PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Dabrafenib (Tafinlar) in Combination with Trametinib (Mekinist) for Metastatic Melanoma

July 21, 2015

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FUNDING

The pan-Canadian Oncology Drug Review is funded collectively by the provinces and territories, with the exception of Quebec, which does not participate in pCODR at this time.

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1 ECONOMIC GUIDANCE IN BRIEF

1.1 Background

The main economic analysis submitted to pCODR by GlaxoSmithKline (GSK) compared dabrafenib and trametinib in combination as first-line treatment of unresectable or metastatic melanoma in patients with BRAF V600 positive mutation in comparison to the following monotherapies: vemurafenib, dabrafenib, trametinib, ipilimumab, and dacarbazine. Dabrafenib and trametinib in combination are both administered orally. For the monotherapies, dabrafenib, trametinib and vemurafenib are administered orally. Ipilimumab and dacarbazine are both administered intravenously.

According to the pCODR Clinical Guidance Panel (CGP), the comparison of dabrafenib and trametinib combination therapy in comparison to the aforementioned monotherapies was appropriate. There were two analyses conducted, the primary analysis which did not consider a class effect for the two BRAF inhibitor treatments, dabrafenib and vemurafenib, which have the same mechanism of action, and the secondary analysis which did consider a class effect for these two treatments. The class effect permitted for a pooling of results of data from the trials of combination therapy (i.e., Combi-V(1), Combi-D(2, 3) and BRF113220(4)). This pooling may yield a more precise estimate of the effect of combination vs. monotherapy in a statistical analysis.

The following modifications to the main analysis by the Submitter included the following:

i) Model timeframe was modified to 8 and 10 years from a time horizon of 5 years.
ii) Four modelling distributions were examined for both progression free survival (PFS) and for overall survival (OS) (Kaplan Meier [trial period], Weibull, log-logistic, Gamma)
iii) Definition of PFS via a blinded independent central review was utilized instead of investigator assessed definition
iv) Dabrafenib-trametinib OS (95% confidence interval (CI) was based on 95% CI of hazard ratio (HR) vs. monotherapy)
v) HRs for PFS and OS for trametinib vs. dabrafenib-trametinib were set to the lower and upper bound of the 95% CI
vi) HRs for PFS and OS for ipilimumab vs. dabrafenib-trametinib were set to the lower and upper bound of the 95% CI
vii) HRs for PFS and OS for DTIC vs. dabrafenib-trametinib were set to the lower and upper bound of the 95% CI
viii) PFS monthly costs (±50% x main analysis case)
ix) Post-progression survival (PPS) monthly costs (±50% x main analysis case)
x) Administration costs (±50% x main analysis case)
xi) Adverse event (AE) costs (±50% x main analysis case)
xii) Post-study anti-cancer therapy (PSACT) costs (±50% x main analysis case, and equal to zero for all therapies)
xiii) Dose intensity (100% for all therapies)
xiv) Utility decrement for progression free vs. perfect health (95% CI)
xv) Utility decrement for post progression vs. progression free (95% CI)

Such modifications to the main analysis were performed in order to demonstrate the variation in the outcomes, i.e., the costs and the utility of the treatment as measured via quality of adjusted life year (QALY).

Patients considered the following factors important in the review of dabrafenib and trametinib combination therapy which are relevant to the economic analysis: overall survival, quality of life and AEs.

The Provincial Advisory Group (PAG) considered the following factors to be important to consider if implementing a funding recommendation for dabrafenib and trametinib combination therapy, and are relevant to the economic analysis: high cost of the dabrafenib and trametinib combination therapy, and the cost-effectiveness of combination therapy compared to monotherapy, i.e., the cost per QALY.

