pCODR EXPERT REVIEW COMMITTEE (pERC)
INITIAL RECOMMENDATION

The CADTH 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 reimbursement decisions. The pCODR process brings consistency and clarity to the assessment of cancer drugs by looking at clinical evidence, cost-effectiveness, and patient perspectives.

Providing Feedback on This Initial Recommendation
Taking into consideration feedback from eligible stakeholders, the pCODR Expert Review Committee (pERC) will make a Final Recommendation. Feedback must be provided in accordance with *pCODR Procedures*, which are available on the pCODR website. The Final Recommendation will be posted on the pCODR website once available, and will supersede this Initial Recommendation.

Drug:
Olaparib (Lynparza)

Submitted Funding Request: As monotherapy maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response to platinum-based chemotherapy

Submitted by:
AstraZeneca Canada Inc.

Manufactured by:
AstraZeneca Canada Inc.

Notice of Compliance Date:
April 29, 2016

Initial Recommendation Issued:
August 31, 2017

Approximate per Patient Drug Costs, per Month (28 Days) Submitted list price of $0.45 per mg	Olaparib regimen costs: $7102.56 per 28-day course

pERC RECOMMENDATION

pERC recommends reimbursement of olaparib conditional on the cost-effectiveness being improved to an acceptable level.

Reimbursement should be for olaparib monotherapy maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline or somatic as detected by approved testing) high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have completed at least two previous lines of platinum-based chemotherapy and are in radiologic response (complete or partial response) to their most recent platinum-based chemotherapy regimen.

Patients must have received at least four cycles of their most recent platinum-based chemotherapy before starting treatment with olaparib. Eligible patients should have had platinum-sensitive disease, defined as disease progression having occurred at least six months after completion of platinum-based chemotherapy. Maintenance therapy with olaparib should begin within eight weeks of the last dose of platinum-based chemotherapy. Treatment should continue until unacceptable toxicity or disease progression. Funding should be for patients who have a good performance status.

pERC made this recommendation because the Committee was satisfied that there is a net clinical benefit of olaparib maintenance treatment compared with placebo, based on a statistically significant and clinically meaningful improvement in progression-free survival (PFS), no appreciable detrimental effect on quality of life (QoL), and a

manageable but not insignificant toxicity profile. pERC agreed that olaparib aligns with patient values because it is an oral treatment that delays disease progression, has no detriment to QoL, and has manageable toxicities.

The Committee concluded that olaparib, at the submitted price and given the high level of uncertainty in the magnitude of long-term overall survival benefit, is not cost-effective in this population compared with best supportive care.

POTENTIAL NEXT STEPS FOR STAKEHOLDERS

Pricing Arrangements to Improve Cost-Effectiveness
Given that pERC was satisfied that there is a net clinical benefit with olaparib, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of olaparib to an acceptable level. pERC noted that a substantial reduction in the price of olaparib would be required in order to improve the cost-effectiveness to an acceptable level.

Accessibility to Reflex Testing for BRCA Mutation Status at Diagnosis
pERC agreed that BRCA mutation (germline or somatic as detected by approved testing) status is required prior to initiating treatment with olaparib. The Committee noted that it would be ideal for jurisdictions to have BRCA mutation reflex testing at the time of diagnosis to manage both the patient population and the budget impact of a reimbursement recommendation.

Time-Limited Need for Olaparib in Patients Treated with Three or More Lines of Platinum-Based Chemotherapy
At the time of implementing a funding recommendation for olaparib, jurisdictions may consider addressing the short-term, time-limited need to offer olaparib to patients currently receiving their third or later line of platinum-based chemotherapy for the treatment of relapsed BRCA-mutated epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.

Accessibility to Olaparib for Patients on Non-Platinum Chemotherapy on a Case-by-Case Basis
pERC recognizes that there will be a small number of patients who may be allergic to or unable to tolerate platinum-based chemotherapy, and therefore would have non-platinum therapy substituted for up to four cycles. pERC noted that jurisdictions will have to assess each individual case on a case-by-case basis to determine if a patient can receive olaparib.

Availability of Tablets
pERC noted that the current Health Canada approval and the reimbursement request are for olaparib capsules 400 mg (8 x 50 mg) twice daily. The SOLO-2 trial submitted for the current review used a dose of olaparib tablets 300 mg (2 x 150 mg) twice daily. pERC noted that, at the time of the review, the 50 mg capsules have Health Canada market authorization; however, the 150 mg tablets do not. pERC noted that information from the manufacturer is required about when the 150 mg tablets will be available in Canada. pERC noted that, until the olaparib tablets are available, olaparib capsules can be used as maintenance treatment for patients with relapsed BRCA-mutated epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.

Guidance on Transitioning From Capsules to Tablets
If Health Canada approves the tablets for market authorization,

	jurisdictions may want to consider developing processes or plans to transition patients who are currently taking capsules to tablets. **Re-Treatment After a Planned Treatment Interruption** pERC noted that if treatment with olaparib was temporarily stopped, the treating oncologist would need to confirm no evidence of progression before re-starting treatment with olaparib. The Committee noted that if there is evidence of progression as determined by the treating oncologist, treatment with olaparib should be permanently discontinued.

