2019

Making Sense Of The Health Canada Cost-Benefit Analysis: Debunking Price Regulations Based On The Pharmacoeconomic Value Factor

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BACKGROUND

The Patented Medicines Price Review Board (PMPRB) was created in 1987 with a mandate to regulate the prices of patented medicines in Canada. Amid growing affordability concerns of patented medicines in Canada, attention is now turning to drug prices as a means to manage drug expenditures. In December 2017, the Government of Canada published a proposal to amend the regulations governing the prices of patented medicines in Canada.[1] Among other factors, the proposed amendments introduce new pharmacoeconomic factors (i.e., cost-utility analysis [CUA] thresholds) to ensure that "prices reflect value and Canada's willingness and ability to pay for patented medicines".

The amendment was accompanied by a Cost-Benefit Analysis (CBA) to describe the impact of the proposed regulatory changes.[2] According to the CBA, the proposed amendments are expected to result in 10-year total savings to public, private and out of pocket-payers of $8.6 billion (present value). In contrast, a PDCI reanalysis reported an estimated impact of $26.1 billion to the revenue of the pharmaceutical industry over ten years.[3]

In an independent assessment of Health Canada's CBA, David Dodge (former Governor of the Bank of Canada) noted that another CBA would need to be commissioned to provide greater transparency regarding the methods, data, and sources used to calculate the price reductions for patented medicines.

According to the updated CBA report[4]:

> *The impact of the pharmacoeconomic value factor was calculated by reducing the price of each high-priority medicine to the cost-effective threshold as published in the publicly available Canadian Agency for Drugs and Technologies in Health (CADTH) reports. For each medicine, the submitted price in the analysis was reduced to one of the three incremental cost-utility ratio (ICUR) thresholds that were assumed to be part of the new PMPRB Guidelines. The thresholds differ based on a medicine's characteristic and are as follows:*
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> - ***$50,000 per quality-adjusted life year (QALY) for high-priority medicines;***
> - ***$150,000 per QALY for high-priority expensive drugs for rare diseases (EDRDs); and***
> - ***$35,000 per QALY for high-priority medicine for a high prevalence disease.***

OBJECTIVE

In an effort to understand how the pharmacoeconomic factors may be implemented under the new PMPRB guidelines, PDCI attempted to reverse-engineer the proposed Pharmacoeconomic Value (PV) price reductions (defined as a % savings) that were published in the updated CBA. Initially, some challenges were evident as the information available in each published recommendation was highly variable. For instance:

- Drug prices redacted or price reanalysis scenarios were not always included
- Specifics on the difference in costs and effects informing the ICUR were not always available
- Multiple base case ICURs reported, or products where there was no ICUR due to dominance
- Products with no published economic analysis available online

PDCI ANALYSIS

A summary of the PDCI analysis, including how the proposed savings from the pharmacoeconomic value factor may have been calculated is provided in *Table 1* below.[i]

Table 1. Summary of Pharmacoeconomic Value Factor Reanalysis[ii,iii]

Data from Published CBA[4]			PDCI Analysis	
Product	**Stated Threshold**	**Savings from Pharmaco-economic Value Factor**	**Information available from CADTH recommendations**	**Calculation to get to % reduction**
GIOTRIF (afatinib)	$50,000/ QALY	45%	ICUR vs. afatinib $25,069; vs. gefitinib (lower) $39,000; vs. gefitinib (upper) $211,000;	Average of 3 ICURs ($91,690) X 0.54 = $50,430
ICLUSIG (ponatinib)	$50,000/ QALY	41%	ICUR vs. dasatinib (lower) $95,311; vs. dasatinib (upper) $102,688; vs. nilotnib (lower) $$94,743; vs. nilotnib (upper) $101,694; vs. SCT (lower) $91,366; vs. SCT (upper) $97,533; vs. hydroxyurea (CP-CML, lower) $94,518; vs. hydroxyurea (CP-CML, upper) $100,065; vs. interferon-alfa (lower) $57,244; vs. interferon-alfa (upper) $68,635; vs. hydroxyurea (AP-CML, lower) $49,082; vs. hydroxyurea (AP-CML, upper) $55,051; vs. hydroxyurea (BP-CML, lower) $66,399; vs. hydroxyurea (BP-CML, upper) $77,535; vs. hydroxyurea (PH+-CML, lower) $87,966; vs. hydroxyurea (PH+-CML, upper) $113,069;	Average of 16 ICURs ($84,556) X 0.59= $49,888
TECFIDERA (dimethyl fumarate)	$35,000/ QALY	46.2%	ICUR vs. glatiramer acetate $65,500	ICUR ($65,500) X 0.538 = $35,239
BANZEL (rufinamide)	$150,000/ QALY	8.7%	ICUR vs. topiramate (TTO) $111 991; vs. topiramate (EQ-5D) $55,715; vs. lamotrigine (TTO) $362,127; vs. lamotrigine (EQ5D) $127,084	Average of 4 ICURs ($164,229) X 0.913 = $149,941

[i] PDCI reached out to Health Canada for clarification on the methods used for the pharmacoeconomic value factor price reductions but specifics were not provided.

