pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Pembrolizumab (Keytruda) for Nonsquamous Non-Small Cell Lung Cancer

May 31, 2019

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TABLE OF CONTENTS

1 ECONOMIC GUIDANCE IN BRIEF

1.1 Submitted Economic Evaluation

The economic analysis submitted to pCODR by **Merck,** compared KEYTRUDA® (pembrolizumab), a high affinity antibody against programmed-death-receptor-1 (PD-1) that inhibits the PD-1 receptor and modulates anti-tumour immunity. Pembrolizumab has been issued marketing authorization without conditions for the treatment of metastatic non-squamous NSCLC in combination with pemetrexed and platinum chemotherapy in adults with no EGFR or ALK genomic tumour abberations and no prior systemic chemotherapy treatment for metastatic NSCLC.

Table 1. Submitted Economic Model

Funding Request	Merck is requesting Pembrolizumab in combination with pemetrexed and platinum chemotherapy, for the treatment of metastatic non-squamous NSCLC, in adults with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC. This aligns with the patient population that the economic model is built on.
Type of Analysis	Cost effectiveness and cost utility analysis
Type of Model	Partitioned-survival model
Comparator	The primary comparison in the model evaluates initial treatment with: •Pembrolizumab 200 mg once every 3 weeks, for up to 24 months, plus Carboplatin 550 mg or Cisplatin 75 mg/m^2, every 3 weeks for 4 cycles, and Pemetrexed 500 mg/m^2 every 3 weeks for 4 cycles, followed by maintenance Pemetrexed Versus •Carboplatin 550 mg or Cisplatin 75 mg/m2, every 3 weeks for 4 cycles, and Pemetrexed 500 mg/m^2 every 3 weeks for 4 cycles, followed by maintenance Pemetrexed
Year of cost	2018
Time Horizon	10-years
Perspective	Publicly funded health care system in Canada
Cost of pembrolizumab	• 100 mg vial at $4,400.00 • 50 mg vial at $2,200.00 • Cost per dose $8,000.00
Cost of chemotherapy	• Carboplatin costs $18.80 per 150 mg vial • Cisplatin costs $9.50 per 50 mg vial or $19.00 per 100 mg vial • Pemetrexed costs $0.83 per mg
Model Structure	The model was comprised of 3 health states: pre-progression, progression (or post-progression), and death.

Key Data Sources	The model effectiveness parameters in the primary analyses were estimated from KN189 patient-level data for time on treatment (ToT), PFS based on blinded independent central review (BICR) and OS. These parameters are included within the model for the overall trial population as well as sub-groups of patients with PD-L1 TPS <50%. The submitter provided analyses for the overall trial population in the base case as well as for the PD-L1 TPS ≥50% and <50% sub-groups in scenario analyses. As an overall modeling approach, parametric models were fit to KM ToT, PFS and OS data to extrapolate outcomes over the model time horizon.

1.2 Clinical Considerations

According to the pCODR Clinical Guidance Panel (CGP), the comparison with pemetrexed and platinum chemotherapy is appropriate. Relevant issues identified included:

- There is a net overall clinical benefit from the addition of pembrolizumab to platinum-pemetrexed chemotherapy in patients with advanced / metastatic non squamous NSCLC. As of the November 8, 2017 data cut-off date, the median follow-up duration was 10.5 months. The OS survival data are still immature. However, the Keynote 189 trial demonstrates clear improvement in both OS (median OS not reached vs 11.3 months, HR 0.49, 95%CI 0.38-0.64) and PFS (median PFS 8.8 vs 4.9 months, HR 0.52, 95%CI 0.43-0.64) for pembrolizumab plus chemotherapy, versus platinum-pemetrexed chemotherapy alone.
- Secondary efficacy parameters including ORR and quality of life were significantly improved for patients receiving the combination of pembrolizumab plus chemotherapy. These improved efficacy outcomes have an acceptable safety profile. The AE profile is largely driven by expected chemotherapy AEs, which are similar between the two groups. There are expected immune related AEs that oncologists are already familiar with managing.
- Non squamous NSCLC represents a significant health burden. Estimates are that over 4000 patients annually across Canada might benefit from the addition of pembrolizumab to platinum and pemetrexed chemotherapy. Therefore this new option for treatment has the potential to improve on a significant unmet need.
- Currently, patients with tumors with high PD-L1 expression (≥ 50%) would receive pembrolizumab in the first line setting. Keynote 189 provides another option for the treatment of this population of patients. There are no randomized trials to address the question of pembrolizumab alone versus pembrolizumab plus chemotherapy in this patient group. An indirect treatment comparison (ITC) was provided suggesting improved efficacy for the combination of pembrolizumab plus chemotherapy. However, the corresponding confidence intervals crossed the null hypothesis value, indicating statistical non-significance. Therefore, the relative efficacy of pembrolizumab plus chemotherapy over pembrolizumab remains uncertain. Both treatments are superior to chemotherapy alone and should be available to clinicians to choose based on individual patient needs and preferences as outlined in the physician input to this review.
- The original Keynote 10 trial used weight based dosing for pembrolizumab, at a dose of 2mg/kg. Subsequent trials of pembrolizumab have adopted a fixed dose of pembrolizumab at 200mg including Keynote 189. The CGP would strongly recommend pembrolizumab be used as per the evidence i.e. 200mg flat dosing. Keynote 10 also evaluated pembrolizumab 10mg/kg and the best OS numerically, was seen in this arm. However, the CGP recognize that prior decisions regarding pembrolizumab have recommended pembrolizumab dosing at 2mg/kg up to a maximum of 200mg.

Summary of registered clinician input relevant to the economic analysis

- The clinicians providing input generally agreed that the combination of pembrolizumab and pemetrexed/platinum-based chemotherapy would be a suitable first line option for all non-squamous (NSQ) NSCLC patients with low expression of PD-L1, as well as for those with high expression of PD-L1 who are eligible for pembrolizumab monotherapy but may benefit from a rapid therapeutic response. According to the clinicians, the combined use of chemotherapy and immunotherapy addresses a therapeutic gap whereby one would usually have to risk a worsening condition after progression on one therapy before trying the other. It is felt that the availability of first line immunotherapy independent of PD-L1 expression increases equity in patients who have no PD-L1 results and those unfit for second line therapy. Safety and tolerability were not seen as major issues by clinicians. They maintained that both combination and monotherapy options should remain available for NSQ NSCLC patients, but agreed that the sequence of therapies should favour first line pembrolizumab therapy (alone or combined with chemotherapy, as determined by PD-L1 status and patient preference) moving forward.

Summary of patient input relevant to the economic analysis

- Patient input indicated that the key treatment outcomes that respondents would most like to address are: to stop or slow the progression of the disease, to reduce or eliminate side effects (e.g., reduce pain, fatigue, cough and shortness of breath), and to improve appetite and energy. Respondents additionally indicated that they would value improved independence and requiring less assistance from others. They would also like there to be less or no cost burden associated with new treatments.

- Pembrolizumab in combination with chemotherapy was seen as an aggressive therapeutic approach for a variety of clinical presentations. It was mentioned that it may be an attractive option for patients wishing to benefit from first line immunotherapy without being limited by tumour PD-L1 expression, and that anticipated side effects would be acceptable to many in view of the promises of gains in length and quality of life.

Summary of Provincial Advisory Group (PAG) input relevant to the economic analysis
PAG considered the following factors important to consider if implementing a funding recommendation for pembrolizumab which are relevant to the economic analysis:

- The dose of pembrolizumab is a fixed dose of 200mg for NSCLC and in the KEYNOTE-189 trial. PAG noted that pembrolizumab for first- and second-line NSCLC can be administered at 2 mg/kg up to a total dose amount of 200 mg (dose capped at 200 mg). Although fixed dose would minimize drug wastage, PAG is seeking guidance on weight-based dosing of 2 mg/kg up to a flat dose cap of 200 mg in this setting, given the high cost of fixed dose compared to weight based dose for patients weighing less than 100 kg. The economic analysis only considered the flat dose of pembrolizumab. There was no option to explore the impact of weight-based dosing.
- Pembrolizumab, being an intravenous drug, would be administered in an outpatient chemotherapy center for appropriate administration and monitoring of toxicities. Intravenous chemotherapy drugs would be fully funded in all jurisdictions for eligible patients, which is an enabler for patients.
- Additional health care resources would be required for pre-medication, drug preparation, chair time and monitoring for toxicities such as immune-mediated reactions post-infusion.