The cost of dabrafenib and trametinib in combination and as monotherapy as used in the main analysis was based on a confidential price submitted by the manufacturer. At the submitted confidential price, dabrafenib costs $[redacted] per capsule of 75 mg, and trametinib costs $[redacted] per tablet of 2 mg. *(The costs of dabrafenib and trametinib are based on confidential prices submitted by the manufacturer and cannot be disclosed to the public according to the pCODR Disclosure of Information Guidelines.)* However, according to the Newfoundland formulary, dabrafenib costs $68.72 per capsule of 75 mg, with a total dose cost of $274.87(5). The cost per 28 days is $7,696.94. Trametinib costs $314.65 per 2mg tablet for a total dose cost of $314.65(6). The cost per 28 days is $9,566.20.

For the comparative monotherapies, vemurafenib costs $46.54 per 240mg tablet with a dose of eight tablets for a total cost of $372.32(7). The cost per 28 days is $10,424.96. Ipilimumab costs $5,800 per vial per 50mg with a dose of five vials for a total dose cost of $29,000(8). The cost per 28 days is $38,677. Dacarbazine costs $0.35 per mg with a total dose cost of $731.90(8). The cost per 28 days is $975.86.

1.2 Summary of Results

The EGP based their estimates on the model submitted by GSK and reanalyses conducted by the EGP. A 5% discount rate was utilized in the economic model submitted. The discount rate reflects the discount in costs that should occur as a result of a value in a specific time period relative to another time period. As per the recommendations by Canadian Agency for Drugs and Technologies in Health (CADTH)(9), a reanalysis was conducted such as to present the results with a discount rate of 0%, and 3%.

The cost of the dabrafenib and trametinib combination therapy and the monotherapies for were considered according to publicly available information. In the Newfoundland formulary, the cost of dabrafenib is $68.72 per 75 mg capsule with a total dose cost of $274.87 and the cost per 28 days is $7,696.94(5). For trametinib, it is $314.65 per 2mg tablet with a total dose cost of $314.65 and the cost per 28 days is $9,566.20(6). For vemurafenib, it is $50.50 per 240mg tablet and the cost per 28 days is $11,311.44(10). As per previous EGRs, the recommendation for the cost of dabrafenib is $63.33 per 75 mg capsule with a total dose cost of $253.32 and the cost per 28 days is $7,092.96(11). For trametinib, it is $290 per 2mg tablet with a total dose cost of $290 and the cost per 28 days is $8,120.00(12).

Dabrafenib-Trametinib Versus Vemurafenib

Primary Analysis Assuming No Class Effect For BRAF Inhibitors

The EGP's best estimate of the incremental cost-effectiveness ratio (ICER) is between $323,454 and $446,238 per QALY when dabrafenib-trametinib is compared with

vemurafenib, assuming no class effect for BRAF inhibitors. The EGP chose the lowest and highest estimate from their reanalyses to define the range. The full range of reanalyses conducted by the EGP and the resultant ICERs can be found in Table 1.

The EGP's estimates were similar to the submitted estimates (Table 1).

Secondary Analysis Assuming A Class Effect for BRAF Inhibitors

The EGP's best estimate of the incremental cost-effectiveness ratio (ICER) is between $259,749 and $357,262 per QALY when dabrafenib-trametinib is compared with vemurafenib, assuming a class effect for BRAF inhibitors. The EGP chose the lowest and highest estimate from their reanalyses to define the range. The full range of reanalyses conducted by the EGP and the resultant ICERs can be found in Table 2.

The EGP's estimates were similar to the submitted estimates (Table 2).

Dabrafenib-Trametinib Versus Dabrafenib

Primary Analysis Assuming No Class Effect For BRAF Inhibitors

The EGP's best estimate of the ICER is between $361,349 and $709,259 per QALY when dabrafenib-trametinib is compared with dabrafenib alone, assuming no class effect for BRAF inhibitors. The EGP chose the lowest and highest estimate from their reanalyses to define the range. The full range of reanalyses conducted by the EGP and the resultant ICERs can be found in Table 1.

The EGP's estimates were similar to the submitted estimates (Table 1).

Secondary Analysis Assuming A Class Effect For BRAF Inhibitors

The EGP's best estimate of the ICER is between $401,698 and $637,954 per QALY when dabrafenib-trametinib is compared with dabrafenib alone. The EGP chose the lowest and highest estimate from their reanalyses to define the range. The full range of reanalyses conducted by the EGP and the resultant ICERs can be found in Table 2.

