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Executive Summary

The CADTH pan-Canadian Oncology Drug Review program (pCODR) is designed to bring consistency and clarity to the assessment of cancer drugs by looking at clinical evidence, cost-effectiveness, and clinician and patient perspectives. Established in 2010 by the provincial and territorial Ministries of Health (with the exception of Quebec), the pCODR program assesses cancer drugs and makes reimbursement recommendations to the participating provincial and territorial Ministries of Health and provincial cancer agencies to guide their drug funding decisions. The pCODR program has been part of CADTH since April 2014.

CADTH is guided by its four core values. One of CADTH’s values is the pursuit of excellence. Specifically, CADTH is committed to ensuring that the needs and expectations of its customers are met in an efficient, credible, affordable, and timely manner. In keeping with the value of excellence, CADTH has adopted and integrated the eight guiding principles into the pCODR program. The measures against which pCODR is assessed are based on CADTH’s core values and guiding principles, which can be read in full on the CADTH website.

As part of this commitment to excellence, CADTH is pleased to publish this third pCODR performance metrics report, which analyses pCODR activity from the time of receiving its first submission in 2011 to March 31, 2016. It is an important part of CADTH’s commitment to bringing greater transparency and accountability to the cancer drug review process.

A. Delivering on Priority Initiatives in 2015-2016

1. Enhancing Patient Engagement Through Collaboration Projects

The pCODR program continues to collaborate with patient groups to support and further enhance cancer patient community involvement in the assessment of new cancer drugs.

In August 2015, the Canadian Cancer Action Network (CCAN) and pCODR co-developed two new narrated slide presentations to make it easier for patient groups to provide input into a pCODR review. The slide presentations, along with our previously released A Guide for Patient Advocacy Groups, offer guidance on how best to collect and present patient evidence. The examples included in both presentations are based on observations and comments from the pCODR Expert Review Committee (pERC).

As of March 31, 2016, of the 75 drug submissions received by pCODR, 72 submissions have had patient input. In a number of instances, pERC has commented in its final recommendations that patient input was extremely helpful in illustrating the lived experience of a patient with a particular type of cancer and helped it to appreciate the impact (both good and bad) that the drug under review may have on those taking it and those caring for patients living with cancer.

“In my initial review of the study data, I was not overwhelmed with [the drug under review]. The patient advocacy group submission reinforced for me that the benefits of [the drug under review versus standard first-line therapy] cannot be summarized by parameters like initial response rate and that long-term effects are of greater value to assess [the drug’s] impact. Additionally, the distress that patients feel having to endure a [standard] treatment that oncologists feel forced to offer first-line was very well captured in this submission and was as valuable to me in weighing the benefits of [the drug under review] in the first-line setting as the clinical data.” — pERC Member

In September 2015, CCAN and pCODR introduced a Cancer Drug Pipeline Information for Patient Advocacy Groups. The objective of this initiative is to provide a centralized source of public information for patient groups that details the anticipated cancer drug products or indications that could enter the Canadian market. It aims to support patient groups by providing longer lead times to make a submission to the pCODR program.

2. New Pilot Initiative to Increase Clinician Input and Feedback in the pCODR Process

On February 1, 2016, CADTH introduced a new pilot initiative that would increase opportunities for clinician input and feedback in the pCODR process. The pilot aims to expand our reach into the clinical community to capture the breadth of clinical practice experiences from the different jurisdictions and to solicit the values of the broad clinical community. This additional input will provide real-world practice evidence from clinical communities across Canada and allow us to gain insights into local and regional issues, and to identify areas of unmet need.

CADTH intends to evaluate this pilot initiative after receiving 25 cancer drug submissions with clinician input, or sooner if appropriate, and will consult with stakeholders on any significant changes to the pCODR process.
B. pCODR Operations: Summary of Key Metrics

Created to bring consistency and clarity to the assessment of cancer drugs, pCODR’s continued operations have contributed to a more transparent and rigorous review system. Under CADTH’s governance, pCODR is meeting its production targets and program objectives.