SUMMARY OF pERC DELIBERATIONS

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

CLINICAL BENEFIT	PATIENT-BASED VALUES
ECONOMIC EVALUATION	ADOPTION FEASIBILITY

In 2015, an estimated 2,800 new cases of ovarian cancer were diagnosed in Canada, with 1,750 deaths directly attributable to the disease. Serous epithelial ovarian cancer is the most commonly encountered histology in advanced ovarian cancers, and 20% to 30% of high-grade serous ovarian cancers have the breast cancer 1 or 2 gene mutation (BRCAm). Standard treatment for ovarian, fallopian tube, or primary peritoneal cancer — hereinafter referred to collectively as ovarian cancer — includes surgery and platinum/taxane combination chemotherapy. Despite expected response rates of 75% to 85%, recurrence is likely in most women. If this recurrence is six months or more after the last platinum-based chemotherapy, patients are classified as platinum-sensitive. After a response is observed following a fixed number of cycles of platinum-based therapy, the current standard treatment strategy is "watch and wait" until further disease progression occurs. All patients will eventually develop platinum resistance, with shortened progression-free survival (PFS) intervals during subsequent lines of chemotherapy. Registered clinicians noted there is currently no therapy known to extend off-chemotherapy remissions, and the durations of remission are generally progressively shorter over time, with increasing disease symptoms and/or chemotherapy exposure. Therefore, there is a significant unmet need for effective therapies that may extend remission.

The present review is a resubmission based on new clinical information. pERC deliberated upon the results of two randomized controlled trials (RCTs), Study 19 and SOLO-2, that both compared olaparib with placebo. pERC considered placebo to be a reasonable comparator, since the current standard treatment strategy is "watch and wait" in this setting. The Committee noted that Study 19 was the basis of the original submission to pCODR for olaparib; as such, the Committee had previously deliberated upon the results of a subgroup analysis within Study 19 in patients with BRCAm ovarian cancer. The SOLO-2 trial was a phase III, double-blind RCT that provided new evidence on the use of olaparib for patients with relapsed BRCAm ovarian cancer with disease in complete or partial response to platinum-based chemotherapy. The Committee noted that the SOLO-2 trial, similar to Study 19, reported a statistically significant improvement in PFS in favour of olaparib compared with placebo. pERC considered that a longer median PFS was observed in the olaparib group in the SOLO-2 trial compared with that reported in the BRCAm subgroup in Study 19. pERC discussed differences between the two trials that may have accounted for the difference in the magnitude of the observed PFS benefit, including differences in baseline patient characteristics and study design.

pERC also discussed the lack of overall survival (OS) data available at this time from the SOLO-2 trial due to the immaturity of the survival data, and noted that even with sufficient follow-up, the OS results may be confounded by post-trial treatments, as patients were permitted to receive subsequent treatment with a poly (adenosine diphosphate [ADP]–ribose) polymerase (PARP) inhibitor upon disease progression. In the absence of OS data, pERC discussed the clinical meaningfulness of PFS in relapsed ovarian cancer. The Committee acknowledged that the Clinical Guidance Panel (CGP) considered PFS to be a clinically important and valid primary end point in studies of relapsed ovarian cancer therapy. Input from registered clinicians also expressed that the goal of maintenance therapy is to improve PFS and delay time to the next chemotherapy treatment for this group of patients. pERC agreed that the delay in progression of disease is a meaningful end point in this clinical setting. Therefore, the Committee concluded that the PFS benefit observed in SOLO-2 was statistically significant and clinically meaningful.

pERC deliberated on the toxicity profile of olaparib and noted that there were more frequent toxicities compared with placebo, including adverse events (AEs) such as nausea, fatigue, vomiting, and diarrhea. In addition, the Committee discussed that anemia occurred in a much higher proportion of patients who received olaparib compared with placebo, and in some instances, led to dose reductions or dose interruptions. However, pERC noted that the majority of anemia cases were low-grade. pERC noted that some potential side effects of olaparib, although rare, could be severe, including developing acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) and chronic myelomonocytic leukemia (CMML). Overall, pERC noted that AEs could be managed in clinical practice through monitoring and appropriate dose adjustments.

pERC discussed the available patient-reported outcomes (PROs) data from the SOLO-2 trial. The Committee noted that although disease-related symptoms, physical functioning, and QoL did not improve among patients treated with olaparib compared with placebo, there was no detriment in PROs for most patients on olaparib compared with placebo over a 12-month period. pERC considered this to be reasonable in the setting of maintenance treatment. Furthermore, pERC also acknowledged that despite the side effects and toxicities associated with treatment with olaparib, there was no appreciable detrimental effect in QoL and other PROs.

pERC therefore concluded that there is a net clinical benefit of olaparib compared with placebo, based on the clinically meaningful results in PFS, no observed detriment in QoL and a manageable, but not insignificant, toxicity profile. In making this conclusion, the Committee acknowledged the unavailability and uncertainty of evidence of olaparib demonstrating a confirmed improvement in OS and a need for more effective treatment options.