The EGP's estimates were similar to the submitted estimates (Table 2).

Indirect Comparisons of Dabrafenib-Trametinib Versus Other Therapies

The results of the reanalyses by the EGP for the comparisons of dabrafenib-trametinib with either trametinib, ipilimumab or dacarbazine are indicated in Table 1 (primary analysis assuming no class effect for BRAF inhibitors) and Table 2 (secondary analysis assuming a class effect for BRAF inhibitors) in comparison to the base case scenario with the results by the Submitter. The estimates provided in Table 1 and Table 2 have a degree of uncertainty that is attributed to i) the utilization of the statistical methodology (network meta-analysis) and ii) methodological concerns of that methodology, as applied by the Submitter. The EGP considered that the pCODR Clinical Guidance Report indicated that the results of the submitted network meta-analysis should be interpreted with caution given the heterogeneity between the included trials and patient populations.

Cost of Combination Therapy has a Large Effect on the ICER

It was assumed that the cost of the combination therapy would not remain as per the manufacturer's identified price. It is possible that this cost for the combination therapy

may change which would have an effect on the ICER, with a decrease in price lowering the ICER and an increase in the price increasing the ICER.

Table 1: Reanalysis conducted by the EGP using the submitted model for the primary analysis assuming no class effect for the BRAF inhibitors

	Dabrafenib-trametinib vs. Vemurafenib*			Dabrafenib-trametinib vs. Dabrafenib*			Dabrafenib-trametinib vs. Trametinib*			Dabrafenib-trametinib vs. Ipilimumab*			Dabrafenib-trametinib vs. Dacarbazine*		
Scenario	QALYs	Costs, $	ICER, $	QALYs	Costs, $	CER, $	QALYs	Costs, $	ICER, $	QALYs	Costs, $	ICER, $	QALYs	Costs, $	ICER, $
1. Submitter Main Analysis (Base-case)	0.345	114,493	332,129	0.408	153,002	374,995	0.505	116,771	231,103	0.719	138,152	192,083	0 887	205,332	231,612
2. Discount rate of 0%	0.369	122,556	331,869	0.448	161,870	361,349	0.551	125,559	227,735	0.786	149,299	189,935	0 967	216,698	224,088
3. Discount rate of 3%	0.142	46,052	323,454	0.109	77,002	709,259	0.156	43,232	276,799	0 206	38,853	188,828	0 256	104,047	405,756
4. Cost in Newfoundland formulary	0.345	153,830	446,238	0.408	186,676	457,529	0.505	151,159	299,162	0.719	185,799	258,330	0 887	252,979	285,357
5. pCODR EGP listing price	0.345	140,242	406,823	0.408	171,202	419,602	0.505	135,353	267,880	0.719	163,901	227,884	0 887	231,081	260,657

***There is uncertainty in the incremental effect and thus the ICERs due to the uncertainty in the estimates of effect derived from the submitted network meta-analysis.**

Table 2: Reanalysis conducted by the EGP using the submitted model for the secondary analysis assuming a class effect for the BRAF inhibitors

	Dabrafenib-trametinib vs. Vemurafenib*			Dabrafenib-trametinib vs. Dabrafenib*			Dabrafenib-trametinib vs. Trametinib*			Dabrafenib-trametinib vs. Ipilimumab*			Dabrafenib-trametinib vs. Dacarbazine*		
Scenario	QALYs	Costs, $	ICER, $	QALYs	Costs, $	CER, $	QALYs	Costs, $	ICER, $	QALYs	Costs, $	ICER, $	QALYs	Costs, $	ICER, $
1. Submitter Main Analysis (Base-case)	0.388	101,502	261,388	0 349	143,951	412,180	0.494	112,213	227,200	0.714	131,814	184,714	0 889	197,372	221,948
2. Discount rate of 0%	0.419	108,850	259,749	0 379	152,254	401,698	0.540	120,848	223,832	0.782	142,644	182,482	0 972	208,414	214,315
3. Discount rate of 3%	0.144	40,463	280,866	0.115	73,128	637,954	0.149	40,204	269,084	0.198	36,152	182,766	0 248	99,832	403,276
4. Cost in Newfoundland formulary	0.388	138,732	357,262	0 349	175,660	502,972	0.494	145,692	294,987	0.714	177,744	249,075	0 889	243,301	273,597
5. pCODR EGP listing price	0.388	126,323	325,306	0 349	161,089	461,251	0.494	130,304	263,830	0.714	156,635	219,496	0 889	222,193	249,860