- From July 2011 to March 31, 2016, pCODR has received a total of 75 submissions, including two expanded indication reviews. The projected production capacity for pCODR for 2015-2016 was between 20 and 25 submissions; pCODR met this target with 22 recommendations issued in 2015-2016.
- 10 of 16 priority review requests have been granted since inception.
- In cases where a manufacturer provides a submission ahead of Health Canada’s approval (pre-Notice of Compliance (NOC)), the time from NOC date to the Notification to Implement date is a median of 86 business days, compared to 201 business days for submissions provided after a NOC, recognizing that there may be delays from the submitter in providing the submission.
- More than 60% of pCODR submissions were pre-NOC submissions, an option that allows the review process to begin earlier resulting in recommendations to be issued shortly after Health Canada’s market approval and may result in an earlier funding decision by the jurisdictions.
- pCODR is working with stakeholders to ensure timely reviews. The process is meeting its review target timelines with a median of 144 business days for all submissions received as of March 31, 2016.
- By March 31, 2016, pCODR issued a total of 65 final recommendations. Of the 65 recommendations, nine (14%) were positive recommendations, 42 (65%) were conditional recommendations, and 14 (21%) were negative recommendations.
- pCODR continues to post an average of nine documents for each of the reviews on the Find a Review (pCODR) page. Interested parties can follow the progress of a review using CADTH’s online process tracking tool.
- pCODR has a roster of approximately 80 active clinical and economic review panel members. Members of the Clinical Guidance and Economic Guidance Review Panels and pERC are listed on the CADTH website.

C. On the Horizon

CADTH, through the pCODR program, is continually assessing how the drug review process can be improved. Knowing what new cancer drugs are on the horizon allows for better planning across the system.

Based on the pipeline information surveyed, pCODR estimates that there may be as many as 293 drug-indication pairs that are being developed with many of these being submitted for review over the next five years. Of these, 185 are new drug-indication pairings and 108 are new indications for existing drugs as of March 31, 2016.

pCODR continues to watch for treatment trends, such as the use of companion diagnostics. As of March 31, 2016, there were 12 different companion diagnostics linked to 33 individual cancer drugs and 44 cancer drug-indication pairs on the horizon.
1. Introduction

The pan-Canadian Oncology Drug Review (pCODR), a CADTH program, assesses cancer drugs and makes reimbursement recommendations to the participating federal drug plans, provincial and territorial Ministries of Health (excluding Quebec), and provincial cancer agencies to guide their funding decisions. pCODR is designed to bring consistency and clarity to the assessment of cancer drugs by looking at clinical evidence, cost-effectiveness, and clinician and patient perspectives.

The pCODR review process is comprehensive, and benefits from the input of patient groups, drug manufacturers, clinicians, and government. It’s a collaborative approach, which means that reimbursement recommendations reflect the thinking of Canada’s most respected oncologists, economists, and administrators, who have had the benefit of hearing from patient groups as well. The pCODR program objectives include:

- Providing consistency and clarity to the cancer drug review process, ensuring that participating federal and provincial drug plans and provincial cancer agencies benefit from a single, clear approach to new cancer drug evaluation; and
- Leveraging best practices and expertise from across Canada to provide public payers with the best possible information to inform their funding decisions.

2. Performance Measures

The measures against which pCODR is assessed are based on CADTH’s core values. These values incorporate pCODR’s guiding principles. Those principles (which can be read in full on the CADTH website) include:

- Efficiency and effectiveness: A review process that is cost-efficient, effective, and streamlined (i.e., reduced duplication) to support timely decision-making
- Evidence-based reviews: A review process with capacity for rigorous and consistent evidence-based clinical and pharmacoeconomic reviews to support evidence-based decision-making
- Representation: A review process that is multidisciplinary, cross-jurisdictional, and collaborative in nature, and includes appropriate input from key stakeholders and links to other key national initiatives.

With these principles in mind, the pCODR program is publishing its third performance report on its business operations and stakeholder engagement activities. This third report, which analyzes pCODR activity to March 31, 2016, is an important part of CADTH’s ongoing commitment to bringing greater transparency and accountability to the cancer drug review process. The results and their implications are provided on the following pages.

3. Results: Operations

The number of reviews, the length of time for those reviews, scope of expertise, and access provided to stakeholders through the review process are important markers of pCODR’s operational efficiency.

