



pan-Canadian Oncology Drug Review Final Economic Guidance Report

Bendamustine (Treanda) for Non-Hodgkin Lymphoma

November 29, 2012

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INQUIRIES

Inquiries and correspondence about the pan-Canadian Oncology Drug Review (pCODR) should be directed to:

pan-Canadian Oncology Drug Review
1 University Avenue, suite 300
Toronto, ON
M5J 2P1

Telephone: 416-673-8381
Fax: 416-915-9224
Email: info@pcodr.ca
Website: www.pcodr.ca

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1 ECONOMIC GUIDANCE IN BRIEF

1.1 Background

First-Line

The economic analysis submitted by **Lundbeck Canada Inc.** evaluated the cost-utility and cost-effectiveness of the combination of bendamustine and rituximab (BR) as **first line treatment** as follows:

- compared to R-CHOP in a mixed population of patients with advanced indolent non-Hodgkin's lymphoma (iNHL) or with Mantle cell lymphoma (MCL), which is similar to the population evaluated in the Rummel 2009 study
- compared to R-CHOP in only patients with indolent NHL
- compared to R-CVP in only patients with indolent NHL

According to the **pCODR Clinical Guidance Panel**, first line treatment of advanced indolent non-Hodgkin's lymphoma (NHL) differs by the specific type of lymphoma. In Canada, for indolent NHL, comparator therapies include both R-CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) and R-CVP (cyclophosphamide, vincristine, and prednisolone). However, in practice R-CVP is the favoured therapy because of concerns regarding the increased toxicity of the R-CHOP regimen, which includes doxorubicin. However, there are no head-to-head randomized clinical trials comparing bendamustine with R-CVP or comparing R-CHOP with R-CVP in this population. For patients with Mantle Cell Lymphoma (MCL), R-CHOP is the treatment regimen used, and this is compared with bendamustine in the Rummel 2009 randomized controlled trial.

Patient advocacy group input raised two points relevant to the economic evaluation.

- Patients report a willingness to accept side effects associated with new therapies provided their net quality of life improves. Both quality of life and adverse events are incorporated in the economic evaluation.
- They noted the impact of indolent NHL on caregivers. The submitted analysis was conducted from a Ministry of Health perspective, which does not consider societal costs such as caregiving, however, it is appropriate for pCODR.

The **Provincial Advisory Group (PAG)** raised the following points relevant to the economic analysis:

- PAG noted that it would be important to consider the costs of maintenance therapy. While the main analysis only included the cost of induction therapy (similar to how treatment was administered in Rummel et al.), submitted sensitivity analyses incorporated the costs of rituximab maintenance therapy, which is now standard clinical practice.
- While the base case assumed a dose of 90 mg/m², PAG noted that the Health Canada approved dosing of bendamustine in the relapse setting is 120mg/m² and this would be an important dosing regimen to consider. The EGP addressed this by conducting additional analyses using the higher doses of bendamustine.
- PAG noted that costs associated with the supportive use of growth factors to treat febrile neutropenia would be important to consider. The economic analysis incorporates costs of growth factors, however, based on adverse events reported in Rummel et al., bendamustine has a lower rate of grade 3/4 neutropenia than R-CHOP, and is likely also lower than R-CVP. Therefore, the EGP considered that costs of growth factors would not negatively impact the cost-effectiveness of bendamustine.

Relapse/Refractory

The economic analysis submitted by **Lundbeck Canada Inc.** evaluated the cost-utility and cost-effectiveness of bendamustine in the **relapse/refractory setting** as follows:

- compared to ibritumomab (i.e. radioimmunotherapy) in rituximab-refractory iNHL patients
- compared to best supportive care in rituximab-refractory iNHL patients
- compared to fludarabine in relapse patients with iNHL or MCL, as evaluated in the Rummel et al. 2010 Study

According to the pCODR Clinical Guidance Panel (CGP), **these comparisons are appropriate**. Currently there is no standard approach to the treatment of relapsed and refractory patients. Retreatment with CVP or CHOP (+/- rituximab), fludarabine (+/- rituximab), radioimmunotherapy and oral alkylating agents (chlorambucil or cyclophosphamide) have all been used in the relapsed/refractory setting. The only RCT evaluating bendamustine in this setting compares bendamustine plus rituximab with fludarabine plus rituximab (Rummel et al., 2010) in patients with relapse iNHL or MCL. In the case of the refractory analysis, the choice of BSC as a supplementary analysis is supported by the observation that radioimmunotherapy is not offered in many hospitals and there may be associated toxicities.

