metric helps both organizations determine the opportunity costs and trade-offs of reimbursing the costs on prescription drugs. Optimizing the gains from new medications and technologies partly depends on the flexible application of pricing thresholds, based on cost per QALY.

The Patented Medicine Prices Review Board's New Framework

Presenter: Tanya Potashnik, Director, Policy and Economic Analysis Branch, Patented Medicine Prices Review Board

Changes in the Pharmaceutical Market

The market for patented pharmaceuticals has evolved considerably as new innovations are being discovered and made available in Canada. In recent years, new medicines have become more specialized. These include precision medicines, gene therapies, and biologics, which treat increasingly serious and unique diseases with high manufacturing and delivery costs for a small patient population. Indeed, Canadian expenditures on drugs—i.e., generic and patented drugs—have increased steadily since the mid-1970s and now represent approximately 15.7 per cent of total health spending.[9] The recent specialization of new medicines contrasts with the

[7] Cost-effectiveness is one of several factors that influence the pCPA's decision to negotiate a confidential rebate agreement. See PCDI Market Access, *Pan-Canadian Pharmaceutical Alliance Negotiation Guidelines*.
[8] In Canada, more information is needed on how modifiers and specialized technologies will be considered in pharmacoeconomic value assessments.
[9] Canadian Institute for Health Information, *National Health Expenditure Trends, 1975 to 2018*.

1990s. In that era, much of the pharmaceutical innovation was not in biological treatment options. Instead, it was in small molecule products that were used to treat highly prevalent conditions, such as heart disease or clinical depression.

Drug Pricing Is a Global Issue

With drug expenditures rising each year, the PMPRB believes drug pricing reform is overdue. However, drug pricing is not solely a Canadian problem and is being discussed in several developed and developing countries around the world. For example, public payers in the United States, such as Medicare Part B, are contemplating introducing measures like the PMPRB's external price referencing framework. Yet, external price referencing can also be challenging because list prices do not represent the actual prices paid to manufacturers by public payers.

An additional challenge is that the current basket of countries used to perform external price references includes the United States. The present PMPRB guidelines state that pharmaceutical prices in Canada cannot exceed the highest international price, which is often set by the United States. In fact, the lack of pharmaceutical pricing restrictions in the United States has led several Canadian stakeholders to question whether the U.S. is an appropriate comparator—given that pricing regulations in Canada, as well as many of its economic comparators, are relatively strong.

Proposed Changes to the PMPRB Guidelines

The Government of Canada identified the PMPRB as a lever to help ensure that medicines are affordable, accessible, and used appropriately. For instance, to improve affordability, the PMPRB has begun examining new guidelines that will change how price reviews are conducted. In addition, the Regulatory Review of Drugs and Devices (R2D2) is designed to improve access to medications.[10] Key changes to the PMPRB's Regulatory and Compliance Framework include the following:

PMPRB12: Currently, PMPRB uses the list prices of patented medicines sold in seven countries (the "PMPRB7") to set maximum prices in Canada. The proposed changes would look at a new basket of 12 countries, called the "PMPRB12," where consumer price protection is a crucial component of health care system design, and where meaningful policies to increase affordability are taking place. New countries proposed for addition to the list include Australia, Belgium, Japan, Netherlands, Norway, South Korea, and Spain. Countries proposed for removal include the United States and Switzerland.[11] This helps to ensure that Canadian drug prices remain consistent with international norms.

Prioritization of Drugs: The PMPRB's new framework places drugs into two categories. Category 1 (high priority) includes drugs which are "first in class," have a cost per QALY of more than $30,000, or for which yearly sales are expected to be more than $20 million. Category 2 (low priority) includes all other drugs. Drugs in Category 1 are subject to more extensive assessment criteria than drugs in Category 2, which include a requirement for manufacturers to disclose the rebates they provide to third parties.[12]

[10] Health Canada, *Improving the Regulatory Review of Drugs and Services*.
[11] Health Canada, *Protecting Canadians from Excessive Drug Prices*.
[12] For more information, see Patented Medicine Prices Review Board, *Guidance Document on Changes to the Guidelines*.