3.1 Volume

pCODR has received 75 submissions, including two expanded indications, since the time of receiving its first submission in the 2011 launch of the program (July 2011 to March 31, 2016). Of the 75 submissions, nine were granted priority review (see Appendix A for priority review criteria and pCODR’s experiences to date). pCODR has also analyzed submission data regarding the tumours treated by the drugs and the drugs’ routes of administration (see Appendix B).
Table 1: Summary of Submissions Received Since Launch of pCODR

<table>
<thead>
<tr>
<th>Total Submissions = 75 (as of March 31, 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Drug</td>
</tr>
<tr>
<td>Total Submissions</td>
</tr>
<tr>
<td>July-Dec 2011</td>
</tr>
<tr>
<td>Jan-June 2012</td>
</tr>
<tr>
<td>July-Dec 2012</td>
</tr>
<tr>
<td>Jan-June 2013</td>
</tr>
<tr>
<td>July-December 2013</td>
</tr>
<tr>
<td>Jan-June 2014</td>
</tr>
<tr>
<td>July-December 2014</td>
</tr>
<tr>
<td>Jan-June 2015</td>
</tr>
<tr>
<td>July-December 2015</td>
</tr>
<tr>
<td>Jan-March 2016</td>
</tr>
</tbody>
</table>

pCODR = CADTH pan-Canadian Oncology Drug Review; pERC = pCODR Expert Review Committee.

Priority Reviews
Submissions are reviewed in the order they are received; however, at time of filing, a submitter may request that a submission be considered a priority review. This request is assessed against clinically based criteria that, if met, allow the submission to be reviewed next. Because the review timeline is not condensed, prioritization affects only the order of review (in the event submissions may be queued) and order of placement on the pERC agenda; see Appendix A for the criteria.

3.2 Access
The pCODR process offers manufacturers and tumour groups the option to submit drugs for review before a Notice of Compliance (NOC) approval is received from Health Canada. Unique in Canada when it was introduced, this mechanism allows for the review process to begin earlier, as the pCODR review runs parallel to Health Canada’s review. The option has been well received; approximately 63% of pCODR’s submissions were submitted prior to NOC approval.
3.2.1 Timeliness

A pre-NOC review is initiated before a manufacturer has received the drug’s NOC from Health Canada. As a result of starting the review in the pre-NOC phase, the funding recommendation is issued sooner after market approval.

In cases where a manufacturer provides a submission ahead of Health Canada’s approval (i.e., pre-NOC), pCODR has found that the time from NOC date to the Notification to Implement date is significantly shorter than for submissions provided after a NOC, as this option allows the review process to begin earlier resulting in recommendations to be issued shortly after Health Canada’s market approval. Figure 2 shows that the average lead time for pre-NOC submissions is approximately 65 business days. Figure 3 shows that significantly fewer overall submission days (86 business days) are required for submissions made pre-NOC compared with post-NOC submissions (201 business days), from the time of receipt of NOC to time of Notification to Implement.

This finding supports pCODR continuing with this approach to accept pre-NOC submissions. pCODR has noted that pre-NOC submissions may require additional clarification with manufacturers, as the review is beginning before all regulatory issues are settled. However, this does not affect patient access because these efforts take place before the drug has been approved for marketing.
Figure 2: Time Between Notice of Compliance and Submission Received

NOC = Notice of Compliance; pCODR = CADTH pan-Canadian Oncology Drug Review.

Figure 3: Time From Receipt of Notice of Compliance to Notification to Implement

NOC = Notice of Compliance; pCODR = CADTH pan-Canadian Oncology Drug Review.
3.2.2 pCODR Review Timelines
pCODR works with stakeholders to ensure drugs and new indications are reviewed and initial recommendations are issued within 180 calendar days of the manufacturer's submission being deemed complete. Key factors for ensuring this timeline is met are good planning (e.g., including an accurate anticipated submission filing date in pre-submission information is important) and accurate information provided by the submitter. Lack of information (e.g., insufficient economic information, and/or incomplete NOC requirements and/or other submission requirements) may significantly affect pCODR review timelines.

Having an accurate anticipated submission filing date is important. It is used to notify patient groups and registered clinicians of a pending drug submission and the target deadline date for providing input in order to maximize the time for these stakeholders to prepare their input into the review process. It is also important for planning and for identifying resources for the review (e.g., managing the review process, assessing the current submission volumes, identifying key experts to participate in the review process, and planning for the proposed new submission).