***There is uncertainty in the incremental effect and thus the ICERs due to the uncertainty in the estimates of effect derived from the submitted network meta-analysis.**

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?

There is a difference in the estimates as different cost estimates for the dabrafenib and trametinib combination therapy and the monotherapies for dabrafenib and trametinib were considered. There are also differences as a result of the number of decimal places included (e.g., cost of the medication). The variation in the discount rate also contributed to the differences in the estimates. There was no difference in ΔE as no other utility scores were considered.

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

Yes, the following factors of overall survival, quality of life (measured in terms of QALYs), and AEs were considered and adequately addressed in the submitted economic analysis. For overall survival, the reanalyses of the main analysis were conducted such as to present the results of the costs and QALYs for dabrafenib and trametinib in combination in comparison to vemurafenib, dabrafenib, trametinib, ipilimumab, and dacarbazine, within the 95% CI (i.e., the range of the values that can occur at the lower and upper bound) of a HR.

For PFS, which has been an outcome reported in clinical trials for metastatic melanoma(13), the reanalyses of the main analysis were conducted such as to present the results of the costs and QALYs for dabrafenib and trametinib in combination, in comparison to vemurafenib, dabrafenib, trametinib, ipilimumab, and dacarbazine, with the 95% CI (i.e., the range of the values that can occur at the lower and upper bound) of a HR.

For the AEs, the costs were set at 50% of base case value and 150% of base case value. The EGP conducted a reanalysis of the main analysis to determine the impact on the QALYs if a discount rate of 0%, and 3% were applied relative to the main analysis value of 5%.

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

The economic model is adequate. However, there are limitations. It is preferred to have clinical trial results where there are direct comparisons for dabrafenib and trametinib in combination in comparison to vemurafenib, dabrafenib, trametinib, ipilimumab, and dacarbazine. There was a statistical technique applied, network meta-analysis, such as to make inferences regarding the anticipated outcomes should such direct comparisons have occurred. The Submitter used the results of the network meta-analysis to generate data for the indirect comparisons of dabrafenib-trametinib with trametinib-alone, ipilimumab, and with dacarbazine for this economic model. The pCODR Clinical Guidance Panel concluded that the results of the submitted network meta-analysis should be interpreted with caution due to the heterogeneity in the trial characteristics included in the network.

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?

The model assumptions were as follows:

a) Patients were similar to those in COMBI-V(1), COMBI-D(2, 3), and BRF113220(4) trials. Not all patients would be similar as there would be variation attributed to inherent characteristics which would be evident as per the outcomes documented (e.g., adverse events, response to treatment). As well, despite efforts to standardize recruitment of

patients into the clinical trials according to research subject eligibility criteria, there would still be variation in the mode by which the patients were selected to partake in the clinical trials.

b) Dabrafenib, trametinib and vemurafenib monotherapies, and ipilimumab and dacarbazine are the most relevant comparators for dabrafenib-trametinib combination. It was assumed that the relative dosing intensities (RDIs) for ipilimumab would be the same as those for dacarbazine but the RDIs may not be the same. There is no data for ipilimumab to calculate the RDI. The proportion of patients receiving PSACTs for ipilimumab was assumed to be the same as that for the vemurafenib arm of COMBI-V(1), but the proportion of patients may not be the same. There was no PSACT data for ipilimumab in the clinical trial, CA184-024(14). Use of ipilimumab, was distributed amongst other therapies in the same proportion as the vemurafenib arm in COMBI-V(1). There is no data for ipilimumab to calculate the use. These assumptions would have an impact on the outcomes.