pERC also discussed the results of supportive evidence from a bioavailability trial (Study 24) that supported continuous dosing of olaparib tablets for olaparib phase III clinical trials. pERC noted that the formulation of olaparib in the SOLO-2 trial was different from that in Study 19. Specifically, the SOLO-2 trial used olaparib tablets (2 x 150mg) twice daily, compared to Study 19 that used olaparib capsules (8 x 50 mg) twice daily. The Committee noted that the results of Study 24 suggest that the 300 mg daily dose of olaparib was better tolerated than higher doses, and showed similar effectiveness in tumour shrinkage. Thus, the study concluded that olaparib tablets are recommended for use in phase III clinical trials, thereby simplifying drug administration from 16 capsules per day to four tablets per day. pERC considered that the capsule formulation of olaparib is currently approved for market authorization by Health Canada and that the tablet formulation does not have market authorization in Canada. pERC discussed that the tablet formulation of olaparib would alleviate the significant capsule burden and reduce the burden of olaparib administration to patients. pERC considered the CGP's conclusion that the bioavailability of the olaparib tablet appears to be greater due to improved solubility compared to the capsule and that the tablet dosage was better tolerated than higher dosages showing similar effectiveness in tumour shrinkage. pERC therefore agreed with the CGP's recommendation that olaparib capsules should be used to treat patients with relapsed BRCAm ovarian cancer until olaparib tablets are available.

pERC acknowledged registered clinician input regarding the value of delaying progression and delaying the next needed chemotherapy course. pERC discussed input from registered clinicians that olaparib is an option to significantly extend remission after completion of chemotherapy for relapse. They noted that there is a significant unmet need for therapies that may extend remission, improve QoL, and extend survival. While pERC acknowledged that olaparib demonstrated an improvement in PFS compared with placebo, the Committee was unable to draw conclusions on the magnitude of OS benefit observed from the available clinical trials. Input from clinicians also indicated that olaparib has improved toxicity compared with chemotherapy; however, pERC was unable to comment on this comparison, as the evidence presented in the SOLO-2 trial was in a setting where the clinical alternative is "watch and wait." pERC acknowledged input provided by registered clinicians and noted that the current review addressed only patients who are relapsed and in response to a second platinum-based treatment and, therefore, data were unavailable to make any statement on the use of olaparib as maintenance treatment following first-line treatment and this would be considered out of scope for this review.

pERC deliberated upon input from one patient advocacy group regarding ovarian cancer and noted that patients value having oral treatment options that help manage disease-related symptoms, prolong survival, prolong time until recurrence, improve QoL, and reduce the number of visits to the cancer centre. Patients show willingness to tolerate side effects with new therapies, even if the benefit of treatment is short-term. However, patients were least willing to tolerate drug-related serious side effects, such as blood cancer and inflammation of the lungs. The majority of patients also expressed a desire to control fatigue. pERC agreed that the results from the SOLO-2 trial did not demonstrate an improvement in PROs, including QoL, but suggested that olaparib showed no detriment in QoL, which pERC considered to be reasonable in the setting of maintenance treatment. Overall, pERC concluded that the oral route of administration and the therapeutic intent of olaparib to delay progression and prolong time off of chemotherapy aligns with patient values. However, the Committee was limited by the immature OS data from the SOLO-2 trial and the quality of clinical evidence provided in Study 19 regarding OS and were unable to conclude that olaparib prolongs survival.

pERC deliberated on the cost-effectiveness of olaparib compared with best supportive care (BSC) and concluded that, at the submitted price, olaparib is not cost-effective. pERC made this conclusion noting

the significant uncertainty regarding the incremental cost-effectiveness ratio (ICER) due to the uncertainty in the clinical effectiveness of olaparib compared with BSC, based on the available clinical data. The Committee discussed that the lack of OS data from the SOLO-2 trial and the use of OS data derived from the subgroup of BRCAm patients in Study 19 increased the uncertainty in the estimates of incremental cost-effectiveness. pERC agreed with the pCODR Economic Guidance Panel (EGP) that, given that OS data were based on the small subgroup of BRCAm patients that was not powered to detect overall survival differences, there is considerable uncertainty around the OS data used. In addition, the Committee also discussed the issue that the use of PARP inhibitors as subsequent therapy post-progression in Study 19 would likely confound the observed OS benefit from Study 19. pERC noted that the main drivers of the incremental cost in the analysis were the cost of olaparib, the time horizon, and the treatment duration. The Committee discussed the fact that the lack of OS data from the SOLO-2 trial, and the limitations of the clinical data in Study 19, increased the uncertainty in the incremental cost-effectiveness estimates for olaparib. pERC discussed that, although the submitter's ICER was included in the EGP's best estimate range of the ICER, the ICER is likely toward the upper range of the EGP's estimates, and likely even higher given a more clinically plausible time horizon, more plausible health utility state values, and the lack of evidence of long term survival. Overall, pERC concluded that a substantial price reduction would be required in order to improve the cost-effectiveness of olaparib to an acceptable level.