Treatment with pembrolizumab, particularly maintenance treatment up to 2 years, would require increased nursing resources, pharmacy resources, clinic visits given treatment is every three weeks, chair time, blood work, laboratory testing (e.g., TSH, cortisol), and supportive care drugs (e.g., vitamin B12, folic acid).

- Re-treatment of pembrolizumab was permitted in the trial following the completion of 35 cycles of treatment if a patient were to relapse. The economic analysis applies a maximum treatment duration of 35 cycles for pembrolizumab (2 years). The impact of re-treatment was not explored directly in the economic analysis. Yet, the submitted model accounts for 7.2% of patients in the pembrolizumab plus chemotherapy arm that received pembrolizumab in the second line as post-discontinuation therapy.
- Sequencing of all available treatments for NSCLC is uncertain. Subsequent lines of therapy after treatment discontinuation was estimated from the Keynote-189 trial. The costs of subsequent therapies are included in the model, however clinical effect could not be altered.

1.3 Submitted and EGP Reanalysis Estimates

The main assumptions and limitations with the submitted economic evaluation were:

The main economic evaluation was conducted using a chemotherapy (pemetrexed and platinum) comparator group as per Keynote 189 trial. Two sensitivity analyses have been submitted for additional comparators: pembrolizumab monotherapy (KN024), and Carboplatin or Cisplatin in combination with Docetaxel or Gemcitabine or Paclitaxel or Pemetrexed or Vinorelbine. These estimations have been obtained by conducting: 1) an indirect treatment comparison (ITC) and 2) a network-meta analysis (NMA), summarized below:

1) **ITC**: An indirect comparison of pembrolizumab-chemotherapy (KN189) and pembrolizumab monotherapy (KN024) was performed using the Bucher method after adjusting trial populations and treatment arms with inverse probability of treatment weighting (IPTW) methodology. The ITC was conducted in a subset of patients from KN189 (n=202) and KN024 (199), i.e. in patients with TPS ≥50%, NSQ histology and chemotherapy with carboplatin/cisplatin + pemetrexed. The submitter noted that the ITC was not powered to demonstrate a statistically significant difference between pembrolizumab-chemotherapy and pembrolizumab monotherapy, but the analysis suggests a numerical benefit in OS with the combination of pembrolizumab-chemotherapy versus pembrolizumab monotherapy in non-squamous NSCLC with PD-L1 TPS≥50%, and without EGFR mutation and ALK translocation. However, these results are statistically non-significant. Therefore, the relative efficacy of pembrolizumab + chemotherapy over pembrolizumab monotherapy remains uncertain in the patient population of interest.

2) **NMA**: The submitter conducted a systematic review of the literature and an NMA to provide estimates of the relative treatment effect (OS and PFS) between pembrolizumab + platinum-pemetrexed chemotherapy and competing interventions for the 1st line treatment of metastatic NSCLC in patients with non-squamous histology who are EGFR mutation and ALK translocation negative.

   The submitted NMA concluded that in the patient population of interest, pembrolizumab + chemotherapy could be superior to most competing interventions in terms of OS and PFS except for the atezolizumab regimen and other pembrolizumab regimens. There was some

degree of heterogeneity in effect modifiers between trials. These results should be interpreted with caution due to limitations that may arise from between-study differences in some covariates; and lack of sufficient evidence to minimize heterogeneity and inconsistency (e.g., by performing meta-regression analysis).

In summary, the key assumptions that have the most impact on the results of the main economic evaluation (comparing pembrolizumab plus pemetrexed and platinum versus pemetrexed and platinum) are: the difference in OS between groups (adjusted or not for post-progression treatment crossover), the clinical benefits after the trial period (maintained or declined after 2-year period) and the time horizon. Utility values by health states versus by time-to-death method have a moderate impact on this economic evaluation, while the extrapolation methods used have only a slight impact. Finally, the submitted model assumed a fixed dose of pembrolizumab, and as such, a drug wastage scenario had only a limited impact in this economic evaluation. Time on treatment extrapolation model has a moderate impact on the ICER. Accounting for the cost of second-line anti-PD1 therapies prescribed to patients in pembrolizumab plus chemotherapy group has only a minor impact on the ICER.

