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:
Eribulin Mesylate (Halaven)

Funding Request:
For the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane administered in either the adjuvant or metastatic setting.

Submitted By: Eisai Ltd.	**Manufactured By:** Eisai Ltd.
NOC Date: December 14, 2011	**Submission Date:** February 9, 2012
Initial Recommendation: June 1, 2012	**Final Recommendation:** August 2, 2012

RECOMMENDATION	The pCODR Expert Review Committee (pERC) **recommends** funding eribulin in patients with metastatic or incurable locally advanced breast cancer **conditional on its cost-effectiveness being improved to an acceptable level.** It should be funded for patients who have had previous treatment with a taxane and an anthracycline, who have had at least two chemotherapy regimens for metastatic or locally recurrent disease and who have progressed after their last therapy. In addition, patients must have good performance status (ECOG ≤ 2). The Committee made this recommendation because they were satisfied that there is an overall clinical benefit of eribulin compared with standard therapies. However, at either the list price or the submitted price, the Economic Guidance Panel's estimates of the incremental cost-effectiveness ratio for eribulin could not be considered cost-effective compared with current therapies.
POTENTIAL NEXT STEPS FOR STAKEHOLDERS	**Pricing Arrangements to Improve Cost-Effectiveness** Given pERC was satisfied there is a net clinical benefit of eribulin, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of eribulin to an acceptable level.

SUMMARY OF pERC DELIBERATIONS

pERC noted that the burden of illness of incurable locally advanced or metastatic breast cancer is considerable, with breast cancer being the most commonly diagnosed malignancy in Canadian women and the second leading cause of cancer deaths in women. pERC noted that there are limited effective treatment options for these patients at a late stage of disease. Treatment options that may be considered include vinorelbine, gemcitabine, capecitabine, taxanes and anthracyclines. One open-label randomized controlled trial (EMBRACE, Cortes 2011) comparing eribulin with a treatment of physician's choice was included in the pCODR systematic review and considered appropriate. It was noted that eribulin was evaluated in patients who had received between two and five prior treatments and this represented a heavily pre-treated population, which is in need of therapeutic options.

pERC's *Deliberative Framework* for drug funding recommendations focuses on four main criteria:	
CLINICAL BENEFIT	PATIENT-BASED VALUES
ECONOMIC EVALUATION	ADOPTION FEASIBILITY

pERC deliberated upon the results of the EMBRACE study, which evaluated eribulin compared with a treatment of physician's choice and concluded that there is a net clinical benefit associated with eribulin. pERC noted that there was a modest but clinically and statistically significant improvement in the overall survival. The observation of a survival advantage was particularly important in this heavily pre-treated population with advanced disease, because there is a lack of evidence supporting a survival benefit of currently available treatment options. pERC also reviewed the safety data for eribulin and noted that serious adverse events were similar between the two treatment groups. pERC discussed that peripheral neuropathy and febrile neutropenia were higher with eribulin compared with the treatment of physician's choice arm. However, pERC noted that these adverse events are commonly observed with other standard chemotherapeutic agents and considered that the toxicity profile of eribulin was acceptable. Overall, pERC considered the quality of the clinical trial to be reasonable; however, some limitations in the trial design were noted, particularly the lack of quality of life data. While blinding would have been impractical due to the variety of treatment options used in the comparator arm, pERC noted that the open-label nature of the trial may have introduced bias into the study results. In addition, pERC noted that there was uncertainty in the dose intensity of the comparator arm and it was unclear how this might have impacted the use of supportive therapies and overall survival results.

