pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pCODR EXPERT REVIEW COMMITTEE (pERC)
FINAL RECOMMENDATION

The pan-Canadian Oncology Drug Review (pCODR) was established by Canada's provincial and territorial Ministries of Health (with the exception of Quebec) to assess cancer drug therapies and make recommendations to guide drug-funding decisions. The pCODR process brings consistency and clarity to the cancer drug assessment process by looking at clinical evidence, cost-effectiveness and patient perspectives.

pERC Final Recommendation
This pERC Final Recommendation is based on a reconsideration of the Initial Recommendation and feedback from eligible stakeholders. This pERC Final Recommendation supersedes the pERC Initial Recommendation.

Drug:
Pertuzumab (Perjeta Herceptin Combo Pack)

Funding Request:
In combination with trastuzumab and a taxane for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease

Submitted By: Hoffmann-La Roche Limited	**Manufactured By:** Hoffmann-La Roche Limited
NOC Date: April 12, 2013	**Submission Date:** November 2, 2012
Initial Recommendation: May 31, 2013	**Final Recommendation:** August 1, 2013

pERC RECOMMENDATION	The pCODR Expert Review Committee (pERC) recommends funding pertuzumab in combination with trastuzumab and a taxane (Perjeta) conditional on the cost-effectiveness being improved to an acceptable level. Funding should be for the palliative treatment of patients with HER2-positive unresectable locally recurrent or metastatic breast cancer with an ECOG status of 0 or 1, who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. In the case of patients who received trastuzumab in the adjuvant setting, pERC considered that a six month interval in which patients had not relapsed to be a clinically reasonable time frame. However, pERC considered the length of this interval should be flexible and based on the judgment of the treating oncologist. pERC made this recommendation because it was satisfied that there is an overall clinical benefit of pertuzumab. However, the Committee noted that pertuzumab could not be considered cost-effective at the submitted confidential price and the Economic Guidance Panel's estimates of the range of incremental cost-effectiveness ratios.
POTENTIAL NEXT STEPS FOR STAKEHOLDERS	**Pricing Arrangements to Improve Cost-Effectiveness** Given pERC was satisfied that there is a net clinical benefit of pertuzumab in combination with trastuzumab and a taxane, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of pertuzumab to an acceptable level.

SUMMARY OF pERC DELIBERATIONS

pERC noted that breast cancer is a common cause of cancer deaths. pERC also noted that the current standard of care in the first-line treatment of women with HER2-positive metastatic breast cancer is trastuzumab plus chemotherapy (usually a taxane), based on evidence of a survival benefit. pERC considered that there is a need for more and better therapies that delay progression and improve survival as current life expectancy is between 18 and 24 months for these patients. One randomized controlled trial (CLEOPATRA, Baselga 2012 & Swain 2013) was included in the pCODR systematic review, which compared pertuzumab plus trastuzumab plus docetaxel with placebo plus trastuzumab plus docetaxel. pERC considered this to be an appropriate and clinically relevant comparison.

pERC's Deliberative Framework for drug funding recommendations focuses on four main criteria:

CLINICAL BENEFIT	**PATIENT-BASED VALUES**
ECONOMIC EVALUATION	**ADOPTION FEASIBILITY**

pERC deliberated on the results of the CLEOPATRA study and considered that there was an overall net clinical benefit for pertuzumab. This was based on a statistically significant improvement in both progression-free survival and overall survival for the pertuzumab group compared with the control group.
pERC noted that the CLEOPATRA study provided evidence for the effectiveness of pertuzumab in combination with trastuzumab and docetaxel. However, after careful consideration and input from pCODR's Provincial Advisory Group, pERC decided that, due to regional variations in the use of different taxanes, it would be reasonable to fund pertuzumab in combination with a taxane. pERC also discussed that the trial included only a small proportion of patients who had received trastuzumab in the neoadjuvant or adjuvant setting. While this likely reflected clinical practice at the time the trial was conducted, pERC noted that the majority of patients would now receive adjuvant trastuzumab. pERC discussed the possibility that pertuzumab plus trastuzumab may not be an effective treatment in patients who were previously exposed to trastuzumab. pERC noted that the CLEOPATRA study restricted patient eligibility for the trial to patients who had not relapsed within 12 months of receiving trastuzumab. However, after careful consideration, and based on clinical practice in the treatment of breast cancer, pERC decided that it would be reasonable to fund pertuzumab in patients who had previously received trastuzumab in the adjuvant setting, provided that there was a six month period in which patients had not relapsed. Upon reconsideration of the pERC Initial Recommendation, pERC discussed feedback received from pCODR's Provincial Advisory Group that indicated that the six-month interval could be considered arbitrary and may differ from how metastatic breast cancer patients are managed in some provinces. Therefore pERC considered that, although six months is a reasonable timeframe from a clinical perspective, this interval should be considered flexible and the decision to reinstitute trastuzumab as part of the combination with pertuzumab and a taxane should be based on the judgment of the treating oncologist.

pERC also discussed the toxicity profile of pertuzumab based on the results of the CLEOPATRA study. pERC noted that adverse events such as diarrhea and febrile neutropenia were more frequently observed in the pertuzumab group compared with the control group. However, in the context of other systemic therapies, pERC considered that the overall tolerability of pertuzumab was acceptable.

pERC deliberated upon the alignment of pertuzumab with patient values. Patient advocacy group input indicated that patients with HER2 positive metastatic breast cancer valued extending life and prolonging progression-free survival. Therefore, based on the improvement in overall survival and progression-free survival demonstrated in the CLEOPATRA study, pERC considered that pertuzumab aligned with these patient values. Patient input also indicated that patients valued treatments that maintained quality of life. pERC noted that based on the limited evidence available for deliberations, quality of life appeared similar between the pertuzumab group and the control group. pERC also considered that patients were willing to accept adverse events if there was a clinical benefit and the toxicity was tolerable as was observed in the CLEOPATRA study. Therefore, overall, pERC considered that access to pertuzumab aligns with patient values.

pERC deliberated on the cost-effectiveness of pertzumab. pERC noted that the estimates of incremental cost-effectiveness provided by the pCODR Economic Guidance Panel (EGP) were slightly higher than the manufacturer's estimates, primarily because the manufacturer's estimates overestimated the survival benefit associated with pertuzumab. pERC considered that it was reasonable from a clinical perspective for the Panel to eliminate the post-progression survival benefit the manufacturer had estimated for the pertuzumab treatment because there is currently no evidence to support this residual effect.

Upon reconsideration of the pERC Initial Recommendation, the Committee discussed feedback from the manufacturer that disagreed with the assumptions made by the EGP. pERC considered additional information provided by the EGP further supporting the conclusion that there is a lack of evidence to support a post-progression survival benefit for pertuzumab and noted that the pCODR Clinical Guidance Panel also agreed with this assessment. Therefore, pERC considered that the EGP's analyses remained valid. pERC also considered assumptions about the potential for pertuzumab to reduce the risk of progression after the clinical trial. pERC agreed with the EGP that it is not realistic to assume that pertuzumab would continue to reduce the risk of progression indefinitely and there is currently no evidence to support this effect. However, pERC noted that the EGP's approach of addressing this by assuming equal risk of progression beyond the trial was a conservative approach.

pERC accepted the pCODR Economic Guidance Panel's estimates of the cost-effectiveness of pertuzumab plus trastuzumab plus docetaxel compared with placebo plus trastuzumab plus docetaxel, which were between $262,000 and $304,000 per quality-adjusted life year (QALY). pERC discussed that the actual ICER is not likely to be either the lower or upper boundary of this range, but that estimates within the lower part of this range were more clinically plausible. pERC noted that these considerations did not change the Committee's assessment that, at the confidential price submitted, pERC did not consider that pertuzumab was cost-effective.

pERC discussed the feasibility of implementing a recommendation for pertuzumab. pERC noted that pertuzumab is only available in a pack that includes both pertuzumab and trastuzumab (Perjeta Herceptin Combo Pack). Upon reconsideration of the pERC Initial Recommendation, pERC discussed feedback from the manufacturer and from pCODR's Provincial Advisory Group about the potential for wastage and agreed that there would likely be little to no wastage of trastuzumab as it will have a 28-day stability when reconstituted in bacteriostatic water and any excess amount of trastuzumab can most likely be used for other patients.