Patient advocacy group input considered the following factors important, which are relevant to the economic analysis: extending either quantity or quality of life; a willingness to trade-off disutility associated with adverse events provided they yield significant benefits; willingness to travel for treatment.

- Quality of life and time spent progression-free are considered in the model
- Patients' concerns with symptoms are adequately incorporated into the model, particularly fatigue.
- Patients sometimes report significant travel in order to receive care. This point is particularly relevant in the case of refractory iNHL. While radioimmunotherapy may not be accessible in all jurisdictions, patients' willingness to travel may enhance its accessibility for some patients. On the other extreme, BSC could be considered a suitable treatment option in some patients during the course of their disease.

The **Provincial Advisory Group (PAG)** considered factors related to bendamustine dosing and implementation costs. In addition to dosing, the PAG raised concerns regarding that bendamustine would increase total costs and budget impact as it could be viewed as an additional treatment (as opposed to a substitute treatment in the respective settings).

At the list price, bendamustine costs \$312.50 per 25 mg vial and \$1250.00 per 100 mg vial. At the recommended dose in the relapse setting of 120 mg/m² IV on days 1, 2 and every 21 days, the average cost per day in a 28-day course is \$182.12 and the average cost per 28-day course is \$5100.00.

1.2 Summary of Results

First-Line

The Economic Guidance Panel's estimate of the incremental cost-effectiveness ratio ranged from \$ 35,081/QALY to \$ 94,071/QALY, depending on the comparator and the patient population considered. These estimates were based on the model submitted by Lundbeck Canada Inc. and reanalyses conducted by the Economic Guidance Panel with a shorter time horizon and increased bendamustine dose. **However, the EGP considered that their best estimates were seriously limited by the submitted model and uncertainty in the data given the lack of individual patient level data and trials with appropriate direct comparisons and estimates compared with R-**

CHOP could be between \$140,000 and \$155,000 per QALY when considering probabilistic sensitivity analyses. The EGP suggests that the same degree of uncertainty likely exists for comparisons with R-CVP.

The incremental cost-effectiveness ratio was based on an estimate of the extra cost (ΔC) and the extra clinical effect (ΔE). More specifically, the EGP's best estimates were that:

- For BR vs R-CHOP in a mixed iNHL/MCL Population: the extra cost (ΔC) is \$23,131, the extra effect (ΔE) is 0.2459 and so the incremental cost-effectiveness ratio ($\Delta C / \Delta E$) is \$94,071 per QALY
- BR vs R-CHOP in only the iNHL Population: the extra cost (ΔC) is \$24,307 and the extra effect (ΔE) is 0.297 and so the incremental cost-effectiveness ratio ($\Delta C / \Delta E$) is \$81,935 per QALY
- BR vs R-CVP in only the iNHL Population: the extra cost (ΔC) is \$17,889 and the extra effect (ΔE) is 0.510, so the incremental cost-effectiveness ratio ($\Delta C / \Delta E$) is \$35,081 per QALY.
- The EGP considered that their best estimates were seriously limited by the inherent uncertainty associated with the lack of appropriate RCTs, the lack of individual patient level data and uncertainty regarding the utility of progressive NHL. To address these data concerns, the EGP suggests that in the comparisons to R-CHOP in the mixed iNHL/MCL and iNHL only populations that the upper end (95%CI) of the ICER from the Submitter's probabilistic sensitivity analysis be considered. This estimate of uncertainty would add another \$60,000 per QALY to the reanalyzed ICERs. Therefore, when compared with R-CHOP, the ICER for BR could be as high as \$155,000 per QALY in a mixed iNHL/MCL population or \$140,000 per QALY in an iNHL population. Probabilistic sensitivity analyses suggested that a similar adjustment for BR vs R-CVP is not required, however, the EGP would suggest that the same degree of uncertainty is likely to exist in this setting given the very limited data in this setting.

The reanalyses conducted by the EGP using the submitted model showed that:

- Using a 120 month time horizon (vs. 68 months as applied in the EGP's best estimates or vs. 240 months used in the main analysis by the submitter) results in an ICER of \$60,609 per QALY for the comparison of R-CHOP in the mixed iNHL/MCL population, \$54,004 per QALY for the comparison with R-CHOP in the iNHL only population and \$19,746 per QALY for the comparison with R-CVP in the iNHL only population.
- Increasing the dose of bendamustine from 90mg/m² to 120mg/m² has a significant impact on the ICER, resulting in \$81,514 per QALY for the mixed iNHL/MCL population; and \$73,917 per QALY or \$34,493 per QALY (vs R-CHOP and R-CVP, respectively) for the iNHL only population.
- Reanalysis of scenarios other than increased dose and time horizon did not result in significant changes to the ICER.