pERC also deliberated upon patient advocacy group input, which indicated that patients value extending life expectancy and maintaining quality of life. pERC noted that in the EMBRACE study, life was extended by approximately 2.5 months in the eribulin group compared with the treatment of physician's choice group. Input from patient advocacy groups indicated that extending life by approximately two to three months was a meaningful improvement for them and pERC considered that eribulin aligned with this patient value. pERC also considered that the effect of new treatments on quality of life was important to patients. However, pERC noted that quality of life was not measured in the EMBRACE study. In addition, pERC considered that the input provided by patient advocacy groups did not provide details or anecdotal evidence on patients' direct experiences with eribulin. As a result, pERC considered it challenging to determine whether or not eribulin aligned with the patient-identified value of maintaining quality of life. pERC acknowledged some of the challenges patient advocacy groups may face in collecting information on patients' direct experiences, especially with a new drug to which Canadian patients may have had little exposure. However, pERC emphasized that it is important to have quality of life information available for their deliberations.

pERC deliberated upon the cost-effectiveness of eribulin. pERC reviewed the estimates presented by the pCODR Economic Guidance Panel, which ranged from $114,000 per quality adjusted life year (QALY) to $272,000 per QALY and agreed that the true estimate was most likely at the higher end of the range, i.e. between $223,840 per QALY and $272,275 per QALY). The latter is based on the more conservative assumption that survival benefit of eribulin would be limited once the patient's disease has progressed. pERC noted that the range presented by the Economic Guidance Panel was wide, reflecting that there is considerable uncertainty in the model and that small changes in survival estimates and the time horizon

for the analysis could have a large impact on cost-effectiveness estimates. pERC discussed that one of the main factors affecting the cost-effectiveness estimates was the survival estimates used in the economic model. In reviewing the clinical data from the EMBRACE trial, pERC noted that while all of the survival benefit in the trial is observed by 18 to 24 months, in the submitted economic model, approximately 60% of the survival benefit of eribulin is based on extrapolated data beyond 18 months. Based on the planned survival analysis from the EMBRACE study, there was no evidence that benefit would accumulate past 24 months. Therefore, pERC considered that the cost-effectiveness of eribulin compared with treatment of physician's choice is likely between $223,840 per QALY and $272,275 per QALY, depending on when the expected cumulative survival benefit stops accruing between 18 and 24 months. As a result, pERC did not consider eribulin to be cost-effective. pERC considered feedback from the manufacturer that survival benefit data beyond 18 months from the EMBRACE trial were not incorporated into the pCODR Economic Guidance Panel's best estimates of the cost-effectiveness of eribulin. pERC reviewed the re-analyses conducted by the Economic Guidance Panel and their rationale for using the 18 month estimates. pERC agreed with the Economic Guidance Panel that the analyses based on clinical data from the 18 month pre-planned analysis are more robust than those based on clinical data from the 24 month unplanned analysis. pERC considered that results observed at 24 months may be biased as a result of multiple unplanned looks at the data and that these more favourable estimates may not be stable over time.

pERC discussed factors that could impact the feasibility of implementing a funding recommendation for eribulin and noted that eribulin is likely to be an additional, sequential therapy to be used in patients with advanced breast cancer. Therefore, it will not necessarily replace other therapies and overall treatment costs will likely increase.

pERC also considered feedback from pCODR's Provincial Advisory Group on the requirement for disease recurrence within six months of last treatment and the challenges this requirement may create when implementing the recommendation. pERC noted that the EMBRACE trial included only patients who had progression within six months or less of latest chemotherapy treatment but that an explicit reason for restricting EMBRACE to this patient population was not provided. pERC was unaware of any reason why eribulin would not be an appropriate treatment for some patients who have progressed more than six months after their last chemotherapy and determined that the six month criterion was not essential for the recommendation.

pERC also considered feedback from pCODR's Provincial Advisory Group on whether the use of eribulin for patients whose disease progressed on hormone therapy would be appropriate. pERC noted that patients are required to have had at least two previous chemotherapies, including an anthracycline and a taxane. If a patient met these criteria, even if their last treatment was a hormone therapy, eribulin could be an appropriate therapy.

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 Canadian Cancer Survivor Network)
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- pCODR's Provincial Advisory Group
- the Submitter (Eisai Ltd.)