As part of the alignment work, CADTH will be implementing changes to its procedures that will require all submitters to provide a minimum 120 calendar days’ advance notification for anticipated drug submissions and resubmissions. This requirement will apply to all CADTH Pre-submission Information Requirements Forms received on May 1, 2016 and onward, and would pertain to all submissions and resubmissions filed on or after September 1, 2016.

Figure 4 shows a snapshot of submitters’ compliance rates on the pre-submission notification period in 2014 and 2015. About 85% of submitters have provided at least four months’ notification in advance of the anticipated filing date in 2014, compared with 78% of submitters in 2015.

**Figure 4: Snapshot of Submitters’ Compliance Rate Regarding Pre-Submission Notification Period**
pCODR typically reviews new submissions within 99 and 149 business days from the date of receipt of a submission to Notification to Implement. Table 2 shows pCODR’s drug review timelines as of March 31, 2016 for all drugs received to date. The median timeline for a pCODR review is 144 business days. The pre-NOC submission reviews included 17 early conversion drug reviews. The post-NOC reviews included seven early conversions.

**Early conversion**
Feedback on an initial recommendation is assessed to determine whether it is eligible to be converted to a Final Recommendation without reconsideration. If it is, the Final Recommendation will be posted on the CADTH website. This step allows recommendations to be finalized sooner.

**Table 2: pCODR’s Drug Review Timelines for all pCODR Submissions Received as of March 31, 2016**

<table>
<thead>
<tr>
<th></th>
<th>Initial Recommendation*</th>
<th>Final Recommendation*</th>
<th>Notification to Implement*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>106 days</td>
<td>137 days</td>
<td>147 days</td>
</tr>
<tr>
<td>Median</td>
<td>96 days</td>
<td>133 days</td>
<td>144 days</td>
</tr>
<tr>
<td>Range</td>
<td>75-208 days</td>
<td>89-222 days</td>
<td>93-233 days</td>
</tr>
</tbody>
</table>

* From time of submission received
NOC = Notice of Compliance; pCODR = CADTH pan-Canadian Oncology Drug Review.
Note: The estimated pCODR review ranges between 99 and 149 business days. The pCODR average review “time clock” begins as soon as a manufacturer submits a drug for review (and not at NOC approval).

**Notification to Implement**
Refers to a full and final funding recommendation. Once a final recommendation has been made, pCODR allows 10 business days for parties who participated in the review process to make an application for a procedural review, if they believe that pCODR did not undertake the review process fully and/or fairly. If there is no procedural review request following the 10 business days, pCODR issues the Notification to Implement, which is the green light for provinces to proceed with making their funding decision.

3.3 Conclusion
The pCODR process has been successfully handling the expected volume of submissions and has seen significant uptake of its pre-NOC submission option. Based on the current trend, pCODR expects to see increases in submission volumes in the near future and will need to explore best practice approaches to manage the potential influx of submissions. The program also identified a pattern with pre-NOC reviews. Generally, they require additional time to resolve administrative issues, as the manufacturer is still seeking regulatory approval; however, this does not affect patient access because without Health Canada approval, the drug under review cannot be sold in Canada. pCODR continues to manage these administrative issues and improve its time investment for pre-NOC submissions because they can yield faster access.
4. Results: Transparency

Transparency is a core value. It is demonstrated through the amount and type of information that is publicly posted, and the nature of the review process itself. CADTH, in collaboration with the participating jurisdictions and with input from stakeholders, has established a common recommendation framework to support its drug expert committees in making recommendations to the participating jurisdictions to guide their reimbursement decisions. The Recommendation Framework for CADTH Common Drug Review and pan-Canadian Oncology Drug Review Programs highlights some of the factors that CADTH’s drug expert committees, in formulating a reimbursement recommendation, will consider to provide guidance to the participating jurisdictions.

4.1 Posted Information

Since its inception, pCODR has committed to posting publicly both the initial and final reimbursement recommendations, as well as the clinical and economic reviews that are considered in formulating a recommendation. pCODR has met this objective for each of the reviews that completed the process and has issued 65 final recommendations as of March 31, 2016. Of the 65 recommendations, nine were positive recommendations, 42 were conditional recommendations, and 14 were negative recommendations.¹ There are, on average, nine documents (e.g., initial and final clinical and economic reports, initial and final recommendations, feedback from eligible participants, conflict of interest declarations) posted per review. Interested parties can follow the progress of a review using CADTH’s online process tracking tool for pCODR submissions.