[ii] Products with a proposed reduction less than 50% were included in PDCI's reanalysis as a 50% reduction cap was applied by Health Canada.

[iii] Due to a lack of transparency on the methods used in the CBA and challenges in variation with available information from the published recommendations, PDCI was not able to reverse-engineer the price reduction for all drugs included in the CBA according to the pharmacoeconomic value factor.

In summary, for the products in *Table 1,* the price reduction is calculated as:

$$\% \textbf{ Price Reduction} = 1 - \left[\frac{\textbf{Stated Threshold}}{\textbf{Average of Publicly Available ICERS}}\right]$$

The fundamental problem with applying this simplistic equation to calculate price reductions is that it disregards the numerous non-drug cost variables driving the resultant ICUR. An ICUR is determined based on calculated total costs *and* QALYs (Quality-adjusted Life Years) for both the treatment *and* comparator.

- ICUR is a ratio that is calculated by dividing the difference in costs between Treatment A and Treatment B by the difference in effects (QALYs) between Treatment A and Treatment B over the time horizon of the analysis:

$$\textbf{Incremental Cost Utility Ratio (ICUR)} = \frac{\textbf{Total Cost}_{\textbf{A}} - \textbf{Total Cost}_{\textbf{B}}}{\textbf{Effects}_{\textbf{A}} - \textbf{Effects}_{\textbf{B}}}$$

Therefore, as multiple structural and input parameters (and associated uncertainty) determine the final ICUR estimate, access to the pharmacoeconomic model would be required to accurately calculate the price required to achieve an ICUR below a chosen threshold. Due to the numerous factors influencing the ICUR, it is not possible to do an accurate back of the envelope calculation with the limited available information as contained in most published CADTH recommendations.

CONCLUSION

Price reduction decisions have a large impact on listing, product launch, and prescribing decisions and therefore must be accurate if they are to be implemented. Until the updated PMPRB guidelines are published, we are only able to speculate on how the Pharmacoeconomic Value factor will be implemented by the PMPRB. This analysis identifies major concerns with a lack of transparency around how ICURs will be used to calculate price reductions under the new PMPRB regulations, the lack of available information from published recommendations to be able to inform price reduction calculations, as well as serious methodological concerns with the price reduction calculation as identified in our analysis.

Issues for Further Consideration:

• What role, if any, is there for incorporating value into pricing decisions for various Canadian markets?

• Is it correct to use economic evaluations, which are developed to inform one question: *cost-effectiveness,* to now answer an entirely different question: *price?*

• What is the appropriateness of using blunt economic thresholds for price setting?

• There is a reason prices are negotiated with drug programs through the pan-Canadian Pharmaceutical Alliance (pCPA): discussions of value, willingness to pay, and affordability are relative to those paying for and delivering healthcare. Reimbursement negotiations consider a wide variety of collaborative approaches for drug reimbursement. The solutions are as varied as the drugs being negotiated on a monthly basis.

REFERENCES

1 Patented Medicine Prices Review Board. (2017). PMPRB Guidelines Scoping Paper: High Level Overview of Potential New Framework – CG1 Consultation Phase. Retrieved from https://www.pmprb-cepmb.gc.ca/CMFiles/Consultations/scoping_paper/pmprb_scoping_paper_e.pdf

2 Amendments to the Patented Medicines Regulations. Patented Medicine Prices Review Board Modernization Cost-Benefit Analysis. Strategic Policy Branch, Health Canada. September 8, 2017.

3 PDCI Market Access. (2018). Proposed Amendments to the Patented Medicines Regulations: A Critical Appraisal of the Cost-Benefit Analysis. Retrieved from http://www.pdci.ca/wp-content/uploads/2018/01/20180129_PDCI-Critical-Assessment-PM-Regs-Amendments_Report-Final.pdf

4 Amendments to the Patented Medicines Regulations Cost-Benefit Analysis. Strategic Policy Branch, Health Canada. May 6, 2019.