The pERC Initial Recommendation was to **recommend** funding eribulin in patients with metastatic or incurable locally advanced breast cancer **conditional on its cost-effectiveness being improved to an acceptable level**. It should be funded for patients who have had previous treatment with a taxane and an anthracycline, who have had at least two chemotherapy regimens for metastatic or locally recurrent

disease and who have progressed within six months of the last chemotherapy. In addition, patients must have good performance status (ECOG ≤ 2). Feedback on the pERC Initial Recommendation indicated that the pCODR's Provincial Advisory Group and Eisai Ltd. agreed with the recommendation in part.

OVERALL CLINICAL BENEFIT

pCODR review scope

The pCODR review evaluated the effect of eribulin monotherapy on patient outcomes compared to chemotherapeutic regimens without eribulin in the treatment of patients who have previously received at least two chemotherapeutic regimens for metastatic breast cancer or incurable locally advanced recurrent breast cancer, and who have previously received both anthracyclines and taxanes in the adjuvant and/or advanced-stage disease setting.

Studies included

The pCODR systematic review included one open-label randomized trial (EMBRACE, Cortes 2011) comparing eribulin to treatment of physician's choice in women with incurable locally advanced or metastatic breast cancer who had received between two and five previous chemotherapy regimens, including an anthracycline and a taxane. The primary outcome of the EMBRACE study was overall survival.

Patient population: Heavily pre-treated women

The EMBRACE study included women with incurable locally advanced or metastatic breast cancer who had received between two and five previous chemotherapy regimens, including an anthracycline and a taxane. The median number of previous chemotherapy regimens received by patients in the trial was four, with a range of one to seven, indicating a heavily pre-treated patient population. pERC noted that the baseline demographic and disease characteristics were balanced between the two treatment groups. pERC also noted that the EMBRACE study included patients with an ECOG score ≤2, indicating patients with good performance status.

pERC discussed that it was unclear how patients who had not previously received an anthracycline or taxane would respond to eribulin. While these patients were permitted in the trial, 99% of patients had previously received an anthracycline and a taxane. In clinical practice this would likely be a small patient population since taxanes and anthracyclines are standard breast cancer treatments. pERC also noted that the trial included two groups of patients, those who received an anthracycline and a taxane in the adjuvant setting and those who received these agents in the metastatic setting. It was not clear to pERC how response may differ between these two groups of patients.

pERC also considered feedback from pCODR's Provincial Advisory Group on the requirement for disease recurrence within six months of last treatment and the challenges this requirement may create if implementing the recommendation. pERC noted that the EMBRACE trial included only patients who had progression within six months or less of latest chemotherapy treatment but that an explicit reason for restricting EMBRACE to this patient population was not provided. pERC considered that there is no reason to believe that eribulin would not be an appropriate treatment for some patients who have progressed more than six months after last chemotherapy. For these reasons, the six month criterion was removed from the recommendation.

pERC also considered feedback from pCODR's Provincial Advisory Group on whether the use of eribulin for patients whose disease progressed on hormone therapy would be appropriate. pERC noted that patients are required to have had at least two previous chemotherapies, including an anthracycline and a taxane. If a patient met these criteria, even if their last treatment was a hormone therapy, eribulin could be an appropriate therapy.

Key efficacy results: Overall survival benefit for eribulin

The key efficacy outcome deliberated on by pERC was overall survival. The primary endpoint of the EMBRACE study was overall survival, defined as the time from randomization to the date of death or the last date the patient was known to be alive (date of censoring). pERC noted that a statistically significant difference in overall survival was observed for eribulin compared to treatment of physician's choice

(hazard ratio = 0.81, 95% confidence interval 0.66 to 0.99, P = 0.041). The median overall survival was 13.1 months in the eribulin group compared with 10.6 months in the treatment of physician's choice group, which pERC considered to be a modest, but clinically meaningful benefit.