EVIDENCE IN BRIEF

pERC deliberated upon:

- a pCODR systematic review
- other literature in the Clinical Guidance Report providing clinical context
- an evaluation of the manufacturer's economic model and budget impact analysis
- guidance from pCODR clinical and economic review panels
- input from two patient advocacy groups (Canadian Breast Cancer Network and Rethink Breast Cancer)
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- pCODR's Provincial Advisory Group.
- the Submitter (Hoffmann-La Roche Limited)

The pERC Initial Recommendation was to fund pertuzumab in combination with trastuzumab and a taxane (Perjeta) conditional on the cost-effectiveness being improved to an acceptable level. Funding should be for the palliative treatment of patients with HER2-positive unresectable locally recurrent or metastatic breast cancer with an ECOG status of 0 or 1, who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease or who have not relapsed within 6 months of receiving trastuzumab in the adjuvant setting. Feedback on the pERC Initial Recommendation indicated that the manufacturer disagreed with the initial recommendation and pCODR's Provincial Advisory Group agreed with the initial recommendation.

OVERALL CLINICAL BENEFIT

pCODR review scope

The pCODR review evaluated the efficacy and safety of pertuzumab in combination with trastuzumab and a taxane in patients with HER2-positive metastatic or locally recurrent unresectable breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

Studies included: one randomized controlled trial

The pCODR systematic review included one study, CLEOPATRA (Baselga 2012 & Swain 2013). The CLEOPATRA study was a double-blind, placebo-controlled randomized controlled trial that compared the safety and efficacy of pertuzumab plus trastuzumab plus docetaxel (n=402) to placebo plus trastuzumab plus docetaxel (n=406). No cross-over was permitted between treatment groups and the study remained blinded until the final overall survival analysis was conducted.

Patient populations: included patients with locally recurrent breast cancer and those who had not relapsed within 12 months of receiving adjuvant or neoadjuvant trastuzumab

The CLEOPATRA study included patients with HER2-positive locally recurrent or metastatic breast cancer who had not received chemotherapy or biologic therapy for their metastatic disease who had an ECOG performance status of 0 or 1. pERC discussed this patient population and considered that because the study permitted inclusion of patients with unresectable locally recurrent breast cancer, it would not be appropriate to limit the funding of pertuzumab to only patients with metastatic breast cancer.

Patients included in the CLEOPATRA study could have received adjuvant or neoadjuvant chemotherapy, provided 12 months or more had elapsed, between the last therapy and the diagnosis of metastatic breast cancer; approximately 10-12% of patients had been exposed to trastuzumab in this way. While this low proportion likely reflected clinical practice at the time the trial was conducted, pERC noted that the majority of HER2 positive breast cancer patients would now receive adjuvant or neoadjuvant trastuzumab. pERC discussed the possibility that pertuzumab plus trastuzumab may not be an effective treatment in metastatic patients who had progressed while receiving adjuvant or neoadjuvant trastuzumab. pERC noted that the CLEOPATRA study was restricted to patients who had not relapsed within 12 months of receiving adjuvant or neoadjuvant chemotherapy. pERC discussed whether or not this was an appropriate time interval and noted that this was a historical standard that did not have a strong biological rationale. After careful consideration and based on common clinical practice in Canada where a six-month relapse-free interval is used in the treatment of breast cancer, pERC decided that it would be reasonable to fund pertuzumab plus trastuzumab in patients who had previously received adjuvant or neoadjuvant trastuzumab and who have not relapsed within six months of receiving trastuzumab. Upon reconsideration of the pERC Initial Recommendation, pERC discussed feedback received from pCODR's Provincial Advisory Group indicating that the six-month interval could be considered arbitrary and may differ from how metastatic breast cancer patients are managed in some provinces. Therefore pERC considered that, although six months is a reasonable timeframe from a clinical perspective, this interval should be considered flexible and based on the judgment of the treating oncologist.