The EGPs estimates were substantially higher than the submitted estimates. This is because the reanalysis conducted by the EGP was based on a shorter time horizon, an increased bendamustine dose and uncertainty in the model and data, which was accounted for by adopting the 95th confidence interval arising from the submitted probabilistic sensitivity analysis.

According to the economic analysis that was submitted by the manufacturer:

- For BR vs R-CHOP in a mixed iNHL/MCL Population: the extra cost (ΔC) is \$16,014, the extra effect (ΔE) is 0.300 and so the incremental cost-effectiveness ratio ($\Delta C / \Delta E$) is \$53,418 per QALY
- BR vs R-CHOP in only the iNHL Population: the extra cost (ΔC) is \$17,009 and the extra effect (ΔE) is 0.345 and so the incremental cost-effectiveness ratio ($\Delta C / \Delta E$) is \$49,365 per QALY

- BR vs R-CVP in only the iNHL Population: the extra cost (ΔC) is \$12,145 and the extra effect (ΔE) is 0.588, so the incremental cost-effectiveness ratio ($\Delta C / \Delta E$) is \$20,646 per QALY.

Relapse/Refractory

In the **relapse** treatment setting, the Economic Guidance Panel's best estimate of the incremental cost-effectiveness ratio is **\$41,613 per quality-adjusted life year** when bendamustine is compared with **fludarabine**. The EGP based these estimates on the model submitted by Lundbeck Canada Inc. and reanalyses conducted by the EGP where the time horizon was shortened. **However, the EGP noted that these estimates were subject to substantial uncertainty given the lack of patient level data available for the analysis and may, in fact, be higher.**

The reanalysis conducted by the EGP using the submitted model showed that:

- Using a time horizon of 100 months (versus 200 months in the submitted analysis) results in an ICER of \$45,949 per QALY.
- As in the case of the evaluation for bendamustine in the first-line treatment, the effect on quality of life is derived from a delay in progression.

In the **refractory** treatment setting, the Economic Guidance Panel's best estimate of the incremental cost-effectiveness ratio is **\$50,134 per quality-adjusted life year** when bendamustine is compared with **radioimmunotherapy**. The EGP based these estimates on the model submitted by Lundbeck Canada Inc. and reanalyses conducted by the EGP where the time horizon was shortened. **However, the EGP noted that these estimates were subject to substantial uncertainty given the lack of randomized controlled trials in this setting and the lack of patient level data available for the analysis and may, in fact, be higher.**

The EGP remains critical of these best estimates given the lack of clinical data informing them and would suggest that the same degree of uncertainty as existed in the first-line setting, also exists in the relapse and refractory settings.

According to the economic analysis that was submitted by the manufacturer:

- In the **relapse** treatment setting, compared with **fludarabine**, the incremental cost-effectiveness ratio was \$38,821 ($\Delta C = \$30,781$ and $\Delta E = 0.79$)
- In the **refractory** treatment setting, compared with **radioimmunotherapy**, the incremental cost-effectiveness ratio was \$35,490 ($\Delta C = \$7,201$ and $\Delta E = 0.203$)
- In the **refractory** treatment setting, compared with **best supportive care**, the incremental cost-effectiveness ratio was \$[REDACTED] ($\Delta C = \$[REDACTED]$ and $\Delta E = [REDACTED]$) (*Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed*).

1.3 Summary of Economic Guidance Panel Evaluation

If the EGP estimates of ΔC , ΔE and the ICER differ from the Submitter's, what are the key reasons?

First-Line

The EGP estimates differed from those of the submitter due to a shorter time horizon (68 months versus lifetime), increased drug dosage and attempts to account for uncertainty in the analyses. The upper bound of the 95% confidence interval from the submitted probabilistic sensitivity analysis were adopted to compensate for the lack of appropriate RCT and individual data. A 68 month time horizon was selected to align with the observed study period in Rummel et al.

Relapse/Refractory

The key limitation of the models stems from the lack of any randomized trials evaluating bendamustine in the refractory treatment setting, inaccessibility of radioimmunotherapy for some patients and reliance on best supportive care in the refractory treatment setting, and lack of patient-level data for both the refractory and relapse analyses. In addition, the limited time period for which clinical data were available required extrapolation which was not viewed favorably by the EGP, thereby necessitating adoption of a more reasonable time horizon.

Were factors that are important to patients adequately addressed in the submitted economic analysis?

First-Line

The economic evaluation adequately took into account the perspective provided by the patient advocacy group input. Patients' willingness to tolerate and trade-off the increased toxicity of R-CHOP as compared to R-CVP could be further examined in future. However, adverse event rates for BR versus R-CVP or R-CHOP versus R-CVP from direct comparisons are not available.

