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: Lapatinib ditosylate (Tykerb) **Funding Request:** In combination with letrozole for the treatment of postmenopausal patients with hormone receptor positive metastatic breast cancer, whose tumours overexpress the ErbB2 (HER2) receptor, and who are suitable for endocrine therapy	
Submitted By: GlaxoSmithKline Inc.	**Manufactured By:** GlaxoSmithKline Inc.
NOC Date: September 30, 2010	**Submission Date:** December 14, 2012
Initial Recommendation: May 2, 2013	**Final Recommendation:** July 5, 2013

pERC RECOMMENDATION	The pCODR Expert Review Committee (pERC) does not recommend funding lapatinib (Tykerb) in combination with letrozole in postmenopausal patients with hormone receptor positive, HER2 receptor positive metastatic breast cancer. The Committee made this recommendation because it was uncertain that there was an overall net clinical benefit of lapatinib plus letrozole when other effective treatment options are available and because lapatinib plus letrozole is not cost-effective compared with letrozole alone or compared with trastuzumab plus anastrozole.
POTENTIAL NEXT STEPS FOR STAKEHOLDERS	No next steps for stakeholders were identified by pERC.

SUMMARY OF pERC DELIBERATIONS

pERC noted that in the treatment of first-line postmenopausal women with hormone receptor positive, HER2 positive metastatic breast cancer a number of comparators exist including trastuzumab plus chemotherapy, lapatinib plus chemotherapy; trastuzumab plus hormonal therapy (such as anastrozole), hormonal therapy alone or chemotherapy alone. pERC discussed that among these comparators, studies evaluating trastuzumab plus chemotherapy have demonstrated an overall survival benefit and noted that in clinical practice the pCODR Clinical Guidance Panel considered this combination to be the standard of care in the first-line setting.

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 one randomized controlled trial included in the pCODR systematic review that compared lapatinib plus letrozole with letrozole alone in the first-line setting (Study EGF30008, Johnston 2009). pERC noted that there was a statistically significant improvement in progression-free survival but there was no statistically significant improvement in overall survival in the trial even though cross-over between treatment groups was not permitted. pERC also noted that an updated survival analysis was requested from the manufacturer but more mature data were not currently available even though the primary data analysis was conducted in 2008 and published in 2009. Considering these factors, pERC agreed with the pCODR Clinical Guidance Panel that from a clinical perspective these results represented only a modest improvement. Therefore, pERC considered that the clinical benefit of lapatinib plus letrozole is uncertain given the other treatment options that are currently available for this population, which have demonstrated an overall survival benefit.

pERC discussed the toxicity profile of lapatinib plus letrozole and noted that there was more toxicity compared with letrozole alone, including adverse events of diarrhea and rash. pERC discussed that these adverse events could be managed in clinical practice through dose adjustments but that monitoring of patients would still be required. pERC noted that although lapatinib is an oral therapy, monitoring of these adverse events and dose adjustments might limit its accessibility in remote areas.

pERC discussed the potential need for lapatinib plus letrozole in a small subpopulation. It was noted that there may be a limited number of patients who cannot receive chemotherapy and who value prolongation of progression-free survival, including elderly patients, those with multiple comorbidities or those who have weakened immune systems (i.e., immunocompromised). However, pERC noted that there would be very few patients for whom this option would be prescribed in clinical practice when other treatment options are available.

pERC considered the alignment of lapatinib plus letrozole with patient values and noted that patient advocacy groups did not provide input on lapatinib plus letrozole. While recognizing the difficulty that patient advocacy groups may have in providing input and accessing patients, pERC considered that it would have been helpful to have information regarding direct patient experiences with lapatinib plus letrozole. Patient advocacy group input from other relevant pCODR reviews of breast cancer treatments indicated that patients with HER2 positive metastatic breast cancer were willing to accept adverse effects if there were a clinical benefit. In addition, patients valued prolonging progression-free survival and treatments that maintained quality of life. pERC noted that given the uncertain clinical benefit of lapatinib plus letrozole, there may be less tolerance among patients for the toxicity associated with lapatinib plus letrozole. pERC also noted that there was no difference in quality of life between lapatinib plus letrozole and letrozole alone in Study EGF30008. pERC also discussed whether or not an oral treatment such as lapatinib plus letrozole that could be taken at home would enhance accessibility for patients who otherwise would have to travel to cancer centers to receive intravenous treatments. However, pERC noted that monitoring and possible dose adjustments would still be required to manage adverse events. Therefore, pERC considered that lapatinib plus letrozole may not align with patient values.