pERC discussed the feasibility of implementing a reimbursement recommendation for olaparib for the treatment of patients with relapsed BRCAm ovarian cancer who are in response to platinum-based chemotherapy. pERC acknowledged, in accordance with the EGP analysis, that the number of eligible patients, the inclusion of BRCAm testing, and the drug cost have the largest impact on the budget impact analysis (BIA). Given that the number of eligible patients with BRCAm is between 20% and 30% and is expected to increase, if testing for *de novo* tumoural mutations becomes available, pERC considered that the submitter's estimates and the reanalysis estimates provided by the EGP likely underestimate the BIA as related to BRCAm testing. In addition, pERC discussed the need for BRCAm testing to implement a reimbursement recommendation for olaparib. pERC noted that BRCAm is not routinely tested in all jurisdictions at this time. Input from the pCODR Provincial Advisory Group (PAG) noted that BRCA test results can take a long time and there may be a delay in the initiation of treatment from completion of platinum-based chemotherapy. Given that BRCAm (somatic and germline) testing is essential to determine susceptibility to PARP inhibition and thus, response to treatment with olaparib, pERC discussed that jurisdictions will need to ensure BRCAm testing is available. Registered clinicians noted that it would be ideal for BRCA mutation reflex testing to be available at the time of initial diagnosis. pERC agreed that it would be ideal for jurisdictions to have BRCA mutation reflex testing at the time of diagnosis to manage both the patient population and the budget impact of a reimbursement recommendation.

The Committee also considered the significant capsule burden with olaparib in Study 19 (16 capsules per day) and acknowledged that the use of the tablet formulation of olaparib in the SOLO-2 trial (4 tablets per day) would significantly reduce the oral medication burden of olaparib administration. pERC noted that if the tablets will be available for use in Canada, jurisdictions may want to consider developing processes to transition patients who are currently taking capsules to tablets. Furthermore, pERC noted that information from the manufacturer is required on when the 150 mg tablets will be available in Canada.

The PAG requested input on the use of olaparib for patients who are already on more than two lines of platinum-based therapy. The Committee agreed that there would be a time-limited need for patients who have received more than two lines of platinum-based therapy. PAG is also seeking guidance on whether olaparib could be considered for patients who have completed platinum-based chemotherapy longer than eight weeks. pERC noted that patients in the SOLO-2 trial were required to complete platinum-based chemotherapy within eight weeks of completing the final dose of the last platinum-containing regimen. However, the Committee considered the CGP's recommendation and agreed that if there is a delay in initiating treatment with olaparib beyond eight weeks, in rare circumstances beyond the control of the patient and physician, it is reasonable that olaparib be initiated as long as there is no evidence of disease progression at the start of olaparib. Furthermore, the Committee discussed whether re-treatment with olaparib would be an option following periods of planned treatment interruption due to patient preference during maintenance treatment. pERC noted that if olaparib treatment was temporarily stopped, clinicians would have to confirm no evidence of progression before re-starting treatment with olaparib. The Committee noted that if there was evidence of progression following a temporary period of stopping treatment with olaparib, as determined by the treating oncologist, treatment with olaparib would likely be permanently discontinued. Finally, pERC discussed the fact that there will be a small

number of patients who may be allergic to or unable to tolerate platinum-based chemotherapy, and therefore would have non-platinum therapy substituted for up to four cycles. pERC noted that jurisdictions will have to assess such situations on a case-by-case basis to determine if a patient who is unable to tolerate platinum-based chemotherapy can receive olaparib.

EVIDENCE IN BRIEF

The CADTH pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC) deliberated on the following:

- a pCODR systematic review
- an evaluation of the manufacturer's economic model and budget impact analysis
- the guidance from the pCODR clinical and economic guidance panels
- a submission from a patient advocacy Ovarian Cancer Canada (OCC)
- input from registered clinicians
- input from pCODR's Provincial Advisory Group (PAG).

OVERALL CLINICAL BENEFIT

pCODR review scope

The purpose of the review is to evaluate the safety and efficacy of olaparib monotherapy, compared with an appropriate comparator, on patient outcomes in the treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline or somatic) epithelial ovarian, fallopian tube, or primary peritoneal cancer — hereinafter collectively referred to as ovarian cancer — who are in response to platinum-based chemotherapy.

Studies included: Two randomized controlled trials

The pCODR systematic review included two randomized trials: Study 19 and SOLO-2. Both trials were international, multi-centre randomized controlled trials (RCTs) and both compared olaparib to placebo.

The present review is a resubmission based on new clinical information. The Committee noted that Study 19 was the basis of the original submission to pCODR for olaparib, and as such, the Committee had previously deliberated upon the results. Study 19 was a double-blind, placebo-controlled phase II trial, comparing olaparib as monotherapy with placebo in patients with recurrent ovarian, fallopian tube, or primary peritoneal cancer with high-grade (2 or 3) serous features who have completed at least two courses of platinum-based chemotherapy, of which their most recent regimen included an objective response. Patients in Study 19 were randomized 1:1 to receive olaparib maintenance therapy at 400 mg (8 x 50 mg capsules) twice daily oral dose continually throughout a 28-day cycle or placebo capsules. SOLO-2 was a double-blind, placebo-controlled phase III trial to confirm the results of Study 19. The trial enrolled platinum-sensitive relapsed BRCA-mutated epithelial ovarian, fallopian tube or primary peritoneal cancer who were in response to platinum-based chemotherapy. Patients were randomized in a 2:1 ratio to receive either oral olaparib maintenance monotherapy at 300 mg (2 x 150 mg tablets) twice daily or placebo tablets.