1) OS benefit and adjustment for crossover: In the KN189 trial, a total of 41.3% of patients in the chemotherapy arm switched to an anti-PD1/PD-L1 therapy (33.5% pembrolizumab alone and 7.8% nivolumab alone). The base case analysis of the model utilizes overall survival for the chemotherapy arm without a switching adjustment. The CGP and EGP considered this appropriate, as it is reflective of the current clinical practice: Pembrolizumab is approved for patients with metastatic NSCLC whose tumors express PD-L1 (tumor proportion score [TPS] ≥1%), with disease progression on or after platinum-containing chemotherapy and nivolumab is approved in the same setting for all levels of expression of PD-L1. However, a 2-stage adjustment method was integrated into the provided model. The EGP performed a re-analysis that has a moderate impact on the ICER.

2) OS benefit and decline of the clinical benefit beyond the trial period: Although different parametric models have been provided through the submitted model to estimate the survival benefit after the trial period, only one scenario was available to alter this beyond the trial period. So, a decline of pembrolizumab clinical benefit after 2-year trial period and up to 5-years was considered as a scenario analysis. This had a moderate effect on the ICER.

3) Time-horizon: The submitted base-case was based on a time horizon of 10 years. The CGP and EGP considered that a time horizon of 10 years was appropriate. However, the EGP notes that the median follow-up of this trial was of only 13 months, and there is uncertainty related to the maintenance of the clinical benefit over the 2-year trial period. The submitted model allowed the EGP to evaluate the impact of different time horizons by performing several re-analyses. Time-horizon had a moderate impact on the ICER.

4) Utility values: The CGP and EGP agreed that the utilities derived from the trial and used by the submitter by time to death in the base-case scenario are appropriate. This is in accordance with some prior pCODR recommendations in similar immunotherapy treatments. Nonetheless, the EGP conducted several re-analyses using the utility values estimated by progression status, which allows better comparability with other submissions, as utilities estimated by progression status are commonly used in submissions involving similar populations.

5) Extrapolation models: Several parametric models have been provided within the submitted model in order to extrapolate the PFS and OS beyond the trial period over the specific time horizons. The impact on the ICER of the many alternative extrapolation methods that were tested was low.

6) Dose of pembrolizumab: The EGP noted that a flat dose of 200 mg was used in this economic model for pembrolizumab, and no re-analysis was possible for this input. Moreover, the drug wastage scenario has only a limited impact in this economic evaluation.

7) Time on treatment (ToT): The submitted model incorporates different parametric models to extrapolate the duration of treatments. The EGP conducted several re-analyses that have moderate to low impact.

8) Cost of post-progression therapies: The percentage of patients who receive subsequent lines of therapy after treatment discontinuation (45.8% for pembrolizumab + chemotherapy and 56.5% for chemotherapy) was estimated from the KN189 trial. While the costs of subsequent therapies are separately included in the model, OS and PFS impacts are assumed to be captured in the OS and PFS Kaplan-Meier data from the KN189 trial, without switching adjustment. According to the anti-PD1 listing criteria in Canada, second line usage of anti-PD1 is not allowed if an anti-PD1 is used in the first line. A scenario analysis was, therefore, conducted where the distributions of the post-discontinuation regimens were altered in a way such that, no patients receiving pembrolizumab plus chemotherapy received an anti-PD1 regimen as a second line therapy The patients who received an anti-PD1 drug (pembrolizumab or nivolumab) were distributed amongst the chemotherapy regimens patients received in the trial in proportion to their usage. No alterations were made to the distribution of second-line therapies in the chemotherapy arm.

Table [2a]. Submitted and EGP Estimates (Deterministic)

Estimates (range/point)	Submitted	EGP Reanalysis Lower bound	EGP Reanalysis Upper bound
ΔE (LY)	1.0	0.93	0.78
Progression-free	7.55 months	7.47	6.50
Post-progression	4.49 months	3.66	2.85
ΔE (QALY)	0.78	0.72	0.58
Progression-free	NA	NA	NA
Post-progression	NA	NA	NA
ΔC ($)	$104,117	$139,784	$113,496
ICER estimate ($/QALY)	$132,760	$194,242	$196,477

NA = Not available

Table [2b]. Submitted and EGP Estimates (Probabilistic)

Estimates (range/point)	Submitted	EGP Reanalysis Lower bound	EGP Reanalysis Upper bound
ΔE (QALY)	0.78	0.71	0.58
Progression-free	NA	NA	NA
Post-progression	NA	NA	NA
ΔC ($)	$104,117	$140,331	$112,587
ICER estimate ($/QALY)	$132,760	$196,406	$194,593

NA = Not available

1.4 Detailed Highlights of the EGP Reanalysis

The submitted economic evaluation is based mainly on valid parameters and presents extensive sensitivity analyses. The EGP performed several re-analyses by varying components of the model that were significant drivers of either the incremental effect or the incremental cost, including time-horizon, assumptions on clinical benefit beyond the trial period and adjusted for crossover and time on treatment extrapolation method.