The majority of the study population (73%) in the EMBRACE trial had prior exposure to capecitabine, whereas only 18% of patients in the treatment of physician's choice arm were prescribed capecitabine as the study treatment. pERC also noted that exploratory subgroup analyses indicated that there is a possibility that patients with prior capecitabine exposure might respond better to eribulin and discussed how this might affect sequencing of treatments. However, pERC noted the exploratory nature of these analyses and discussed that there is an ongoing trial comparing eribulin and capecitabine (NCT00337103) in patients previously treated with anthracyclines and taxanes that may provide more clarity on this point.

Quality of life: No information available

pERC noted that quality of life information was not collected in the EMBRACE study and considered this to be a significant short-coming. pERC further noted that treatments that do not negatively affect quality of life are important to patients and that trial investigators and manufacturers should collect and report good quality data for this outcome in clinical trials. pERC also considered it challenging that input from patient advocacy groups did not provide information on patient's direct experiences with eribulin, which could have provided a sense of the impact of eribulin on quality of life.

Safety: Acceptable toxicity profile

pERC considered the toxicity profile of eribulin to be similar to the range of chemotherapy options studied in the EMBRACE trial. Serious adverse events (Grade 3 or higher) occurred in 25.0% of patients in the eribulin arm and in 25.9% of patients in the treatment of physician's choice arm. However, two clinically important toxicities, peripheral neuropathy and febrile neutropenia, were noted by pERC to be higher with eribulin. Grade 3 or 4 peripheral neuropathy occurred in 8.2% of patients in the eribulin arm and in 2.0% of patients in the treatment of physician's choice arm. Febrile neutropenia occurred in 4.6% of patients in the eribulin arm compared to 1.6% of patients in the treatment of physician's choice arm. However, pERC considered that the rates of these two adverse events in the EMBRACE study were comparable to other standard chemotherapeutic agents administered in the metastatic breast cancer setting, such as taxanes.

Limitations: No quality of life data, open-label design and uncertain dose intensity

The Committee considered that the overall quality of the clinical trial was good although some limitations were noted, including the lack of quality of life data. pERC noted that EMBRACE was an open-label trial. While pERC recognized that as treatment of physician's choice was used as the control arm in the trial, implementing blinding in this trial design would have been extremely difficult, this may have had an impact on trial results. In addition, pERC noted that there is a lack of clear information on the dose intensity of treatments used in the physician's choice comparator arm. In regard to the dose intensity, there was greater use of granulocyte colony stimulating factor in the eribulin arm (18%) compared to the treatment of physician's choice arm (8%), which may have influenced overall survival results.

Comparator information: Appropriate mix of comparators

The agents most commonly administered to patients in the treatment of physician's choice arm included vinorelbine, gemcitabine, capecitabine, taxanes, anthracyclines, and hormone therapy. Although there is currently no standard of care in this particular treatment setting, pERC noted that the agents delivered on the treatment of physician's choice arm were in line with the chemotherapeutic agents available and used in Canadian practice today.

Need: New treatment options that extend life

pERC discussed that there are many women living with breast cancer and that it can have a variable clinical course. It was noted that breast cancer is the most commonly diagnosed malignancy in Canadian women, with an estimated incidence of 23,600 new cases in Canada in 2011. Breast cancer deaths account for 14.4% of all annual cancer deaths and are the second leading cause of cancer deaths in

women. An estimated 5,100 Canadian women died from breast cancer in 2011. Over the past 10 to 15 years there have been a number of new agents for the treatment of metastatic breast cancer, but both physicians and patients are looking for new agents that are tolerable and can extend life while maintaining quality of life.