BRCA mutation (BRCAm) status was not required at trial entry in Study 19; however, testing was done in the post-study period and retrospective pre-planned subgroup analysis was performed in patients with the BRCAm. In the SOLO-2 trial, patients were required to have a predicted deleterious, or suspected deleterious, BRCA mutation based on blood or tumor testing. Patients also consented to provide two blood samples for BRCA mutation testing using Myriad BRCAAnalysis®. Patients who had a known BRCA mutation before randomization were able to enter the trial based on this information and were required to provide blood samples for a confirmatory test. A key inclusion criterion for both trials was that patients had to have been initiated on the study within eight weeks of completing their final dose of a platinum-containing regimen. Patients must have received at least four cycles of their most recent platinum-based chemotherapy before starting treatment with olaparib. Eligible patients should have had platinum-sensitive disease, defined as disease progression having occurred at least six months after completion of platinum-based chemotherapy.

Treatment with olaparib continued until objective disease progression, as defined by Response Evaluation Criteria in Solid Tumors (RECIST) guidelines or unacceptable toxicity in Study 19. Treatment with olaparib continued until disease progression or until investigator deemed that a patient was no long benefitting from treatment in SOLO-2. If required, toxicities could be managed by treatment interruptions and dose reductions. Assessments for disease progression were conducted in strictly defined periods regardless of CA-125 values in the SOLO-2 trial. However, in Study 19, CA-125 progression could trigger an unscheduled tumour assessment to determine progression by RECIST. Crossover was not permitted in either trial for patients in the placebo group; however, treatment with another PARP inhibitor was allowed following

disease progression. Furthermore, in Study 19, patients were allowed a non-platinum regimen between the penultimate and last platinum regimen, whereas this was not allowed in the SOLO-2 trial.

pERC also discussed the results of supportive evidence from Study 24, a bioavailability trial that supported continuous dosing of olaparib tablets for olaparib phase III clinical trials. pERC noted that the formulation of olaparib in the SOLO-2 trial was different from that in Study 19. Specifically, the SOLO-2 trial used olaparib tablets (2 x 150mg) twice daily compared to Study 19 that used olaparib capsules (8 x 50 mg) twice daily. The Committee noted that the results of Study 24 suggest that the 300 mg daily dose of olaparib was better tolerated than higher doses and showed similar effectiveness in tumour shrinkage. Thus, the study concluded that olaparib tablets are recommended for use in phase III clinical trials, thereby simplifying drug administration from 16 capsules per day to four tablets per day. The capsule formulation of olaparib is currently approved for market authorization by Health Canada and that the tablet formulation requires regulatory approval and is not currently available in Canada. pERC noted that the tablet formulation of olaparib will reduce the significant oral medication burden and improve olaparib administration to patients. pERC noted the Clinical Guidance Panel (CGP)'s conclusion that the bioavailability of the olaparib tablet appears to be greater due to improved solubility compared to the capsule and that the tablet dosage was better tolerated than higher dosages showing similar effectiveness in tumour shrinkage. Therefore, pERC agreed with the CGP's recommendation that it is reasonable for patients to be treated with olaparib capsules until olaparib tablets are available in Canada.

Patient populations: BRCA mutation-positive patients

Among 265 enrolled patients in Study 19, 136 of 265 (51.3%) had BRCAm status (74 and 62 in the olaparib and placebo arms, respectively). Baseline characteristics were mostly balanced between treatment groups for the overall trial population and within the BRCAm subgroup of patients. Fewer patients in the olaparib arm had Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) 1 (15% versus 24% in placebo arm) while more patients in the olaparib arm had ECOG PS 0 (84% versus 73% in placebo arm). Similarly, in the BRCAm subgroup, fewer patients in the olaparib arm had a complete response to their most recent platinum-based regimen (49% versus 55% in placebo arm), while more patients in the olaparib arm had a partial response (51% versus 45% in placebo arm). Given that data were reported on the subgroup of patients with BRCAm, a Cox proportional hazards model was used to adjust the progression-free survival (PFS) and overall survival (OS) data for baseline covariates that were considered to be important prognostic factors. These included ethnic descent (Jewish versus non-Jewish), time to progression on penultimate platinum therapy (six to 12 months versus more than 12 months), and response to platinum therapy before randomization (complete response versus partial response).

The SOLO-2 trial randomized 295 patients with BRCAm status (195 and 99 in the olaparib and placebo arms, respectively). Baseline characteristics were mostly balanced between treatment groups; however, differences were observed between patients in the olaparib and placebo groups. Fewer patients in the olaparib arm had an ECOG PS 1 (16% versus 22%), while more patients in the olaparib arm had ECOG PS 0 (83% versus 77%). Fewer patients had two lines of prior chemotherapies in the olaparib arm (55% versus 61%). pERC noted that there was a higher proportion of more heavily pre-treated patients (≥ 3 or more lines of prior chemotherapy) in Study 19 compared with SOLO-2.

Key efficacy results: Progression-free survival

The key efficacy outcome deliberated on by pERC was PFS, the primary outcome in the trial. In Study 19, subgroup analysis for PFS in the BRCAm population was a pre-planned exploratory end point. In the BRCAm subgroup of patients, median PFS was 11.2 versus 4.3 months (hazard ratio [HR] = 0.18; 95% confidence interval [CI], 0.10 to 0.31, $P < 0.0001$) in the olaparib group compared with placebo groups. This translated into a 6.9-month gain in PFS in the BRCAm-positive subgroup. pERC acknowledged that improvement in PFS within the BRCAm subgroup of patients was consistent with the overall trial results and would be meaningful in this population; however, uncertainty remained, due to the small sample size of the study, the exploratory nature of the subgroup analysis, and the use of a one-sided alpha level of 0.2 in the intention-to-treat (ITT) analysis, which allowed a 20% risk for concluding a statistical difference in PFS in favour of olaparib when there is no difference.