New Factor Analysis: The Minister of Health has proposed that price assessments consider market size, GDP, GDP per capita, and pharmacoeconomic value. The introduction of pharmacoeconomic value has received considerable attention because it will link a drug's price to the sustainability of the health care system. It also grounds Canada's definition of an excessive price in the context of population health. Including pharmacoeconomic value in pricing decisions will help the PMPRB measure the opportunity costs for the health care system, and for purchasing drugs. Pharmacoeconomic value will also provide a common unit of measurement across all drugs.

Enhanced Compliance Framework: The PMPRB will enhance its compliance framework by determining whether the average transaction price of a drug matches its maximum rebated price.

Flexible Threshold for New Drug Applications: The PMPRB believes that reducing the gap between the price ceiling set by the PMPRB and the price accepted by the pCPA could expedite the negotiation process.

Summary

The Government of Canada has proposed several reforms to the PMPRB's drug pricing guidelines. These reforms are designed to maintain affordability and access for patients while continuing to incentivize investment in pharmaceutical innovation. Key reforms include the inclusion of pharmacoeconomic value in pricing decisions, and revisions to the set of countries whose list prices are used to determine maximum drug prices in Canada.

Key Lessons Learned

HTA Roundtable participants from government, industry, and patient organizations shared a variety of perspectives on how drug pricing in Canada can be improved. Throughout the half day of presentations and discussions, four key lessons emerged.

- HTA can be a useful tool in informing price ceilings for medical treatments. However, the unique nature of some highly innovative and expensive treatments suggests that HTA should be applied with flexibility (as “a tool not a rule”) when required, to ensure that the benefits of innovative treatments are as accessible as possible.

- The cost per QALY metric is a useful tool for determining the value of patented drugs. There may be an opportunity to refine the QALY metric to more accurately represent patients’ varying degrees of health, the length of time they spend in a health state, and the role of non-treatment factors in health gains made by patients.

- Patients and patient organizations can provide valuable input on how drug prices affect Canadians’ access to treatments, especially to new and innovative treatments. Incorporating this input into pharmaceutical pricing decisions and policy could help ensure that pricing decisions focus on saving and improving lives, in addition to creating a cost-effective system for payers and fair pricing for manufacturers.

- Collaboration between health care stakeholder groups (the PMPRB, Health Canada, CADTH, pCPA, manufacturers, and patient organizations) is necessary to create consistent, equitable decision-making that generates better outcomes for Canadians.

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Appendix A: Presenter Biographies

Michael Drummond

Mike is Professor of Health Economics and he was the Director of the Centre from December 1995 to September 2005. His field of interest is in the economic evaluation of health care treatments and programmes. He has undertaken evaluations in a wide range of medical fields including care of the elderly, neonatal intensive care, immunisation programmes, services for people with AIDS, eye health care, and pharmaceuticals.

Mike is the author of two major textbooks and more than 600 scientific papers, has acted as a consultant to the World Health Organization and was Project Leader of a European Union Project on the Methodology of Economic Appraisal of Health Technology. He has also served on the Boards of Directors of the International Society of Technology Assessment in Health Care and the International Society for Pharmacoeconomics and Outcomes Research. He has been President of the International Society for Pharmacoeconomics and Outcomes Research. Mike is currently Co-Editor-in-Chief of *Value in Health*.

Tanya Potashnik

A career public servant, Tanya Potashnik possesses a breadth of knowledge—in Canada and internationally—in the areas of pharmaceutical policy, market dynamics, and pricing.

Since January 2013, Tanya has served as Director of Policy and Economic Analysis Branch at the Patented Medicine Prices Review Board. Tanya is responsible for leading the development of strategic policy advice, economic analysis, and management of stakeholder relations for the Review Board.

Prior to this role, Tanya served as Manager and Senior Economist at the Review Board. She was on charge of, among other things, the National Prescription Drug Utilization Information System (NPDUIS) initiative. Tanya has also held various policy and management positions in the federal government and the BC Ministry of Health.

Tanya received her Bachelor of Arts in economics and business from the University of Winnipeg and her Master of Arts from the University of Victoria.

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