a) Costs and quality of life (utility scores) are conditioned on treatment and expected time in the PFS and PPS health states. The following relationship: OS = PFS + (OS – PFS) = PFS + PPS was assumed. OS is the time from treatment randomization to the date of death(15, 16). PFS is defined as the time from randomization until objective tumor progression or death from any cause(17). If PFS is utilized as an outcome, important measures such as cost may be excluded. It includes the possible three scenarios of:
   i) objective tumor progression
   ii) death from any cause
   iii) objective tumor progression and death from any cause

   Hence, for the group which had experienced only tumor progression, there is a cost that would be excluded since the cost of tumor progression versus cost of death would be less. It is contingent upon when the data was cut and which patients were included at which stage of their cancer in the data considered for this economic analysis.

c) PFS and OS for vemurafenib was assumed to be the same as that for dabrafenib. There has been no clinical trial to examine such a class effect. Data on OS for dabrafenib-trametinib combination and vemurafenib from COMBI-V(1) were incomplete. The full complement of data should be considered if possible as this will lead to better estimates for the outcomes.

   To illustrate with one example where there may be a bias, patients randomized to chemotherapy were allowed to crossover to an optional extension arm of the study in which they could receive trametinib in the METRIC clinical trial(18) upon initial progression confirmed by independent review. The ITT analyses of OS may result in biased estimates of the causal effect of respective treatments on survival. Patients randomized to dabrafenib monotherapy were allowed to crossover to an optional extension arm of the study in which they could receive combination therapy upon progression. The ITT analyses of OS in BRF113220(4) may result in biased estimates of the causal effect of combination therapy on survival. To adjust the survival data in the respective clinical trials for the potential confounding effects of crossover, two approaches were conducted:

i) Rank Preserving Structural Failure Time Model (RPSFTM)

ii) Iterative Parameter Estimation (IPE)

Two sets of analyses were conducted:

- Treatment group analysis where it is assumed the treatment effect is maintained until death regardless of treatment duration
- On Treatment analysis where it is assumed treatment effect disappears upon treatment discontinuation

For the Treatment group analysis, this active effect is to be further clinically determined(19). The HRs for the Treatment group would be overestimating the benefit.

Comparisons with dabrafenib, trametinib, ipilimumab and dacarbazine were based on a Bayesian network meta-analysis (i.e., a pooling of data) of the HRs for PFS and OS. Differences in the trials in duration of follow-up and other trial characteristics may have affected the treatment effects. This would lead to less accurate estimates in outcomes.

d) Utilities and costs are invariant with respect to time since therapy initiation and conditional on progression status and treatment.

Different utility instruments were used. EuroQol-5D (EQ-5D) quality of life questionnaire(20) was used for the clinical trials, COMBI-V(1), COMBI-D(2, 3), BREAK-3(21). The Functional Assessment of Cancer Therapy–Melanoma (FACT-M) quality of life questionnaire(22, 23) for the clinical trial, BRIM-3(24), was used. No utility instrument was used for the clinical trials BRF113220(4) and CA184-024(14). The utility value for dacarbazine during PFS was assumed to be the same as that for vemurafenib. The utility values for ipilimumab were assumed to be the same as those for dacarbazine. The mean standard error (SE) of utility for PPS was assumed to be the same for all comparators, i.e., 0.691 (0.0110). It was not indicated if the disutility from side effects were considered. This may lead to inaccurate outcomes for utility scores (i.e., the QALYs). The study personnel, treating physicians, and patients were not blinded to treatment assignment in the COMBI-V trial(1). This could have affected the results, especially for patient-reported outcomes, in favour of whichever arm the assessor felt was likely to provide benefit.

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?

For the data derived from the clinical trials of which the manufacturer had access to such unpublished data, the estimates of clinical effect would have been utilized by the EGP for answering the relevant question. The study personnel, treating physicians, and patients were not blinded to treatment assignment in the COMBI-V trial(1). This could have affected the results, especially for patient-reported outcomes, in favour of whichever arm the assessor felt was likely to provide benefit. Tumour response and progression-free survival (the primary outcome) were unbiased outcomes in the COMBI-V trial(1), as a blinded and independent committee conducted tumour assessments.