Relapse/Refractory

The submission adequately took into account the perspective provided by the patient advocacy group input.

Is the design and structure of the submitted economic model adequate for summarizing the evidence and answering the relevant question?

First-Line

A partitioned survival analysis model with three separate health states was employed: progression-free NHL, progressive NHL and death. It is uncertain if the structure of the economic model is adequate and there are serious concerns with the lack of patient level clinical data and appropriate RCTs, which results in substantial uncertainty in the ICERs from the submitted model.

Relapse/Refractory

The design and structure of the submitted Markov model appear adequate for the analyses and are consistent with the literature and standard economic practice. However, the lack of appropriate trial and patient level clinical data in the case of relapse and refractory settings limits the analyses.

For key variables in the economic model, what assumptions were made by the Submitter in their analysis that have an important effect on the results?

First-Line

The deterministic sensitivity analysis suggested that time horizon, utility estimates and rituximab maintenance therapy were important assumptions in the model.

For BR vs R-CHOP in the mixed iNHL/MCL population, the time horizon was truncated at 68 months, which was the observed study period for Rummel et al., resulting in an ICER of \$[REDACTED]/QALY. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).* This result reflects the fact that the ICER is largely driven by the increased PFS beyond the time period for which clinical benefit had been observed (68 months). The extrapolation techniques were appropriate however in need of cautious interpretation. A sensitivity analysis of 120 months (ICER of \$[REDACTED] /QALY) provided by the submitter serves as a halfway point between the observed study period (68 months) and the lifetime horizon (240 months) used in the main analysis. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).*

Because no survival benefit was demonstrated for BR vs R-CHOP in the Rummel et al. study, no survival benefit was modeled in the economic analysis. Therefore, the results are strongly driven by the quality of life assumptions. The main analysis uses utility estimates (0.618 95% CI 0.51 to 0.73) for progressive disease derived from EQ-5D data collected in a previous study (Pettengell et al., Ray et al.). The sensitivity analyses submitted by the manufacturer only consider utility value at the lower end of the confidence interval (0.500) which produces a more favourable ICER of \$[REDACTED] per QALY (vs. R-CHOP, mixed iNHL/MCL population) compared with \$53,418 per QALY at a utility value of 0.618. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).* However, the EGP also considered utility values at the upper end of confidence interval (0.73), the ICER increases to \$[REDACTED] per QALY. Modest differences were noted when varying the utilities associated with adverse events. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).*

The Clinical Guidance Panel suggested that in clinical practice, rituximab maintenance therapy is used with dosing every 2-3 months for up to 2 years. Including the cost of maintenance therapy resulted in an increase in the ICER to \$[REDACTED]/QALY for the comparison with R-CHOP in the mixed iNHL/MCL population. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).*

Similar changes in variables and magnitudes of changes were observed for BR versus R-CHOP in the iNHL only population. With the exception of time horizon, the same holds true for the analysis of BR versus R-CVP in the iNHL only population. However, in the iNHL only population, the parameters used to model PFS could produce significant changes in the model. This is particularly important to note as there are no head-to-head trials or individual patient level data to support the PFS estimates used in the analysis versus R-CVP in the iNHL only population.

Relapse/Refractory

With the exception of time horizon, the assumptions for the model were conservative. It should be noted that the price of bendamustine has a significant impact on the ICER in the case of the refractory setting. However, the lack of appropriate RCT and individual data were viewed unfavorably by the EGP.

Were the estimates of clinical effect and costs that were used in the submitted economic model similar to the ones that the EGP would have chosen and were they adequate for answering the relevant question?

First-Line

No, the estimates of clinical effect were not adequate. The economic model relies primarily on data obtained from Rummel 2009. However, Rummel's study is a randomized phase III evaluation of BR as compared to R-CHOP. These data are inadequate for comparison with R-CVP, especially as there are no trials directly comparing R-CHOP with R-CVP to contribute to a formal indirect comparison. In addition, the Rummel study consisted of both MCL and iNHL patients and data were not available for each subgroup separately (i.e. MCL and iNHL). Furthermore, the lack of patient level data available for the analyses leads to considerable uncertainty in the analyses for both R-CHOP and R-CVP and were not adequate.

To account for the inherent uncertainty associated with the lack of appropriate RCTs, lack of individual data and uncertainty regarding the utility of progressive NHL contributes to a high degree of uncertainty in comparisons of BR to R-CHOP in the mixed and indolent populations. In essence, the 95% confidence interval from the probabilistic sensitivity analysis constitutes a 'best guess.' Another \$60,000/QALY (and rounding to the nearest \$5,000) could then be added to the base case ICERs for the comparison with R-CHOP. Probabilistic sensitivity analyses suggested that a similar adjustment was not required for BR versus R-CVP.