PATIENT-BASED VALUES

Values of patients with metastatic breast cancer: extending life, maintaining quality of life
Patient advocacy group input indicated that patients with advanced/metastatic breast cancer may experience a number of debilitating symptoms, stemming from the disease itself and also from the various therapies used to treat the disease. Patients are seeking treatment options that have a tolerable side effect profile that will allow them to maintain their quality of life. pERC noted that the input provided by patient advocacy groups did not provide details or anecdotal evidence on patients' direct experiences with eribulin. As a result, pERC considered it challenging to determine whether or not eribulin aligned with the patient-identified value of maintaining quality of life. pERC discussed some of the challenges patient advocacy groups may face in collecting information on patients' direct experiences, especially with a new drug to which Canadian patients may have had little exposure. However, pERC emphasized that it is important to have this information available for their deliberations.

From a patient perspective, access to additional therapies that will increase life expectancy is also an important consideration and an extension of two to three months of life is valued by patients. pERC considered that patients who received eribulin in the EMBRACE study had an overall median survival improvement of approximately 2.5 months, which aligns with patient values. Although patient input indicated that they are looking for treatments with manageable side effect profiles, they also indicated 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.

Patient values on treatment: acceptable side effects
Patients are seeking treatments with manageable side effect profiles that will not adversely affect their quality of life, especially as their disease progresses. pERC noted that the toxicity profile was similar between eribulin and the range of chemotherapy options studied in the EMBRACE trial. While peripheral neuropathy and febrile neutropenia were shown to occur more frequently with eribulin in the EMBRACE trial, pERC noted that these event rates were comparable to other standard chemotherapeutic agents administered in the metastatic breast cancer setting, such as taxanes.

ECONOMIC EVALUATION

Economic model submitted: Cost-effectiveness analysis
The pCODR Economic Guidance Panel assessed an economic evaluation looking at the cost-effectiveness of eribulin compared to treatment of physician's choice in women with locally recurrent or metastatic breast cancer who had received two to five prior chemotherapy regimens, including an anthracycline and a taxane component. The treatment of physician's choice was based on the EMBRACE study and represented a combination of possible alternatives including vinorelbine, gemcitabine, capecitabine, taxanes and anthracyclines. pERC considered this comparison to be appropriate, and reflected the fact that there is no specific standard of care and that metastatic breast cancer is most often treated with a series of treatments, rather than one single therapy or combination.

Basis of the economic model: Clinical and economic inputs
Costs include drug acquisition and administration costs, as well as costs related to toxicities. The key cost drivers included the price of eribulin and treatment of physician's choice.

Key clinical effects were based primarily upon the overall survival advantage associated with eribulin when compared to treatment of physician's choice in the EMBRACE trial. The biggest influences on clinical effects were the estimates of overall survival included in the model and the time horizon.

Drug costs: Lower confidential price submitted

Eribulin costs $540.00 per mg at the list price and $[redacted] at the submitted confidential price. (*Non-disclosable economic information was provided to pERC in the pCODR guidance reports for deliberation on a recommendation 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.*) At the list price, and at the recommended dose of 1.4 mg/m^2, and assuming an average body area of 1.7 m^2 and accounting for wastage, the average cost per treatment cycle would be $3,427. At the confidential price, and at the recommended dose of 1.4 mg/m^2, and assuming an average body area of 1.7 m^2 and accounting for wastage, the average cost per treatment cycle would be $[redacted]. (*Non-disclosable economic information was provided to pERC in the pCODR guidance reports for deliberation on a recommendation 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.*) Treatment courses continue every 21 days until the patient's disease progresses.