Key efficacy results: improved progression-free survival and overall survival

Key outcomes deliberated on by pERC included progression free survival, the primary outcome of the CLEOPATRA study based on independent assessment, and overall survival. pERC considered the results of both a pre-planned primary interim analysis after 19.3 months of follow-up (Baselga 2012) and a subsequent analysis that was requested by European health authorities one year later (Swain 2013) and determined that there was an overall net clinical benefit for pertuzumab.

pERC noted that a statistically and clinically significant difference in independently-assessed median progression free survival favoured pertuzumab compared with placebo in the primary analysis (18.5 versus 12.4 months, respectively; HR=0.62, 95% confidence interval 0.51 to 0.75; P<0.001). Differences in overall survival were not statistically significant based on the primary analysis. However, the subsequent analysis of overall survival (Swain 2013) demonstrated a clinically and statistically significant difference in favour of the pertuzumab arm (median not yet reached) compared to the placebo arm (median 37.6 months; HR=0.66 95% CI 0.52 to 0.84; P=0.0008).

Quality of life: limited data but appears similar between placebo and pertuzumab

pERC discussed the time to deterioration of health-related quality of life, which was evaluated in the CLEOPATRA study using the Functional Assessment of Cancer Therapy – Breast (FACT-B) questionnaire. pERC noted that although detailed data were not available and results were only reported in abstract-form, quality of life outcomes appeared similar between the two treatment arms. pERC also considered that patient advocacy group input indicated that patients valued treatments that maintained quality of life.

Safety: acceptable toxicity profile

pERC discussed the toxicity profile of pertuzumab based on the results of the CLEOPATRA study and concluded that the overall tolerability of pertuzumab was acceptable. pERC noted that the number of deaths and the rates of withdrawal due to adverse events were similar between the pertuzumab group and the placebo group. pERC discussed that more patients receiving pertuzumab than placebo experienced febrile neutropenia, diarrhea, rash, mucosal inflammation and dry skin but determined that these were manageable toxicities in the context of systemic therapy.

Need: therapies that delay progression and extend life

pERC noted that breast cancer deaths are the second most common cause of cancer mortality in Canadian women (5,100 deaths in 2012) and that approximately 15 to 20% of all breast cancers are HER2 positive. pERC also noted that HER2 positive breast cancer is considered more aggressive and may result in a poorer prognosis. A number of treatment options exist in the first-line setting for women with HER2 positive metastatic breast cancer. pERC noted that the pCODR Clinical Guidance Panel considered trastuzumab plus a taxane to be the most relevant and clinically appropriate comparator. pERC discussed that studies evaluating trastuzumab plus chemotherapy have demonstrated an overall survival benefit in this setting. However, the majority of patients with metastatic breast cancer who initially respond to trastuzumab demonstrate disease progression within one year of treatment initiation and currently, life expectancy is between approximately 18 to 24 months for these patients. Therefore, pERC considered that there remains a need for new and better therapies for the treatment of metastatic breast cancer.

PATIENT-BASED VALUES

Values of patients with metastatic breast cancer: delay progression and extend survival

Input from two patient advocacy groups indicated that patients with metastatic breast cancer valued treatments that extend overall survival and progression free survival in order to maintain the best possible quality of life. Therefore, pERC considered that the improvements in progression-free survival and overall survival demonstrated in the CLEOPATRA study align with patient values.