pERC deliberated upon the cost-effectiveness of lapatinib plus letrozole and discussed the challenges of using letrozole alone as a comparator and/or using trastuzumab plus anastrozole as a comparator. pERC also noted that there were structural limitations in the economic model that resulted in an overestimate of the survival benefit. Therefore, pERC was more confident in the Economic Guidance Panel's estimates of incremental cost-effectiveness, which were higher than the manufacturer's estimates. pERC concluded that based on the pCODR Economic Guidance Panel's best estimates, lapatinib plus letrozole could not be considered cost-effective compared with letrozole alone. pERC also discussed that from an economic perspective, lapatinib plus letrozole is dominated by trastuzumab plus anastrozole, i.e., if a conservative assumption were made that the efficacy is similar, patients would get the same clinical benefit but, at the list prices, lapatinib plus letrozole would cost more. Therefore, pERC did not consider lapatinib plus letrozole to be cost-effective.

pERC also considered the feasibility of implementing a funding recommendation. pERC discussed that the demand for the combination of a tyrosine kinase inhibitor and hormonal therapy would be expected to be low. It was also noted that trastuzumab plus anastrozole is not currently funded in all jurisdictions.

Upon reconsideration of the pERC Initial Recommendation and based on feedback received from the manufacturer, pERC discussed factors related to the pERC Initial Recommendation including the lack of mature overall survival data, the potential need for lapatinib plus letrozole in a small subpopulation and the potential alignment of lapatinib plus letrozole with patient values. However, pERC concluded that the feedback from the manufacturer did not provide sufficient justification to change the pERC recommendation.

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 (Name of Group)
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- pCODR's Provincial Advisory Group.
- the Submitter (GlaxoSmithKline Inc.)

The pERC Initial Recommendation was to not fund lapatinib (Tykerb) in combination with letrozole in postmenopausal patients with hormone receptor positive, HER2 receptor positive metastatic breast cancer.

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 lapatinib + letrozole compared with placebo + letrozole in postmenopausal women with hormone receptor-positive and epidermal growth factor receptor 2 positive (HER2+) metastatic breast cancer.

Studies included: one randomized controlled trial compared with letrozole

The pCODR systematic review included one randomized controlled trial, Study EGF30008 (Johnston, 2009). This was a double-blind, randomized controlled trial in the first-line setting comparing lapatinib (1500 mg) plus letrozole (2.5 mg) with placebo plus letrozole (2.5 mg). Cross-over of letrozole patients to the lapatinib plus letrozole arm at the time of progression was not permitted.

The pCODR review also provided contextual information on an indirect comparison of lapatinib plus letrozole and trastuzumab plus anastrozole, which was used to inform the cost-effectiveness analyses.

Patient populations: ECOG performance status 0 or 1, HER2 positive subpopulation

Study EGF30008 randomized 1286 postmenopausal women with hormone receptor-positive metastatic breast cancer who had an ECOG performance status of 0 or 1 and who were suitable for endocrine therapy. Of these, 17% (n=219) were HER2 positive (111 in the lapatinib plus letrozole arm and 108 in the placebo plus letrozole arm).

Prior treatment with anti-estrogen therapy in the adjuvant setting was allowed and prior treatment with an aromatase inhibitor and/or trastuzumab in the adjuvant setting was allowed if it had been completed more than one year before entering the study.

Key efficacy results: modest improvement in PFS and no overall survival benefit even though cross-over between treatment groups not permitted

The key efficacy outcomes on which pERC deliberated were progression-free survival in HER2+ patients, which was the primary endpoint in Study EGF30008, and overall survival. pERC discussed that in the HER2+ subpopulation, a statistically significant improvement in median progression-free survival was observed with lapatinib plus letrozole compared to placebo plus letrozole alone (8.2 and 3.0 months, respectively, hazard ratio 0.71; 95% confidence interval 0.53 to 0.96, P=0.019). pERC also noted that median overall survival was not statistically significantly different between lapatinib plus letrozole and letrozole alone. pERC discussed that in many trials, differences in overall survival results may not be statistically significant because cross-over is permitted from the control group to the treatment group. However, cross-over was not permitted in Study EGF30008. pERC also noted that an updated overall survival analysis had been requested from the manufacturer but more mature data were not currently available even though the primary data analysis was conducted in 2008 and published in 2009. pERC also noted that there would have been value in understanding the subsequent treatment patients received in Study EGF 300008, but these data were not available.