Clinical effect estimates: Influenced by survival estimates and time horizon

The two main factors affecting the clinical effect estimates were the survival estimates used in the economic model and the time horizon over which they were modeled. In reviewing the clinical data from the EMBRACE trial, pERC noted that all of the clinical benefit in the trial is observed by 18 months and survival curves converged at about 18 months. In the economic model, approximately 60% of the benefit attributed to eribulin occurs after 18 months, based on an extrapolation of the trial data and not observed trial data. Based on the planned survival analysis from the EMBRACE study, there was no evidence that benefit would accumulate past 24 months. Therefore, pERC considered it was more realistic to assume that in this patient population, cumulative survival benefit stops accruing between 18 and 24 months, rather than accumulating over a lifetime. By projecting a survival benefit beyond the end of the trial, as well as assuming a benefit from eribulin beyond progression, the mean overall survival benefit of eribulin over treatment of physician's choice, as modeled by the manufacturer, may be significantly overestimated. pERC considered feedback from the manufacturer that survival benefit data beyond 18 months from the EMBRACE trial were not incorporated into the pCODR Economic Guidance Panel's best estimates of the cost-effectiveness of eribulin. pERC reviewed re-analyses conducted by the Economic Guidance Panel and their rationale for using the 18 month estimates. pERC agreed with the Economic Guidance Panel that the analyses based on clinical data from the 18 month pre-planned analysis are more robust than those based on clinical data from the 24 month unplanned analysis. pERC considered that results observed at 24 months may be biased as a result of multiple unplanned looks at the data and that these more favourable estimates may not be stable over time.

Cost-effectiveness estimates: Not cost-effective

pERC reviewed the estimates presented by the pCODR Economic Guidance Panel, which ranged from $114,000 per quality adjusted life year (QALY) to $272,000 per QALY. pERC agreed with the Panel that the true estimate was most likely at the higher end of this range, i.e. between $223,840 per QALY and $272,275 per QALY, depending on when the expected benefit stops accruing between 18 and 24 months. pERC noted that the range presented by the Economic Guidance Panel was wide, reflecting the considerable uncertainty in the model and demonstrating that small changes in survival estimates and the time horizon could have a large impact on cost effectiveness estimates. pERC concluded that, at either the list price or the submitted price, eribulin is not cost-effective compared with treatment of physician's choice.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: additional line of therapy and wastage

pERC considered that eribulin is likely to be an additional therapy to be used in patients with advanced breast cancer and would not necessarily replace other therapies. This will likely increase overall treatment costs. pERC noted that eribulin would need to be administered in specialized centres and that a shorter infusion time (two to five minutes) for eribulin compared with standard chemotherapies would result in less chemotherapy chair time. pERC also noted that there may be considerable wastage with eribulin but that availability of different vial sizes could provide more dosing flexibility and potentially

minimize costs for jurisdictions. pERC noted that the Economic Guidance Panel considered the clarity of the budget impact analysis to be poor and that as a result, provinces may find it challenging to assess the budget impact of eribulin.

DRUG AND CONDITION INFORMATION

Drug Information	• Microtubule dynamic inhibitor • 1mg/2mL IV solution was reviewed by pCODR • Recommended dosage of 1.4mg/m^2 IV on days 1 and 8 of a 21 day cycle (infusion time, approximately two to five minutes)
Cancer Treated	• Incurable locally advanced or metastatic breast cancer
Burden of Illness	• Most commonly diagnosed malignancy in Canadian women. • Second leading cause of cancer deaths in women.
Current Standard Treatment	• Currently no standard of care in this setting. Treatment options include vinorelbine monotherapy, capecitabine monotherapy, gemcitabine monotherapy, gemcitabine combination therapy with a platinum agent or taxane, taxane monotherapy, or anthracycline monotherapy.
Limitations of Current Therapy	• Need for improved chemotherapeutic agents, both in terms of 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. Chaim Bell and Jo Nanson who were not present for the meeting
- Dr. Maureen Trudeau and Carole McMahon who were excluded from voting due to a conflict of interest

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

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

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 eribulin for metastatic breast cancer, through their declarations, eight members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, three of these members were 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.

The pERC Final Recommendation may also be informed by feedback on the pERC Initial Recommendation from pCODR's Provincial Advisory Group, patient advocacy groups that provided input at the beginning of the review and the Submitter and/or the manufacturer of the drug under review if they were not the Submitter. Feedback on the pERC Initial Recommendation that was considered is posted on the pCODR website.

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*. Eisai Ltd., as the primary data owner, did not agree to the disclosure of some economic information, therefore, this information has been redacted in this recommendation and publicly available guidance reports, as needed.

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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