Patient values on treatment: manageable side effects and acceptable quality of life

pERC noted that metastatic breast cancer patients are looking for treatments that will extend life expectancy while offering acceptable quality of life with manageable side effect profiles. pERC also noted that many patients would be willing to tolerate the potential adverse effects of a treatment if it was found to prolong their survival, even for a short period of time. pERC discussed the results from the CLEOPATRA study that indicated a manageable adverse events profile and similar quality of life outcomes between the two treatment groups. pERC also noted that two Canadian patients living with HER2 positive metastatic breast cancer had received pertuzumab in the CLEOPATRA study and both reported that pertuzumab had a positive impact on their disease and did not negatively impact their quality of life. Therefore, pERC concluded that pertuzumab aligns with patient values.

ECONOMIC EVALUATION

Economic model submitted: cost-utility

The pCODR Economic Guidance Panel assessed a cost-utility analysis comparing pertuzumab, trastuzumab and docetaxel to placebo, trastuzumab and docetaxel in patients with HER2 positive metastatic breast cancer who have not received prior chemotherapy or anti-HER2 therapy for metastatic disease.

Basis of the economic model: clinical and economic inputs

Costs included the drug acquisition costs, chemotherapy administration costs, costs associated with the treatment of adverse events, and the costs of supportive and subsequent treatments.

Key clinical effects included progression-free survival estimates, overall survival estimates and utility estimates.

Drug costs: confidential price submitted

pERC discussed that pertuzumab is only available as a pack that includes both pertuzumab and trastuzumab (Perjeta Herceptin Combo Pack). The pack includes one 420 mg vial of pertuzumab and one 440 mg vial of trastuzumab, which has a 28 day stability when reconstituted in bacteriostatic water for injection.

At the submitted confidential price, which the Economic Guidance Panel and manufacturer analyses were based upon, Perjeta Herceptin Combo Pack (pertuzumab plus trastuzumab) costs $ 5,063.

At the list price, the Perjeta Herceptin Combo Pack (pertuzumab plus trastuzumab) costs $6,448.

- The recommended dose is 840 mg pertuzumab and 8 mg/kg trastuzumab on day one, followed by 420 mg pertuzumab and 6 mg/kg trastuzumab every three weeks. For the first 28-day course, which includes the recommended loading dose and assumes a weight of 70 kg, the average daily cost is $465 and the average cost per 28-day course is $13,031 based on the list price. For subsequent 28-day courses, the average daily cost is $301 and the average cost per 28-day course is $8,418.

Trastuzumab is available as 440 mg/vial at a cost of $2,700 per vial

- The recommended dose of trastuzumab is 8 mg/kg on day one, followed by 6 mg/kg every three weeks. For the first 28-day course, which includes the recommended loading dose and assumes a patient weight of 70 kg, the average daily cost is $154 and the average cost per 28-day course is $4,292. For subsequent 28-day courses, the average daily cost is $123 and the average cost per 28-day course is $3,434.

Docetaxel is available as 10mg/mL, 20mg/0.5mL or 80mg/2mL vials at a cost of $4.45 per vial.

- The recommended dose of docetaxel is 75 mg/m^2 on day one and every three weeks. The average cost per day is $27.05 and the average cost per 28-day course is $757.35.

Cost-effectiveness estimates: not cost-effective at the confidential price

pERC deliberated upon the cost-effectiveness of pertuzumab and discussed the pCODR Economic Guidance Panel's critique of the manufacturer's economic analysis. pERC noted that the estimates of incremental cost-effectiveness provided by the pCODR Economic Guidance Panel were slightly higher than the manufacturer's estimates, primarily because the manufacturer estimated a higher survival benefit associated with pertuzumab. This was due to two factors: the manufacturer's assumption that there is a post-progression survival benefit associated with pertuzumab and the assumption that pertuzumab would continue to reduce the risk of progression indefinitely. pERC did not agree with these assumptions and, therefore, eliminated the survival benefits that the manufacturer attributed to pertuzumab in the economic model.

