How Does Conditional Regulatory Approval Affect Price Negotiations for Drugs in Canada?

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BACKGROUND

- In 1998, Health Canada established a conditional regulatory policy known as Notice of Compliance with conditions (NOC/c) to provide earlier access to promising new drugs for areas with unmet needs.[1]
- Through NOC/c, a drug can be marketed with the condition that the sponsor conducts further studies to validate its clinical benefits.
- The growing need to expedite access to pharmaceuticals for areas with substantial unmet needs has resulted in an increase in the utilization of NOC/c.
- The pan-Canadian Pharmaceutical Alliance (pCPA), representing the Canadian provinces, territories and federal plans, negotiates confidential public payer pricing with pharmaceutical companies following recommendations from CADTH and/or INESSS.[2]

OBJECTIVE

This study aims to assess how conditional regulatory approval and price reduction recommendations made by the Canadian Agency for Drugs and Technologies in Health (CADTH) impact outcomes at the pan Canadian Pharmaceutical Alliance (pCPA).

METHODS

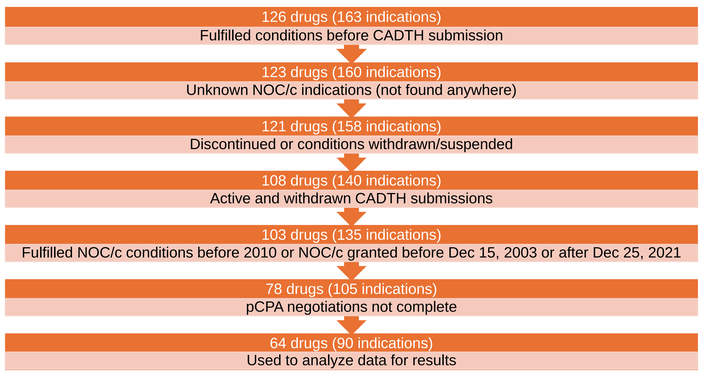
DRUG INDICATIONS INCLUDED

- 163 indications from126 drug products were reviewed by Health Canada and issued NOC/c between 1998-2023 (cut off: May 23, 2023)
- Drugs/indications that fulfilled NOC/c conditions before going to CADTH, had unknown NOC/c indications, were discontinued, withdrawn, or had active or withdrawn CADTH submissions were excluded from the analysis.
- Drugs granted NOC/c before Dec 15, 2003 were excluded as earlier reports are not publicly available on the CADTH site.[4]
- CADTH-relevant filters were applied as drugs tend to go through CADTH before going to pCPA.
- Drugs that fulfilled conditions prior to 2010 were excluded as pCPA was established in 2010.
- Drugs granted NOC/c within 536 days of the last extracted pCPA status (June 14, 2023) were excluded from the analysis, as the average timeframe from NOC to the end of pCPA negotiations was 536 days (2016-2020).[3]

DATA SOURCES

- 126 NOC/c drugs were sourced from Health Canada's NOC/c webpage (last updated May 23, 2023).[5]
- NOC/c indications were pieced together from qualifying notices (if available), Health Canada's Summary Basis of Decision database, CADTH reports, and Sponsor press releases.[4,6]
- The pCPA Negotiation Status database was assessed for factors including the negotiation outcome and time taken to complete negotiations (last extracted June 14, 2023).[7]
- Drugs were then cross-referenced using reports from CADTH's website to identify any price reduction recommendations.[4]

Figure 1: Flowchart for identifying relevant drugs to analyze

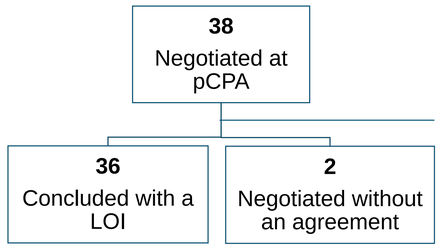


RESULTS

COMPLETED CADTH REVIEW DID NOT ALWAYS RESULT IN PCPA NEGOTIATIONS FOR NOC/c INDICATIONS

- 53% (56/105) NOC/c indications were submitted to CADTH while only 42% (38/90) completed pricing negotiations with pCPA

Figure 2: NOC/c Indications That Completed pCPA Negotiations



Excluded:
- Active negotiations (n=2)
- Under consideration for negotiation (n=3)
- Negotiations not pursued (n=10)

THE DURATION OF SUCCESSFUL pCPANOC/c NEGOTIATONS DO NOT DIFFER SIGNIFICANTLY FROM INDUSTRY AVERAGES.

- NOC/c does not appear to affect successful pCPA negotiation times for oncology drugs, but can double the negotiation time in non-oncology
- Negotiations that concluded with an LOI took 0-382 days for Oncology (n=31), 153-691 days for Rare disease (n=3), and 209-210 days for 'Other' indications

Figure 3: Mean Duration of pCPA Negotiations for Oncology NOC/c Drugs vs Industry Standard (2017-2020)[8]