OS, an exploratory secondary end point in the subgroup analysis, was analyzed at multiple time points without adjustments for multiplicity. Significance was not demonstrated at any of the interim analyses. At the latest OS analysis, in patients with the BRCAm and with 70% maturity, the median OS was 34.9 compared with 30.2 months in the olaparib and placebo arms, respectively (HR 0.62; 95% CI, 0.41 to 0.94, $P = 0.02480$, not adjusted for multiple testing). Adjustments were made for multiple testing in the ITT OS analysis and statistical significance was not demonstrated at any interim analysis. Therefore, the

Committee agreed that considerable uncertainty remains regarding the conclusions that could be drawn from the OS results. Overall, due to the type 1 error rate, the sample size of the trial, analysis of results based on a small subgroup of patients, and multiple testing for outcomes, pERC agreed that considerable uncertainty remained regarding the magnitude of benefit associated with olaparib observed in Study 19.

Results from the SOLO-2 trial confirmed the primary end point of PFS was improved with maintenance treatment with olaparib compared with placebo for adult patients with platinum-sensitive relapsed BRCAm epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response to platinum-based chemotherapy. The median PFS was 19.1 months in the olaparib group, compared with 5.5 months in the placebo group, translating into a 70% reduction in the risk of disease progression or death with olaparib versus placebo (HR 0.30; 95% CI, 0.22 to 0.41, $P < 0.0001$). A sensitivity analysis of PFS, measured by blinded independent central review (BICR) at 51% maturity, also demonstrated a statistically significant improvement in PFS in patients receiving olaparib versus placebo (HR 0.25; 95% CI, 0.18 to 0.35, $P < 0.0001$; median 30.2 months versus 5.5 months). pERC noted the discrepancy in median PFS point estimates obtained from BICR and investigator-assessment was explained by the investigators as possibly resulting from informative censoring. A sensitivity analysis adjusting for this informative censoring, where potentially informatively censored patients (14% in the olaparib arm and 14% in the placebo arm) were assumed to have an event at the next 12-week scan, resulted in a PFS that remained significantly longer with olaparib over placebo (HR 0.26; 95% CI, 0.19 to 0.35, $P < 0.0001$; median 19.6 versus 5.5 months).

Furthermore, the Committee noted that the SOLO-2 trial, similar to Study 19, reported a statistically significant improvement in PFS in favour of olaparib compared with placebo. pERC considered that a longer median PFS was observed in the olaparib group in the SOLO-2 trial compared to that reported in the BRCAm subgroup in Study 19. pERC noted differences between the two trials that may have accounted for the difference in the observed magnitude of the PFS benefit, including but not limited to: a higher proportion of more heavily pretreated patients (greater than 3 or more lines of prior chemotherapy) in Study 19 compared with SOLO-2; and non-platinum regimens between the penultimate and last platinum regimen was allowed in Study 19, but not allowed in SOLO-2. Furthermore, the definition of PFS in the SOLO-2 trial and Study 19 differed in that progression was declared based on the results of RECIST scans that were conducted in strict defined periods regardless of the CA-125 values in the SOLO-2 trial, whereas in Study 19, CA-125 progression could trigger an unscheduled tumour assessment to determine progression by RECIST thereby resulting in placebo patients being declared to have progressed earlier than they would have been if based on the scheduled RECIST scan assessments.

Overall survival (OS) data in the SOLO-2 trial were immature, with 24% of patients having an event at the time of data collection; therefore, median OS was not reached in either arm. The reported 20% reduction in the risk of death in olaparib-treated patients compared with placebo-treated patients is based on a total of 72 OS events in 295 patients. This did not reach statistical significance (HR 0.80; 95% CI, 0.50 to 1.31, $P = 0.43$). A total of 69% of patients were alive and continuing in the study at the latest data cut-off in September 2016. Although crossover was not permitted in the trial, patients randomized to the placebo group were permitted to receive a PARP inhibitor as subsequent therapy after progression. Among patients who were deemed to have progressive disease, 28.3% received a PARP inhibitor as subsequent therapy; of these, 22.2% received a PARP inhibitor as their first subsequent therapy. pERC noted that the OS data will likely be confounded from use of subsequent PARP inhibitors. The Committee noted that while OS data were immature at the time of data collection, any long-term follow-up could be evaluated in the future; however, any benefit will likely be confounded by post-trial treatments, making the actual degree of long-term benefit of olaparib uncertain. pERC noted, and agreed with the pCODR CGP that PFS is a clinically meaningful end point for second-line, relapsed ovarian cancer.