pERC accepted the pCODR Economic Guidance Panel's reanalysis, which excluded any post-progression survival benefits from the model while assuming an equal risk of death from the time of disease progression in both the pertuzumab and the placebo groups. Upon reconsideration of the pERC Initial Recommendation, the Committee discussed feedback from the manufacturer that disagreed with the assumptions made by the EGP. pERC considered additional information provided by the EGP indicating that there is no evidence to support a post-progression survival benefit for pertuzumab and noted that the pCODR Clinical Guidance Panel agreed with this assessment. Therefore, pERC considered that the EGP's analyses eliminating the post-progression survival benefit remained valid. pERC also considered assumptions about the potential for pertuzumab to reduce the risk of progression after the trial. pERC agreed with the EGP that it is not realistic to assume that pertuzumab would continue to reduce the risk of progression indefinitely and there is currently no evidence to support this effect. However, pERC noted that the EGP's approach of addressing this by assuming equal risk of progression beyond the trial was a conservative approach.

The Economic Guidance Panel's estimate of the cost-effectiveness of pertuzumab plus trastuzumab plus docetaxel is between $262,263 to $303,726 per quality-adjusted life year when compared with placebo

plus trastuzumab plus docetaxel. pERC accepted these estimates but noted that the actual ICER is likely to be at the lower end of this range. pERC noted that the estimate of $304,000 per QALY only provided an upper boundary for the range, indicating that the EGP did not identify scenarios in which estimates would be a higher than this upper boundary. pERC also noted that these considerations did not change the Committee's assessment that at the confidential price submitted and based on these estimates, pertuzumab was not cost-effective.

pERC also considered feedback from the manufacturer indicating that they could not replicate the Economic Guidance Panel's estimates. pERC noted that, while the exact estimates were not obtained, the manufacturer's attempt to reanalyze the data produced estimates that were similar to the Economic Guidance Panel's estimates. pERC further noted that, in response to the manufacturer's feedback, the Economic Guidance Panel had provided more clarity and transparency in their report to allow for better replication of their reanalyses.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: clinic resources and use with taxanes

pERC noted that the pertuzumab is only available in a pack that includes both pertuzumab and trastuzumab (Perjeta Herceptin Combo Pack). Upon reconsideration of the pERC Initial Recommendation, pERC discussed feedback from the manufacturer and from pCODR's Provincial Advisory Group about the potential for wastage and agreed that there would likely be no wastage of trastuzumab as it will have a 28-day stability when reconstituted in bacteriostatic water and any excess trastuzumab will most likely be used for other patients.

pERC also discussed that trastuzumab plus chemotherapy is currently the standard first-line treatment in post-menopausal women with HER2 positive breast cancer. Therefore, pERC noted input from pCODR's Provincial Advisory Group that the addition of pertuzumab would not significantly increase chemotherapy clinic time and resources because it would be administered in the same patient population as trastuzumab for which similar treatment and monitoring protocols apply. Upon reconsideration of the pERC Initial Recommendation, pERC discussed feedback from pCODR's Provincial Advisory Group that pertuzumab would increase chair time in chemotherapy clinics. pERC discussed this feedback and agreed that, although pertuzumab would be administered in the same patient population as trastuzumab, the length of time spent at the clinic would be longer for each clinic visit. pERC also noted that if patients receiving pertuzumab have longer progression-free survival, this could lead to more visits to the chemotherapy clinics and increase resource use.

pERC also discussed the potential for use of pertuzumab and trastuzumab with other chemotherapies based on input from pCODR's Provincial Advisory Group. pERC noted that the CLEOPATRA study provided evidence for the effectiveness of pertuzumab in combination with trastuzumab and doectaxel. However, after careful consideration and based on input from pCODR's Provincial Advisory Group, pERC decided that, due to regional variations in the use of different taxanes, it would be reasonable to fund pertuzumab in combination with any taxane.