Considering these factors, pERC agreed with the pCODR Clinical Guidance Panel that from a clinical perspective these results represented only a modest improvement. Therefore, pERC considered that the clinical benefit of lapatinib plus letrozole is uncertain given the other treatment options that are available for this population (e.g. trastuzumab plus chemotherapy), which have demonstrated an overall survival benefit. Upon reconsideration of the pERC Initial recommendation and based on feedback received from the manufacturer, pERC discussed whether or not a positive funding recommendation should be made for lapatinib plus letrozole in the absence of mature overall survival data. pERC noted that the lack of mature overall survival data was only one factor contributing to the recommendation to not fund lapatinib plus letrozole. Other factors such as the choice of comparator in Study EGF30008, the limited need for lapatinib plus letrozole and the lack of alignment with patient values also influenced the pERC recommendation.

Quality of life: similar between treatment groups

In Study EGF30008, quality of life was measured using different scales including the Functional Assessment of Cancer Therapy-Breast, the Functional Assessment of Cancer Therapy-General and Trial Outcome Index. pERC noted that scores were similar between the two treatment groups but that a large proportion of patients did not contribute to the quality of life data because they did not complete the study. This created uncertainty in the quality of life data and pERC had challenges interpreting the results. pERC discussed these results and noted that previous patient advocacy group input indicated that breast cancer patients value maintaining their quality of life while on treatment.

Safety: adverse events manageable but dose adjustments and monitoring required

Based on data from Study EGF30008, pERC noted that more patients reported serious adverse events (22% versus 15%, respectively), grade 3 or 4 diarrhea and grade 3 or 4 rash with lapatinib plus letrozole compared to letrozole alone. pERC discussed that these adverse events could be managed in clinical practice through dose adjustments but that monitoring of patients would still be required. Therefore, pERC noted that although lapatinib is an oral therapy, monitoring of these adverse events and making dose adjustments would limit its accessibility in remote areas.

Comparator information: indirect comparison with trastuzumab plus anastrozole
While Study EGF30008 compared lapatinib plus letrozole with letrozole alone, pERC noted that the manufacturer had also conducted an indirect comparison comparing lapatinib plus letrozole with trastuzumab plus anastrozole to inform the cost-effectiveness analyses. Contextual information provided in the pCODR Clinical Guidance Report discussed the limitations of doing an indirect comparison between lapatinib plus letrozole with trastuzumab plus anastrozole. Therefore, pERC found it challenging to assess the comparative efficacy of lapatinib plus letrozole with trastuzumab plus anastrozole. pERC also discussed that although trastuzumab plus anastrozole is a comparator for lapatinib plus letrozole, it is not funded in many jurisdictions in Canada.

Need: trastuzumab plus chemotherapy is preferred first-line therapy in clinical practice
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 discussed that in the treatment of first-line postmenopausal women with hormone receptor positive, HER2 positive metastatic breast cancer, a number of treatments exist including trastuzumab plus chemotherapy, lapatinib plus chemotherapy; trastuzumab plus hormonal therapy, and hormonal therapy alone or chemotherapy alone. pERC discussed that among these comparators, studies evaluating trastuzumab plus chemotherapy have demonstrated an overall survival benefit and noted that in clinical practice the pCODR Clinical Guidance Panel considered this combination to be the standard of care in the first-line setting. Therefore, pERC discussed whether or not there was a need for lapatinib plus letrozole. Upon reconsideration of the pERC Initial Recommendation and based on feedback from pCODR's Provincial Advisory group, pERC further discussed whether or not use of lapatinib plus letrozole prior to use of trastuzumab plus chemotherapy could negate some of the overall survival benefit that would normally be expected with trastuzumab plus chemotherapy. pERC noted that while there may be some clinical rationale for this, evidence supporting this hypothesis would need to be extrapolated from clinical trials of other agents and was not specific to lapatinib plus letrozole.