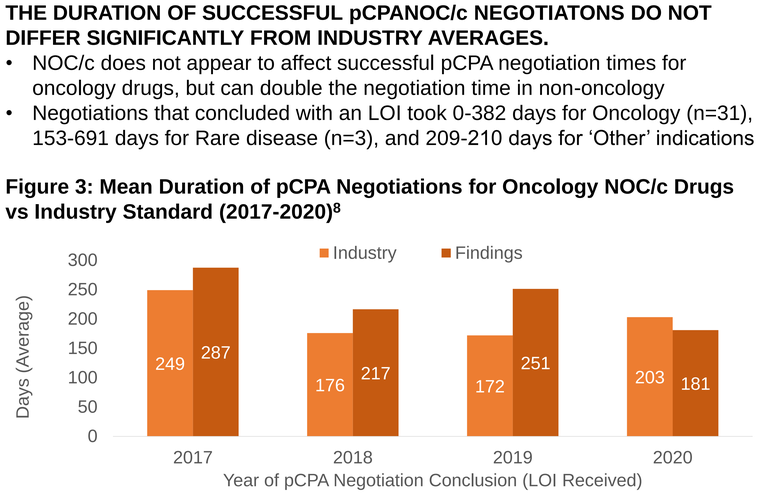
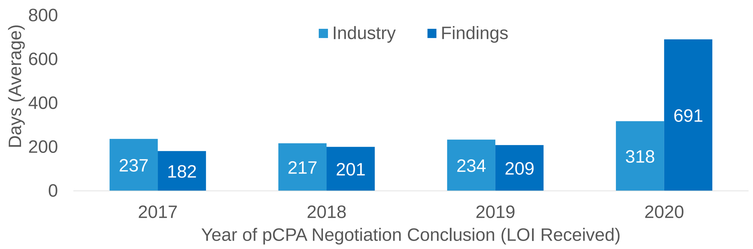


Figure 4: Mean Duration of pCPA Negotiations for Non-oncology NOC/c Drugs vs Industry Standard (2017-2020)[8]



DESPITE SIGNIFICANT PRICE REDUCTION STATEMENTS, NOC/c DRUGS WENT TO pCPA AND 95% RECEIVED A POSITIVE OUTCOME

- All NOC/c indications that received a price reduction recommendation from CADTH still negotiated at pCPA (n=16) and 94% received a positive outcome (LOI).

DRUGS WITH PRICE REDUCTION RECOMMENDATIONS ≥90% WERE ABLE TO SUCCESSFULLY COMPLETE NEGOTIATIONS

- 6 drugs had a price reduction recommendation ≥90%, however all of them still negotiated at pCPA, and 83% concluded with a LOI.

ABBREVIATIONS AND ACRONYMS

CADTH = Canadian Agency for Drugs and Technologies in Health
INESSS = Institut national d'excellence en santé et services sociaux
pCPA = pan-Canadian Pharmaceutical Alliance
LOI = Letter of intent
NOC/c = Notice of Compliance with conditions
RD = Rare Disease

Figure 5: CADTH Price Reduction Recommendations

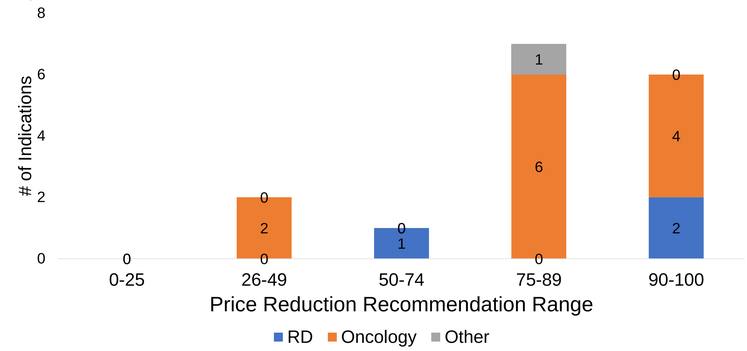


Table 1: Drugs with a CADTH Price Reduction Recommendation ≥90%

Drug	Type	CADTH Price Reduction Recommendation (%)	pCPA Status (as of June 14, 2023)
Kanuma	Rare Disease	96-98	Concluded with an LOI
Keytruda	Oncology	100	Concluded with an LOI
Lenvima	Oncology	100	Concluded with an LOI
Retevmo	Oncology	70-93	Concluded with an LOI
Strensiq	Rare Disease	91	Concluded without agreement
Vitrakvi	Oncology	90+	Concluded with an LOI

LIMITATIONS

- Assessing the reasons why some NOC/c files were submitted to CADTH and others were not was not part of this analysis. This may contribute to a bias for a higher likelihood of positive CADTH review and pCPA negotiation for NOC/c files as those with less chance of success may not have even been assessed for funding.
- The small sample size of rare disease and 'other' NOC/c drugs that received LOI at pCPA compared to the overall drug pool can limit comparative conclusions that can be drawn from this analysis.

CONCLUSION

- Historically, conditional regulatory approval has been associated with unfavorable reimbursement recommendations leading to lack of reimbursement.
- This is likely associated with CADTH policy changes in reviewing NOC/c files. Submission sponsors are developing a deeper understanding of payer needs, leading to strategic decisions made prior to engaging with health technology agencies and pricing negotiations.
- These findings indicate that NOC/c does not significantly affect the duration of pricing negotiations when compared to industry findings for oncology drugs but in recent times has doubled the negotiation timelines in non-oncology
- Despite price reduction recommendations; even those ≥90%, NOC/c drugs have not still been able to successfully negotiate pricing.

REFERENCES

[1]Health Canada. Guidance Document: Notice of Compliance with Conditions (NOC/c). 14 Sep 2016
[2]pCPA. About pCPA. 2023
[3]Dobrescu A. Innovative Medicines Canada. Canadian Public Insurance Plans and Delays in Patient Access to Innovative Medicines. 2021.
[4]CADTH. Reimbursement Review Reports. 19 Oct 2023
[5]Health Canada. Notice of Compliance with conditions (NOC/c). 23 May 2023
[6]Health Canada. The Drug and Health Product Register. 14 July 2021
[7]pCPA. Brand Name Drug Negotiations Status. 2023
[8]IQVIA. Market Access Metrics Database. Feb 2023

DISCLOSURES

Anna Liovas are employed by Ipsen Biopharmaceuticals Canada Inc. Yulia Privolnev and Lovette Chan were employed by Ipsen Biopharmaceuticals Canada Inc. at the time of analysis.

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