The costs referenced in this model are valid parameters as it is based upon previous citations by pCODR and credible reference sources. The only exception is to consider the cost of the medications based upon publicly available information, i.e., published formulary listing costs. Of note, two references to published formulary listing costs are incorrect; dacarbazine cost is not publicly available on a provincial formulary in Ontario or British Columbia.

Hence, the data and the costs were adequate with the limitations as noted by the EGP.

1.4 Summary of Budget Impact Analysis Assessment

What factors most strongly influence the budget impact analysis estimates?

The cost of the combination treatment, dabrafenib and trametinib, the target population size and the market share of the treatment under consideration would have a large impact on the final result.

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

The estimated market shares are not reflective of accurate data in terms of the actual utilization of such treatments evaluated. Hence, this may have an impact in terms of the uptake of the dabrafenib and trametinib combination treatment and the displacement of vemurafenib and dabrafenib monotherapies.

1.5 Future Research

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

This economic evaluation could be improved if there were data from clinical trials with direct comparisons between dabrafenib and trametinib combination therapy and all of the comparator therapies.

Is there economic research that could be conducted in the future that would provide valuable information related to dabrafenib and trametinib in combination as first-line treatment of unresectable or metastatic melanoma in patients with BRAF V600 positive mutation?

Three studies may be further conducted. One study should conduct a similar analysis with the utilization of the full complement of data from the relevant clinical trials such that there are non-disconcordant cut-off dates for the data. Another trial may be conducted whereby utility scores are collected for patients who receive ipilimumab. Lastly, there can be a retrospective cohort analysis whereby administrative data could be utilized to determine the actual utilization of the treatments of interest and the related outcomes. Subsequently, another economic evaluation and budget impact analysis can be generated rather than to utilize the assumptions via the network meta-analysis and displacement of monotherapies with the increased utilization of the combination treatment respectively.

Other economic evaluations have been conducted albeit from different countries apart from Canada as summarized by Johnston et al (2015)(25) and Cashin et al (2008)(26). No presentation of results by Cashin et al (2008)(26) will occur as the article by Johnston et al (2015)(25) is most recent and identifies one study with reference to Canada. There is one economic evaluation from a societal perspective which examined the cost-effectiveness of first-line treatment of trametinib versus dacarbazine and vemurafenib in Canada for

patients with BRAF V600+ advanced or metastatic melanoma(27). The methodology utilized was as follows. A partitioned survival analysis model with 3 health states (pre-progression, post-progression, dead) estimated direct and indirect costs and QALYs. Clinical inputs for trametinib and dacarbazine were from the METRIC trial(28), 87%, 6% and 6% of patients received dacarbazine, paclitaxel, and no drug, respectively. Clinical inputs for vemurafenib were from an indirect, treatment comparison of data from the METRIC(28) and BRIM-3(29) studies. Resource utilization data were derived from physician survey results, drug costs from the manufacturers' price and Quebéc medications lists, and other costs from published sources. Consistent with a prior evaluation of vemurafenib, a 5-year time horizon was used. Costs and QALYs were discounted at 5% annually. The results from this evaluation were as follows. QALYs gained with trametinib were 0.4160 vs. dacarbazine. QALYs gained with trametinib were 0.1241 vs. vemurafenib. Compared with dacarbazine, incremental costs for trametinib were $61,226, resulting in a cost of $147,177 per QALY gained. The incremental costs for trametinib versus dacarbazine were not reported. There is uncertainty in the vemurafenib comparison given the lack of head-to head data (i.e., direct comparisons with the treatment).

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 Melanoma 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 dabrafenib and trametinib for metastatic melanoma. A full assessment of the clinical evidence of dabrafenib and trametinib for metastatic melanoma 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*. The manufacturer, as the primary data owner, did not agree to the disclosure of some economic information, therefore, this information was redacted from 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.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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