Patient-reported outcomes: No detriment in PROs for most patients

Patient-reported outcomes (PROs) were measured using the Total Functional Assessment of Cancer Therapy – Ovarian (FACT-O), FACT-O Symptom Index (FOSI), and Trial Outcome Index (TOI) in both Study 19 and SOLO-2. TOI captures a patient's ability to lead a normal, fulfilling life and is derived from the physical and functional well-being and ovarian cancer subscales of the FACT-O questionnaire. In both Study 19 and SOLO-2, the compliance rates for planned visits of FACT-O were generally high in both groups.

In the majority of patients, differences were not observed after treatment with olaparib or placebo for all scales. Overall, pERC agreed that the results from Study 19 suggest olaparib showed no detriment in PROs or quality of life (QoL), which pERC considered to be reasonable in the setting of maintenance treatment.

The SOLO-2 trial reported similar results, with no apparent detriment in any PROs or QoL. Specifically, there was no statistically significant or clinically relevant difference between olaparib and placebo groups over 12 months. Secondary planned analyses investigated the duration of "good quality of life" by time without symptoms of disease or toxicity (TWiST) and quality-adjusted PFS (QAPFS; a single measure of PFS and QoL outcomes), which also found no significant detrimental effect of olaparib compared to placebo on QoL. Although patient input indicated value in treatment that increased QoL, pERC agreed that results observed with olaparib in terms of PROs are in alignment with the values expressed by patients. Furthermore, pERC agreed that despite moderate, but not insignificant toxicities, there was no detriment in QoL for patients on olaparib.

Safety: More frequent grade 3 or 4 toxicities

The majority of patients who experienced any adverse event (AE) of any grade in the SOLO-2 trial was similar in both groups (99% olaparib versus 95% placebo). The most common AEs of any grade were higher in the olaparib group, including nausea (76% versus 33%), fatigue/asthenia (66% versus 39%), and anemia (44% versus 8%). Similarly, the most common grade 3 or 4 AE was anemia which was higher in the olaparib group, including anemia (20% versus 2%). Similar AEs and toxicity profiles were observed in patients who received olaparib in Study 19.

There was one case of AML reported that resulted in death and one case of myelodysplastic syndrome (MDS) reported in the olaparib group during the study and 30-day follow-up period. No cases of AML or MDS were reported in the placebo group. Additional cases of AML (olaparib group, n = 1; placebo group, n = 1), MDS (placebo group, n = 3), and CMML (olaparib group, n = 1) were reported after the 30-day follow-up period, resulting in an overall incidence of AML/MDS/CMML of 2.1% in the olaparib group (n = 4/195) and 4.0% in the placebo group (n = 4/99). pERC noted that blood disorders or blood cancer were the side effects that patients were least willing to tolerate. MDS occurred in two patients — one each in patients with BRCAm receiving olaparib and placebo.

A greater proportion of patients in the olaparib group versus placebo experienced AEs leading to dose interruptions (45.1% versus 18.2%), dose reductions (25.1% versus 3.0%), and discontinued study treatment (10.8% versus 2.0%). The most common reasons for dose reduction in the olaparib arm were anemia (12.8%), asthenia (3.1%), and fatigue (3.1%). The most common AEs leading to dose interruption in the olaparib arm were anemia (21%), vomiting (7.2%), and nausea (5.6%). The most common AEs leading to discontinuation in the olaparib group include anemia (3.1%) and neutropenia (1.5%). Anemia led to temporary dose interruptions in one out of five patients and to dose reductions in one out of 10 patients. In some instances, grade 3 anemia was managed through blood transfusions. A greater proportion of patients in the olaparib group (17.9%; n = 35) received blood and related products. Blood transfusions were required most often during the period from 2 to 5 months. Overall, pERC noted that olaparib is associated with moderate, but not insignificant toxicities, and can be managed appropriately with dose adjustments.

Need: Active maintenance treatment to prolong progression-free survival and time to next treatment

In 2015, an estimated 2,800 new cases of ovarian cancer were diagnosed, and 1,750 deaths were attributed directly to the disease. Standard therapy includes surgery and platinum/taxane combination chemotherapy. Despite expected response rates of 75% to 85%, recurrence is unfortunately likely in most women. If this recurrence is six months or more after the platinum chemotherapy, patients are classified as platinum-sensitive. Serous epithelial ovarian cancer is the most commonly encountered histology in advanced ovarian cancers, and 20% to 30% of high-grade serous ovarian cancers have BRCA mutations. Although all patients will eventually develop platinum resistance with shortened PFS intervals during subsequent lines of chemotherapy, there is currently no standard maintenance therapy given to patients. The standard practice after response is observed in patients following a fixed number of cycles of platinum-based regimen is to "watch and wait" until further disease progression occurs. pERC acknowledged registered clinician input that stressed the value of delaying symptomatic progression and time to the next treatment.

Registered clinician input: Disease burden, delay in progression, and time to next treatment

In total, four registered clinician inputs were received. Two clinician inputs were provided as a joint submission from a total of 10 oncologists. Two clinician inputs were received from two individual oncologists. According to registered clinician input, there are currently no approved medications with evidence for maintenance therapy of ovarian cancer after induction of remission with chemotherapy. As

such, registered clinicians echoed that there is an unmet need for additional therapies that can increase the chemotherapy-free interval with an opportunity to improve OS. The key benefits of olaparib as identified by the registered clinician inputs include the significant improvement in PFS in BRCAm patients, good tolerability, and the convenience of administering an oral take-home cancer agent. They noted that PARP inhibitors have a significantly improved toxicity profile in comparison with chemotherapy, and that patients' QoL is better on PARP inhibitors compared with any standard cytotoxic chemotherapy. Myelodysplasia or leukemia were identified as possible harms associated with treatment with PARP inhibitors; however, current data from studies demonstrate that the incidences of these serious AEs are minimal. The clinicians providing input identified that olaparib would be an additional therapeutic option as single-agent maintenance therapy, and would not displace any current therapies. They noted that the availability of olaparib may reduce chemotherapy use over time for patients who have long response.