pERC considered that, whenever possible, patients should be treated with therapies that have demonstrated an overall survival benefit. However, pERC noted that there may be a very limited number of patients who are not medically suitable for chemotherapy and who may value prolonged progression-free survival. pERC noted that this may include patients who are older, who are immunocompromised or who have multiple co-morbidities but emphasized that this is not the same as having a poor performance status. However, given the uncertainty in the overall net clinical benefit of lapatinib plus letrozole and the additional toxicity associated with lapatinib plus letrozole, pERC did not consider this need to be great enough to justify a funding recommendation for this very limited patient population. Based on feedback received from the manufacturer on the pERC Initial Recommendation, pERC reconsidered the need for treatment in a small population who cannot tolerate toxic chemotherapy regimens but did not consider that the feedback provided sufficient justification to change the pERC recommendation. pERC also noted that the manufacturer originally requested funding in patients appropriate for endocrine therapy but did not specifically consider the subset of these patients who are both appropriate for endocrine therapy and not suitable for toxic chemotherapy.

PATIENT-BASED VALUES

Values of patients with metastatic breast cancer: delay progression and extend survival
pERC noted that no patient advocacy groups provided input on the review of lapatinib plus letrozole. Therefore, the Committee discussed patient advocacy group input from other relevant pCODR reviews of breast cancer treatments. Input indicated that patients with metastatic breast cancer value delaying progression and extending their life expectancy. pERC noted that based on Study EGF30008, there were only modest improvements in progression-free survival and no overall survival benefit associated with lapatinib plus letrozole.

Patient values on treatment: manageable side effects and acceptable quality of life
pERC considered that it would have been helpful to get direct patient experiences with lapatinib plus letrozole to assist in determining patient values on treatment. While recognizing the difficulty that patient advocacy groups may have in providing input and accessing patients, pERC suggested that approaches to identifying patients who may be able to provide useful input, such as global patient group collaborations, may be appropriate.

In the absence of patient input directly related to lapatinib plus letrozole, pERC noted that metastatic breast cancer patients are looking for treatments with manageable side effect profiles that will extend life expectancy while offering an acceptable quality of life. pERC considered that given the uncertain clinical benefit of lapatinib plus letrozole, there may be less tolerance among patients for the additional toxicity (e.g. serious diarrhea and rashes) associated with lapatinib plus letrozole. pERC also noted that there was no difference in quality of life between lapatinib plus letrozole and letrozole alone in Study EGF30008 and there were challenges interpreting the results given the large number of patients who did not provide quality of life data. pERC also discussed whether or not lapatinib plus letrozole was a more accessible option for patients in remote areas, since it is a combination of oral drugs. However, pERC noted that monitoring of adverse events and making dose adjustments would limit its accessibility in remote areas. pERC also noted that lapatinib requires six tablets per day, which may not be appealing for some patients. Therefore, considering all of these factors, pERC determined that lapatinib plus letrozole may not align with patient values. Upon reconsideration of the pERC initial recommendation and based on feedback received from the manufacturer, pERC discussed whether or not lapatinib plus letrozole aligns with patient values because it provides convenience and enhanced choices. However, pERC noted that other factors such as monitoring of adverse events, lack of survival benefit, and lack of quality of life data were also considered when determining if lapatinib plus letrozole aligns with patient values.

ECONOMIC EVALUATION

Economic model submitted: cost-effectiveness and cost utility analysis

The pCODR Economic Guidance Panel assessed a cost-utility analysis comparing lapatinib plus letrozole to letrozole alone, as well as to trastuzumab plus anastrozole in post-menopausal women with hormone receptor positive, HER-2 positive metastatic breast cancer.

Basis of the economic model: clinical and economic inputs

Costs included drug costs, healthcare costs associated with routine follow-up, disease progression or death and costs associated with the management of adverse events.

Key clinical effects included progression-free survival estimates, overall survival estimates and utility values. The comparison with letrozole alone was based on the clinical results of the HER2 positive subpopulation in Study EGF30008 and the comparison with trastuzumab plus anastrozole was based on an indirect comparison.

Drug costs:

At the list price, lapatinib (Tykerb) costs $23.50 per 250 mg tablet and letrozole costs $1.38 per 2.5 mg tablet.

- At the recommended dose of lapatinib 1500 mg once daily, the average daily cost of lapatinib is $141 and the average cost per-28 day course is $3948.
- At the recommended dose of letrozole 2.5 mg once daily, the average daily cost is $1.38 and the average cost per-28 day course is $38.58.

Trastuzumab is available as 440 mg/vial at a cost of $2698 per vial and anastrozole is available as a 1mg tablet at a cost of $1.27 per tablet.