In addition, the members of the Clinical Guidance and Economic Guidance Review Panels and of the pCODR Expert Review Committee (pERC) are listed on the CADTH website.

Figure 5: Summary of pERC’s Final Recommendations as of March 31, 2016

pERC = CADTH pan-Canadian Oncology Drug Review Expert Review Committee

4.2 Procedural Fairness

A number of groups — provincial government representatives, patient groups, manufacturers, clinicians, and academics — were involved in developing the current pCODR process to ensure its effectiveness and fairness. pCODR has also held several webinars and information sessions since 2011 to explain how the process works. The steps are also summarized in a short video. One of those steps is a procedural review, should a group feel that the steps have been applied unfairly. To date, pCODR has received one procedural review request. It was determined that the request did not meet the grounds for a procedural review, and the final recommendation was implemented without any changes.²

4.3 Conclusion

The current pCODR process is working well. pCODR will assess the benefits of posting additional information as opportunities arise, if the information is useful, understandable, and helpful to stakeholders in terms of contributing to the review process.

¹ pCODR is observing a trend whereby a number of recent submissions to pCODR used non-comparative data as the pivotal study, and in particular where there are ongoing randomized controlled trials for the drug under review. In many of these instances, pERC has indicated that non-comparative data create considerable uncertainty regarding the magnitude of the observed clinical benefit and makes it challenging for pERC to conclude whether there is a net clinical benefit. In light of this observation, if non-comparative data are used, it is important for a submitter to consider the following factors:
- If there is an important therapeutic need that a drug under review may fill
- A randomized trial is not feasible due to various reasons (e.g., the rarity of disease, unethical to randomize, among others)
- Significant outcomes in a large sample of patients when compared with historical data on current standard of care.

² pCODR received its first procedural review request in February 2015. In accordance with section 6 of the pCODR Procedural Review Guidelines, the procedural review request was reviewed by the President and Chief Executive Officer of CADTH, with advice from the pCODR Advisory Committee Chair and Vice-Chair. It was concluded that the request did not meet the grounds for a procedural review.
5. Results: Stakeholder Engagement

Activities to support patient group submissions, the amount of patient input and feedback received, engaging tumour groups and registered clinicians provide data to assess pCODR’s level of stakeholder engagement.

5.1 Patient Group Support

The pCODR program continues to collaborate with patient groups to support and further enhance cancer patient community involvement in the assessment of new cancer drugs. Building on the existing Patient Engagement Collaboration Project, pCODR continues to collaborate with the Canadian Cancer Action Network (CCAN) to co-develop and implement resources to support patient groups, including:

- Creating **two narrated, interactive slide presentations** to help illustrate some of the key components of the *Guide for Patient Advocacy Groups: How to Provide Patient and Caregiver Input for a pCODR Drug Review*. The examples included in both presentations are based on observations and comments from pERC.
- Introducing *Cancer Drug Pipeline Information for Patient Advocacy Groups*. The objective of this initiative is to provide a centralized source of information from public sources for patient groups that details the anticipated cancer drug products or indications that could enter the Canadian market. It aims to support patient groups by providing longer lead times to make a submission to the pCODR program.

pCODR continues to explore opportunities to identify needs, develop resources, and provide support to the Canadian cancer patient community.

5.2 Patient Group Input

Patient group input allows reviewers and pERC to understand patients’ perspectives about the experience of living with cancer and undergoing treatment for it. Since inception, 72 of 75 drug reviews have had patient group submissions.

Figure 6: pCODR Submissions with Patient Group Input since Inception

![Graph showing pCODR submissions with patient group input]

As of March 31, 2016:
- 96% of submissions had patient input (72/75 submissions)
- Total Patient Group Submissions = 101*

*Note: Certain drug/indication submissions had more than 1 patient group submission

pCODR = CADTH pan-Canadian Oncology Drug Review.

A unique aspect of patient group input into the pCODR process is the ability to comment on an initial recommendation. Of the initial recommendations, approximately 64% of the submissions received patient group feedback.
5.3 Tumour Group Engagement

Tumour groups are clinical and/or research groups affiliated with a provincial cancer agency or a provincial or territorial Ministry of Health, where cancer specialists, health care professionals, and researchers with expertise in tumours related to a specific area work together. As part of the process, tumour groups are eligible to make a submission to pCODR for review. Since its inception, pCODR has received three tumour group submissions and worked with tumour groups to review data, offer counsel on the process, and explain the nature of the information needed by the evaluators. For more information, please review pCODR’s Process in Brief.