In consultation with the pCODR Clinical Guidance Panel, it was considered that a shorter time horizon (68 months) and a higher dose of bendamustine (120mg/m²) may be more appropriate than the estimates provided by the submitter.

Relapse/Refractory

No, the estimates of clinical effect were not adequate. There are no randomized controlled trials evaluating bendamustine in the refractory setting and individual patient data were not available for either the analysis in the refractory setting or the relapse setting. In addition, the Economic Guidance Panel suggested a decrease in the time horizon from 200 months to 100 months, which resulted in comparable decreases in both clinical effects and costs.

1.4 Summary of Budget Impact Analysis Assessment

What factors most strongly influence the budget impact analysis estimates?

In both the first-line setting and the relapse/refractory setting, a number of assumptions were evaluated through the use of sensitivity analysis: (1) market share rate (2) prevalence rate (3) proportion of prevalent cases treated as first-line (4) percentage of prevalent cases treated as active (5) number of rituximab cycles (6) bendamustine dose (Relapsed/refractory 120mg/m²; First-line 90mg/m²).

Of these factors, only the number of rituximab cycles does not have a significant impact on budget, because it is expected to be used equally with bendamustine or with the comparators of CHOP or CVP.

The base case assumed a dose of 90mg/m² for first line and 120mg/m² for secondary settings. With the exception of the BR dosage and reduction of rituximab cycles, all other parameters were varied by an arbitrary █%. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).*

What are the key limitations in the submitted budget impact analysis?

A number of limitations were identified in the budget impact analysis:

- Drug wastage was not considered, however, it is not likely to have a significant impact given that bendamustine is available in two vial sizes.
- Market share estimates may be uncertain. For comparators, they are based on drugs dispensed on the basis of multiple indications. There is no data available for the estimation of increase in bendamustine market share.
- The choice of █% for variation in underlying parameters used in the majority of sensitivity analyses is not justified. *(Non-disclosable information was used in this pCODR Guidance Report and the manufacturer requested this information not be disclosed pursuant to the pCODR Disclosure of Information Guidelines. This information will remain redacted until notification by manufacturer that it can be publicly disclosed).*
- Sensitivity analyses were not provided with respect to the prices of bendamustine and its comparators. As in the case of dose however, the variation in total costs are expected to be proportional to the variations in drug prices. In other words a 10% decrease in the price of bendamustine should result in approximately 10% lower incremental costs.
- Finally, only univariate sensitivity analysis were conducted. Multivariate sensitivity analyses simultaneously accounting for differences in drug wastage, market share and drug prices could lead to much higher estimates of budget impact.

1.5 Future Research

What are ways in which the submitted economic evaluation could be improved?

First-Line

- Use of direct comparative RCT data for BR to R-CVP (BRIGHT trial data when available)
- Introduction and use of individual level patient data
- Further analysis of utilities associated with progressive NHL

Relapse/Refractory

- Use of comparative randomized controlled trial data in refractory setting
- Consideration of other active comparators in the refractory setting
- Introduction and use of individual level patient data

Is there economic research that could be conducted in the future that would provide valuable information related to Bendamustine (Treanda) for iNHL?

First-Line

No prior economic evaluation has been completed comparing cost and clinical effect of BR to either R-CVP or R-CHOP. Rather the submission demonstrates that the bulk of economic analysis

has focussed on the addition of rituximab to CVP and CHOP. In future, when the data are available, an economic analysis of the data from the BRIGHT trial would considerably enhance our understanding our assessment of the clinical and economic effectiveness of bendamustine relative to R-CVP.

Relapse/Refractory

The primary limitation in this study could be addressed thorough the generation of appropriate clinical trial data for bendamustine and its comparators in both settings, in the Canadian context and an economic analysis based on individual patient level data.

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 Lymphoma 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 Bendamustine (Treanda) for iNHL. A full assessment of the clinical evidence of Bendamustine (Treanda) for iNHL 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.pcodr.ca).

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. The manufacturer, as the primary data owner, did not agree to the disclosure of some economic information, which was provided to pERC for their deliberations and has been redacted in this publicly available Guidance Report.

This Final Economic Guidance Report is publicly posted at the same time that a pERC Final Recommendation is issued. The Final Economic Guidance Report supersedes the Initial Economic Guidance Report. Note that no revisions were made in between posting of the Initial and Final Guidance Reports.

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.pcodr.ca). 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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