- The recommended dose of trastuzumab is 8 mg/kg on day one, followed by 6 mg/kg every 3 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 $215 and the average cost per 28-day course is $6009. For subsequent 28-day courses of treatment, which do not include the loading dose, the average daily cost is $90 and the average cost per 28-day course is $2575.
- At the recommended dose of anastrozole 1 mg once daily, the average daily cost is $1.27 per day and the average cost per-28 day course is $35.64.

Cost-effectiveness estimates: not cost-effective compared with letrozole or trastuzumab plus anastrozole

pERC deliberated upon the cost-effectiveness of lapatinib plus letrozole and discussed the pCODR Economic Guidance Panel's critique of the manufacturer's economic analysis. pERC noted that the Panel had identified structural limitations in the submitted economic model that overestimated the survival

benefit of lapatinib plus letrozole. Therefore, pERC placed more confidence in the Economic Guidance Panel's estimates of cost-effectiveness that corrected for this and which were higher than the manufacturer's estimates. pERC had challenges determining which was the more relevant comparator, letrozole alone or trastuzumab plus anastrozole, therefore, the Committee considered both analyses. pERC noted that based on the pCODR Economic Guidance Panel's best estimates, lapatinib plus letrozole could not be considered cost-effective compared with letrozole alone. pERC also discussed that cost-effectiveness estimates compared with trastuzumab plus anastrozole were uncertain because of limitations associated with the indirect comparisons. The pCODR Economic Guidance Panel reanalysis justified and used a more conservative assumption that assumed similar efficacy between letrozole plus lapatinib and trastuzumab plus anastrozole. Based on this reanalysis, pERC noted that from an economic perspective, lapatinib plus letrozole is dominated by trastuzumab plus anastrozole, i.e., if similar efficacy is assumed, patients would get the same clinical benefit but, at the list prices, lapatinib plus letrozole would cost more.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: limited access due to dose adjustments and monitoring for adverse events

pERC considered the feasibility of implementing a funding recommendation for lapatinib plus letrozole. pERC discussed the relevance of different comparators and noted that the Provincial Advisory Group had indicated that trastuzumab plus chemotherapy is the standard first-line treatment in post-menopausal women with hormone receptor positive, HER2 positive breast cancer, which supported the pCODR Clinical Guidance Panel's position. pERC considered other comparators and noted that accessibility to trastuzumab plus anastrozole is limited as it is not funded in many jurisdictions. pERC also noted that demand for the combination of a tyrosine kinase inhibitor and hormonal therapy would be expected to be low as there is no randomized controlled trial evidence that this combination has a survival benefit. pERC also discussed whether or not an oral treatment such as lapatinib plus letrozole would enhance accessibility for patients who would have to travel to cancer centers to receive intravenous treatments. However, due to the need for monitoring of adverse events and dose adjustments associated with lapatinib plus letrozole, access would still be limited for patients in remote areas.

DRUG AND CONDITION INFORMATION

Drug Information	• Tyrosine kinase inhibitor of epidermal growth factor receptor (EGFR or HER1) and HER2 • 1500 mg once daily in combination with 2.5 mg letrozole once daily, administered orally
Cancer Treated	• Hormone receptor-positive and HER2+ metastatic breast cancer in post-menopausal women
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 HER-2 positive, resulting in more aggressive clinical phenotype and a poorer prognosis.
Current Standard Treatment	• Anti-HER2 treatment (trastuzumab) in combination with chemotherapy (paclitaxel, docetaxel or vinorelbine) for those suitable to received chemotherapy is standard first-line treatment and has demonstrated a survival benefit • Aromatase inhibitor (anastrozole or letrozole) alone in patients who are not suitable for chemotherapy.
Limitations of Current Therapy	• Need for new and improved targeted therapies in patients that are either not medically fit and can't be treated with chemotherapy.

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. Bill Evans who was not present for the meeting
- Carole McMahon, Jo Nanson, Dr. Maureen Trudeau 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:

- Carole McMahon, Jo Nanson, Dr. Maureen Trudeau and Dr. Tallal Younis who were excluded from voting due to a conflict of interest.
- Dr. Chaim Bell, Dr. Scott Berry, Dr. Bill Evans and Dr. Sunil Desai who were not present

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 lapatinib(Tykerb) with letrozole for MBC, through their declarations, ten members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, but four 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*. There was no non-disclosable information in this recommendation document.

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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