5.4 New Pilot Initiative to Increase Clinician Input and Feedback in the pCODR Process

On February 1, 2016, CADTH introduced a new pilot initiative that would increase opportunities for clinician input and feedback in the pCODR process. The pilot aims to expand our reach into the clinical community to capture the breadth of clinical practice experiences from the different jurisdictions and to solicit the values of the broad clinical community.

Clinicians are required to register with pCODR in order to submit their input. In order to be eligible to provide input, a clinician must:

- Be an actively practising physician
- Be a member of a provincial cancer agency or similar body or a national cancer organization and
- Submit a declaration of conflict of interest.

CADTH strongly encourages collaboration among registered clinicians. Input and feedback from registered clinicians for a specific drug under review may be submitted jointly. If the input is a joint clinician submission, the lead registered clinician must list the names of the other registered clinician contributors, their titles, and their specialties, and each contributor must complete and submit their individual conflict of interest declaration form.

Registered clinicians must use the pCODR Registered Clinician Input on a Drug Review template, which outlines very specific questions, including:

- Confirming whether the physician has experience with using the drug under review (e.g., has either prescribed the drug or has used it in a clinical trial setting)
- Identifying current standard treatment(s) in their jurisdiction for the defined patient population according to the funding request
- Identifying key benefits and harms of the drug under review reported by the registered clinician(s) observed as part of their practice
• Identifying whether there is a high incident and/or prevalent patient population for the new drug under review based on the funding request, and describing whether there is any population group for whom the drug under review should not be used
• Explaining, based on the physician’s practice experience, if the drug under review is clinically superior to current treatments for the defined patient population, and if so, explaining how it is superior
• Explaining how the new drug under review could be sequenced with current therapies
• Explaining whether the new drug under review could replace any current treatments in practice
• Identifying any unmet needs that the drug under review would fulfill
• Confirming whether companion diagnostic testing is required for the new drug under review.

This additional input will provide real-world practice experience from clinical communities across Canada to gain insights into local and regional issues, and to identify areas of unmet need.

CADTH intends to evaluate this pilot initiative after receiving 25 cancer drug submissions with clinician input, or sooner if appropriate, and will consult with stakeholders on any significant changes to the pCODR process.

5.5 Conclusion
The pCODR program will continue to support patient group and clinician involvement and build the capacity of stakeholder groups to participate meaningfully in the review process.
6. Provincial Drug Funding Decisions at a Glance

The pCODR review process results in reimbursement recommendations to the participating jurisdictions; the final decision on whether to publicly fund a cancer drug rests with each jurisdiction. There are many factors that go into a province’s (or cancer agency’s) decision to fund an oncology drug. These include, but are not limited to, available budget, regional health system priorities, and local priorities. A pCODR recommendation is one of the many factors that are considered prior to making a funding commitment.

Given that pCODR was created to assist the participating jurisdictions with their decision-making, there is value in examining how the provinces use pCODR’s reimbursement recommendations. Figure 8 shows the current provincial concordance rate with pCODR recommendations.

Figure 8: Provincial Concordance Rate with pCODR Recommendations as of March 31, 2016

In late 2014, pCODR commissioned a research project\(^3\) to explore whether the time from NOC issued by Health Canada to provincial drug funding decisions has shortened, and whether more consistent decisions have been made across the provinces since its inception. A retrospective review was undertaken. The researchers, through the support of the pCODR program and the Provincial Advisory Group, collected and analyzed public drug funding data for the period pre-pCODR (2003 to 2010) and after pCODR’s inception (2011 to December 31, 2014). The research study took into consideration that the drug review process provides recommendations only, and the final funding approval is a jurisdictional decision that takes into account the individual province’s needs and financial constraints at a given period of time. It was concluded that the implementation of pCODR was associated with greater concordance in cancer drug funding decisions across provinces (see Figure 9) and decreased time to funding decisions (see Table 3).