DRUG AND CONDITION INFORMATION

Drug Information	• A recombinant humanized monoclonal antibody that inhibits dimerizaton of HER2 with other HER receptors (HER3, HER1, and HER4) • Pertuzumab will be supplied in a kit containing 420 mg vial of pertuzumab and 440 mg vial of trastuzumab • The recommended dose, administered i.v. is 420 mg pertuzumab, 6mg/kg trastuzumab administered i.v. every 3 weeks with a loading dose of 840mg pertuzumab and 8mg/kg trastuzumab
Cancer Treated	• HER2-positive metastatic or locally recurrent unresectable breast cancer.
Burden of Illness	• Breast cancer is the most common cancer in women and the 2nd most common cause of cancer mortality in Canadian women • Approximately 15-20% of all breast cancers are HER2-positive, resulting in a more aggressive clinical phenotype and a poorer prognosis
Current Standard Treatment	• Anti-HER2 treatment (trastuzumab) in combination with chemotherapy (paclitaxel, docetaxel or vinorelbine) is standard first-line treatment and has demonstrated a survival benefit
Limitations of Current Therapy	• The majority of patients with metastatic breast cancer who initially respond to trastuzumab will demonstrate disease progression within one year, therefore, there is a need for therapies with improved efficacy and tolerability

ABOUT THIS RECOMMENDATION

The pCODR Expert Review Committee (pERC)
Recommendations are made by the pCODR Expert Review Committee following the pERC Deliberative Framework. pERC members and their roles are as follows:

Dr. Anthony Fields, Oncologist (Chair)
Dr. Maureen Trudeau, Oncologist (Vice-Chair)
Dr. Chaim Bell, Economist
Dr. Scott Berry, Oncologist
Bryson Brown, Patient Member
Mario de Lemos, Pharmacist
Dr. Sunil Desai, Oncologist
Mike Doyle, Economist
Dr. Bill Evans, Oncologist
Dr. Allan Grill, Family Physician
Dr. Paul Hoskins, Oncologist
Danica Lister, Pharmacist
Carole McMahon, Patient Member Alternate
Jo Nanson, Patient Member
Dr. Peter Venner, Oncologist
Dr. Tallal Younis, Oncologist

All members participated in deliberations and voting on the initial recommendation except:

- Dr. Maureen Trudeau, Dr. Paul Hoskins and Jo Nanson who were not present for the meeting
- Dr. Chaim Bell who was not present at the time of voting
- Carole McMahon and Dr. Tallal Younis who were excluded from voting due to a conflict of interest

All members participated in deliberations and voting on the final recommendation except:

- Dr. Maureen Trudeau, Carole McMahon, Jo Nanson and Dr. Tallal Younis who were excluded from voting due to a conflict of interest
- Dr. Chaim Bell and Mario de Lemos who was not present at the time of voting

Avoidance of conflicts of interest

All members of the pCODR Expert Review Committee must comply with the *pCODR Conflict of Interest Guidelines*; individual conflict of interest statements for each member are posted on the pCODR website and pERC members have an obligation to disclose conflicts on an ongoing basis. For the review of pertuzumab (Perjeta Herceptin Combo Pack) for metastatic breast cancer, through their declarations, five members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, but none of these members was excluded from voting.

Information sources used

The pCODR Expert Review Committee is provided with a *pCODR Clinical Guidance Report* and a *pCODR Economic Guidance Report*, which include a summary of patient advocacy group and Provincial Advisory Group input, as well as original patient advocacy group input submissions to inform their deliberations. pCODR guidance reports are developed following the pCODR review process and are posted on the pCODR website. Please refer to the pCODR guidance reports for more detail on their content.

Consulting publicly disclosed information

pCODR considers it essential that pERC recommendations be based on information that may be publicly disclosed. All information provided to the pCODR Expert Review Committee for its deliberations was handled in accordance with the *pCODR Disclosure of Information Guidelines*.

Use of this recommendation

This recommendation from the pCODR Expert Review Committee (pERC) is not intended as a substitute for professional advice, but rather to help Canadian health systems leaders and policymakers make well-informed decisions and improve the quality of health care services. While patients and others may use this Recommendation, it is for informational and educational purposes only, and should not be used as a substitute for the application of clinical judgment respecting the care of a particular patient, for professional judgment in any decision-making process, or for professional medical advice.

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