1. The assumption of a 10 year time horizon was felt to be reasonable by the CGP. Though the CGP supported the choice of the base case time horizon, the uncertainty in this long term projection should be acknowledged as a limitation. In addition, as a main assumption in this model is that the survival benefit for pembrolizumab is maintained after the trial period, a shorter time horizon decreases the impact of this assumption. To explore uncertainty related to the maintenance of the clinical benefit over the 2-year trial period, a 5 year time horizon was used in the upper bound estimate.

2. Several re-analyses were performed to assess the impact of the PFS, OS and ToT extrapolation methods. This included adjustment methods for cross-over.

3. As KN189 trial did not provide a clinical rationale for PD-L1 testing in this population (since the survival benefit observed with pembrolizumab plus chemotherapy in this indication was independent of PD-L1 expression), there was no re-analysis conducted by EGP incorporating PD-L1 testing. However, this was included in the sub-group analysis by PD-L1 expression.

4. In the ITC used to compare pembrolizumab plus chemotherapy versus pembrolizumab monotherapy, the CGP and EGP noted that despite using valid statistical techniques to adjust trial populations and treatment arms (Bucher methods, inverse probability of treatment weighting (IPTW) methodology) and the 2-stage adjustment to account for crossover, there might still be residual differences between compared populations. In addition, this ITC analysis is potentially unpowered to detect a statistically significant difference. The submitted model did not make it possible to alter the HR for OS calculated using the ITC, which was used to estimate the clinical benefits between pembrolizumab plus chemotherapy and pembrolizumab monotherapy. The EGP considered this as an important limitation of the submitted model and concluded that there was too much uncertainty with the methodology to consider this economic analysis further in its review. As a result, the EGP did not undertake re-analysis estimates for the comparison against pembrolizumab plus chemotherapy and pembrolizumab monotherapy.

The Submitter provided feedback on the pERC Initial Recommendation disagreeing with the EGP's reanalysis. Specifically, the Submitter did not agree with the use of 2-stage adjustment for crossover for OS in the lower bound ICER estimate and the use of a 5-year time horizon in the upper bound ICER estimate. The EGP, however maintains their reanalysis estimates for the lower bound and upper bound ICER estimates.

The EGP notes that the submitted base-case was based on a time horizon of 10 years and the EGP lower bound estimate maintained the 10-year time horizon. The CGP and EGP considered that a time horizon of 10 years was appropriate. However, the EGP re-iterated that the median follow-up of the KEYNOTE-189 trial was of only 13 months, and there is uncertainty related to the maintenance of the clinical benefit over the 2-year trial period. The submitted model allowed the EGP to evaluate the impact of different time horizons by performing several re-analyses. To explore uncertainty related to the maintenance of the clinical benefit over the 2-year trial period, a 5-year time horizon was used in the upper bound estimate.

Overall, the EGP explored a cross-over adjustment and a 5-year time horizon to account for the uncertainty of the long term benefits of pembrolizumab, mainly due to the short duration of KEYNOTE-189 and the uncertainty related to the pembrolizumab benefits beyond the trial, specifically for the PE model and analysis provided for this review.