\(^3\) Amirrtha Srikanthan, Helen Mai, Nianda Penner, Eitan Amir, Andreas Laupacis, Mona Sabharwal, Kelvin KW Chan. *The Impact of pCODR on Cancer Drug Funding Decisions*. Poster presented at: Canadian Association of Medical Oncologists Annual Scientific Meeting 2016; April 28, 2016; Toronto, ON.
Agreement of decisions among provinces prior to and after implementation of pCODR was examined by computing agreement kappa statistics using the methods of Brennan Prediger to account for multiple raters.

pCODR = CADTH pan-Canadian Oncology Drug Review.

Source: Amirtha Srikanthan, Helen Mai, Nianda Penner, Eitan Amir, Andreas Laupacis, Mona Sabharwal, Kelvin KW Chan. The Impact of pCODR on Cancer Drug Funding Decisions. Poster presented at: Canadian Association of Medical Oncologists Annual Scientific Meeting 2016; April 28, 2016; Toronto, ON.

Table 3: Change in Time to Funding Estimates (pre-pCODR versus pCODR)

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Mean reduction in the number of days(^a)</th>
<th>pre-pCODR (calendar days)</th>
<th>pCODR (calendar days)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from submission date to funding date</td>
<td>236</td>
<td>732</td>
<td>496</td>
<td>83 to 389</td>
<td>0.003</td>
</tr>
<tr>
<td>Time from NOC date to funding date</td>
<td>270</td>
<td>768</td>
<td>497</td>
<td>89 to 453</td>
<td>0.004</td>
</tr>
</tbody>
</table>

CI = confidence interval; NOC = Notice of Compliance; pCODR = CADTH pan-Canadian Oncology Drug Review.

\(^a\) Adjusted for province and indication.

Source: Amirtha Srikanthan, Helen Mai, Nianda Penner, Eitan Amir, Andreas Laupacis, Mona Sabharwal, Kelvin KW Chan. The Impact of pCODR on Cancer Drug Funding Decisions. Poster presented at: Canadian Association of Medical Oncologists Annual Scientific Meeting 2016; April 28, 2016; Toronto, ON.
Figure 10: Provincial Funding Decisions on pERC Recommendations as of March 31, 2016

a. Provincial Funding Decisions: Positive Recommendations

b. Provincial Funding Decisions: Conditional Recommendations

As of March 31, 2016

© 2016 CADTH: pCODR Metrics Report
b. Provincial Funding Decisions: Conditional Recommendations (cont’d)

As of March 31, 2016

c. Provincial Funding Decisions: Negative Recommendations

As of March 31, 2016

pCODR = CADTH pan-Canadian Oncology Drug Review; pERC = pCODR Expert Review Committee.

Notes:
- "Under Provincial Consideration" means that the province is reviewing pCODR’s recommendation. This may include the province working with the drug manufacturer to reach an agreement for a drug product that both parties can accept, in particular in cases where pERC has recommended that the drug be funded only on the condition of cost-effectiveness being improved to an acceptable level. This may occur before or after the pan-Canadian negotiations. Please contact the specific provincial drug program and/or cancer agency in your province for information about the status of a given drug product.
- "Under Negotiation with Manufacturer" means that the Pan-Canadian Pricing Alliance is conducting a joint pan-Canadian negotiation for this drug. More information on the Pan-Canadian Pricing Alliance can be found at http://www.pmprovinceterritories.ca/en/initiatives/358-pan-canadian-pharmaceutical-alliance or by contacting the specific provincial drug program and/or cancer agency in a province for information about the status of a given drug product.
- The manufacturer made a resubmission to pCODR for Xalkori for advanced non–small cell lung cancer after receiving a negative recommendation; as such, provinces agreed to wait for the final recommendation resulting from the resubmission.
- While pERC recommends funding ramucirumab (Cyramza) in combination with paclitaxel, conditional on its cost-effectiveness being improved to an acceptable level, pERC does not recommend funding ramucirumab monotherapy for the treatment of patients with advanced or metastatic gastric cancer or gastro-esophageal junction adenocarcinoma with disease progression following first-line chemotherapy.
As of March 31, 2016, pCODR had issued 62 Notifications to Implement\(^4\) for cancer drug products. Figure 11 shows the number of positive funding decisions made by the provinces (includes positive and conditional recommendations from pERC).