Table [3]: Detailed Description of EGP Reanalysis: Pembrolizumab in combination with pemetrexed and platinum chemotherapy versus chemotherapy				
	ΔC	ΔE (QALY)	ICER ($/QALY)	Δ from baseline submitted ICER
Baseline (Submitter's best case)	$104,117	0.78	$132,760	--
LOWER BOUND (deterministic)				
1. *OS with 2-stage adjustment for crossover*	$142,546	0.89	$159,590	$26,830
2. *Clinical benefit decline after 2-years*	$101,553	0.62	$162,772	$30,012
Best case estimate of above 2 parameters	$139,784	0.72	$194,242	$61,482
UPPER BOUND (deterministic)				
3. *5 year time horizon*	$100,362	0.62	$162,802	$30,042
4. *Time on treatment: pembrolizumab discontinued at disease progression*	$117,966	0.78	$150,420	$17,660
5. *Utilities value by progression status*	$104,117	0.74	$141,133	$8,373
Best case estimate of above 3 parameters	$113,496	0.58	$196,477	$63,717
LOWER BOUND (probabilistic, 5000 iterations)				
Best case estimate based on above 1, 2	$140,331	0.71	$196,406	$63,646
UPPER BOUND (probabilistic, 5000 iterations)				
Best case estimate based on above 3, 4, 5	$112,587	0.58	$194,593	$61,833

1.5 Evaluation of Submitted Budget Impact Analysis

The factors that most influence the budget impact analysis include number of patients eligible to be treated with pembrolizumab and the extent of market expansion.

The submitter perform several sensitivity analysis, which mainly affect the number of patients eligible to pembrolizumab plus chemotherapy.

The EGP considered the BIA assumptions and estimations to be reasonable.

1.6 Conclusions

The EGP's best estimate of ICUR for Pembrolizumab in combination with chemotherapy when compared to chemotherapy is:

- between $194,242/QALY and $196,477/QALY.
- The EGP was unable to evaluate the use of pembrolizumab at 2 mg/kg for this patient population as the base case used a flat dose of 200 mg. There is uncertainty on how weight-based dosing would impact the cost estimates.
- The extra cost of pembrolizumab is between $113,496 and $139,784. The factor that most influences the costs is duration of treatment.
- The extra clinical effect of pembrolizumab is between 0.58 QALY to 0.72 QALY. The factors that most influence the incremental clinical benefit are the time horizon, and the clinical benefits declined after 2-year period.
- The probabilistic results for the EGP's best case estimates were similar to the deterministic results.

Overall conclusions of the submitted model:

The submitted model included many appropriate assumptions and an extensive set of sensitivity analysis for the primary comparison. The ITC used to compare pembrolizumab plus chemotherapy versus pembrolizumab monotherapy comported several technical issues and the EGP considered this as an important limitation of the submitted model and concluded that there was too much uncertainty with the methodology to consider this economic analysis further in its review. Finally, pembrolizumab was evaluated at a flat dose of 200mg. The submitted model did not allow the EGP to explore the impact of different dosing schedules and no vial wastage was considered for pembrolizumab.

2 DETAILED TECHNICAL REPORT

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in Section 1. Pursuant to the *pCODR Disclosure of Information Guidelines*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations.

3 ABOUT THIS DOCUMENT

This Economic Guidance Report was prepared by the pCODR Economic Guidance Panel and supported by the pCODR Lung Clinical Guidance Panel and the pCODR Methods Team. This document is intended to advise the pCODR Expert Review Committee (pERC) regarding resource implications and the cost-effectiveness of pembrolizumab (Keytruda) non-squamous NSCLC. A full assessment of the clinical evidence of pembrolizumab (Keytruda) non-squamous NSCLC is beyond the scope of this report and is addressed by the relevant pCODR Clinical Guidance Report. Details of the pCODR review process can be found on the pCODR website (www.cadth.ca/pcodr).

pCODR considers it essential that pERC recommendations be based on information that can be publicly disclosed. Information included in the Economic Guidance Report was handled in accordance with the pCODR Disclosure of Information Guidelines. There was no information redacted from this publicly available Guidance Report.

The Final Economic Guidance Report is publicly posted at the same time that a pERC Final Recommendation is issued. The Final Economic Guidance Report will supersede the Initial Economic Guidance Report.

The Economic Guidance Panel is comprised of economists selected from a pool of panel members established by the pCODR Secretariat. The panel members were selected by the pCODR secretariat, as outlined in the pCODR Nomination/Application Information Package and the Economic Guidance Panel Terms of Reference, which are available on the pCODR website (www.cadth.ca/pcodr). Final selection of the pool of Economic Guidance Panel members was made by the pERC Chair in consultation with the pCODR Executive Director. The Economic Guidance Panel is editorially independent of the provincial and territorial Ministries of Health and the provincial cancer agencies.

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