Figure 11: Provincial Uptake for CADTH pan-Canadian Oncology Drug Review Recommendations

Note: Total of 50 pCODR positive recommendations (includes both positive + conditional) as of March 31, 2016

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\(^4\) Notification to Implement refers to a full and final funding recommendation. Once a final recommendation has been made, pCODR allows 10 business days for parties who participated in the review process to make an application for a procedural review, if they believe that pCODR did not undertake the review process fully and/or fairly. If there is no procedural review request following the 10 business days, pCODR issues the Notification to Implement, which is the green light for provinces to proceed with making their funding decision.
7. On the Horizon

CADTH, through the pCODR program, is continually assessing how the drug review process can be improved. Knowing what new cancer drugs are on the horizon would allow for better planning. As of March 31, 2016, pCODR estimates that there are 293 drug-indication pairs (see note below) that may be submitted for review over the next five years. Of these, 185 are new drug-indication pairings and 108 are new indications for existing drugs. Most of the drug-indication pairs would treat lung, lymphoma and myeloma, and genitourinary cancers.

Figure 13: Estimated Upcoming Drug-Indication Pairs

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>New Drug</th>
<th>New Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynecology</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Breast</td>
<td>22</td>
<td>14</td>
</tr>
<tr>
<td>Endocrine</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Leukemia</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Lung</td>
<td>42</td>
<td>10</td>
</tr>
<tr>
<td>Lymphoma &amp; Myeloma</td>
<td>21</td>
<td>25</td>
</tr>
<tr>
<td>Melanoma</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Neurological</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Note: These numbers include drugs that are in both phase 2 and phase 3 trials. Phase 3 trials are estimated to be complete in or around 2016 to 2020. These numbers are estimates only and may be subject to regulatory delays, or the manufacturer may decide not to pursue licensing and marketing in Canada. “Drug-indication pairs” means a particular drug prescribed for a particular indication. In certain cases, a drug manufacturer may provide a submission with more than one drug-indication pair for a particular drug product.

pCODR continues to watch for treatment trends, such as the use of companion diagnostics. As of March 31, 2016, there were 12 different companion diagnostics linked to 33 individual cancer drugs and 44 cancer drug-indication pairs on the horizon.
The pCODR program will continue to assess its performance and report back to its stakeholders each year. Created to bring consistency and clarity to the assessment of cancer drugs, pCODR’s continued efforts have contributed to a more transparent and rigorous review system.
APPENDIX A: Priority Review

Submissions to the CADTH pan-Canadian Oncology Drug Review (pCODR) process are reviewed in the order they are received (i.e., first come, first served). However, at time of filing, a submitter may request that their submission be assessed to determine whether it meets priority review criteria. Request for priority review must be initiated by a manufacturer or tumour group. The request is assessed by a three-person panel consisting of the pCODR Expert Review Committee (pERC) Chair, the pERC Vice-Chair, and one additional pERC member, according to the following clinically based criteria:

- A new oncology drug, or an oncology drug with a new indication and employed for the active treatment of cancer, where use offers potential substantial improvements on significant outcomes, such as (but not limited to):
  - Improved overall survival in the adjuvant setting; or
  - Elimination or substantial reduction of treatment side effects associated with standard of care; or
  - Measurable and substantial improvements in quality of life over other available therapies in Canada

OR

- A new oncology drug, or an oncology drug with a new indication and employed for the active treatment of cancer, where no other comparable drug or treatment is currently marketed in Canada.

What Is pCODR’s Experience With Priority Requests?

To date, pCODR has assessed 16 requests for priority review. Priority status has been granted for 10 of the 16 requests.

For submissions that were granted priority review:
- There were no other viable treatment options available in Canada, and the drug or indication demonstrated some certainty in the magnitude of benefit in the outcomes of interest.
- There was certainty in the magnitude of benefit in the outcomes of interest, and the magnitude of benefit was substantial compared with currently available treatments.

For submissions that were not granted priority review:
- The pivotal studies provided by the submitter required further in-depth analyses (i.e., a full review) to reduce uncertainty in the results (e.g., subgroup analyses, non-validated surrogate outcomes).
- The magnitude of improvement in outcomes of interest was not considered to be sufficient to warrant priority status over other submissions, given other relevant available treatments.
APPENDIX B: Submissions by Route of Administration and Tumour Type

Figure B1: Submissions by Route of Administration

Note: Submissions received as of March 31, 2016.

Figure B2: Submissions by Tumour Type

Top submissions were for melanoma, leukemia, lymphoma & myeloma as of March 31, 2016