PATIENT-BASED VALUES

Values of patients with ovarian cancer: Impact on daily life and quality of life

Input from one national patient organization noted that patients' lives were profoundly affected by ovarian cancer, including having significant psycho-social impacts, such as fear, depression, worry, and anxiety. Other areas that were most significantly affected include sexual relationships, sleep, work life, and physical activity and well-being. Caregivers reported that their sleep, sexual relationships, work life, and self-esteem were most significantly affected when caring for someone with ovarian cancer.

Input from 17/36 patients and caregivers agreed or strongly agreed that their current or past treatments for ovarian cancer were able to manage the disease; however, according to patients, their treatments were difficult and not as effective as they hoped. Common side effects that had a negative influence on their lives include fatigue, bowel problems, hair loss, blood problems, neuropathy, and nausea and vomiting. Patients indicated that they were willing to tolerate additional side effects even if the benefits of the treatment were considered to be short-term.

Patient experience with Olaparib: Prolonging recurrence, and improving quality of life

Overall, 21 respondents who were not treated with olaparib provided input about their expectations with olaparib. Fifteen respondents had direct experience with olaparib. The majority of patients expressed that they would consider taking olaparib as it would prolong the time to recurrence, can be taken at home, and does not cause hair loss. Patients noted that they value treatment that prolongs survival, lengthens the time until recurrence, improves QoL, and reduces the number of visits to the cancer centre. Patient input also indicated that the majority of respondents were willing to deal with some side effects, including nausea, fatigue, taste changes, blood problems, and bruising, but were less willing to tolerate serious AEs, such as blood disorders, blood cancer, and inflammation of the lungs. Among the 15 patients who had direct experience with olaparib, the majority of side effects reported include tiredness, weakness, nausea, taste changes, blood problems (e.g., anemia), dizziness, and diarrhea. Twelve respondents agreed that olaparib had improved their QoL compared with previous treatments.

Overall, pERC concluded that the oral route of administration, the clinically meaningful improvement in PFS, and the therapeutic intent of olaparib aligned with patient values. However, pERC was unable to conclude that olaparib prolongs OS.

ECONOMIC EVALUATION

Economic model submitted: Cost-effectiveness and cost-utility analysis

The pCODR Economic Guidance Panel (EGP) assessed cost-effectiveness and cost-utility analyses comparing olaparib monotherapy as maintenance treatment in patients with platinum-sensitive recurrent BRCAm-positive ovarian cancer.

Basis of the economic model: Overall survival from Study 19; progression-free survival from SOLO-2

Included costs were for drugs, follow-up, AE treatment, subsequent treatments, and end-of-life care. pERC noted that the factor most significantly affecting cost was drug cost. Key clinical effects considered in the analysis were obtained from Study 19 and SOLO-2. OS data were derived from a BRCAm subgroup of Study 19 as opposed to the OS data from the SOLO-2 trial because OS data in SOLO-2 were immature at

the time of analysis. pERC noted that OS data were based on a relatively small number of patients, and the Committee noted that the uncertainty in the OS data had the largest impact on the incremental cost-effectiveness ratio (ICER). Other uncertainties in the clinical effect estimates included the use of subsequent PARP inhibitors following progression in Study 19, which may confound the OS data. The EGP was unable to assess the effects of confounding due to subsequent PARP inhibitor usage on the ICER.

Drug costs: High drug cost

Olaparib costs $16.74 per 50 mg capsule. At the recommended dose of eight capsules twice per day, this amounts to $267.84 per day and $7,499.52 per 28-day course. Given the high dose intensity observed in the trial and the 50 mg capsule size, pERC does not anticipate that olaparib would be associated with significant wastage.

Cost-effectiveness estimates: Uncertainty in OS benefit

pERC deliberated on the cost-effectiveness of olaparib compared with best supportive care (BSC). The submitter's best estimate of the incremental cost-effectiveness ratio (ICER) is $243,249 per quality-adjusted life year (QALY). The EGP's best estimate of the ICER was between $195,112 per QALY and $421,637 per QALY.

pERC noted the significant uncertainty in the ICER due to the uncertainty in the clinical effectiveness of olaparib compared with BSC, given the limitations in available clinical trials. The Committee noted the lack of OS data from the SOLO-2 trial and the use of OS data derived from the subgroup of BRCAm patients in Study 19 increased uncertainty in the estimates of incremental cost-effectiveness. pERC agreed with the pCODR EGP that, given that OS data were based on the small subgroup of BRCAm patients that was not powered to detect OS differences, there is considerable uncertainty around the OS data used. In addition, the Committee discussed the issue that the use of PARP inhibitors as subsequent therapy post-progression in Study 19 would likely confound the observed OS from Study 19. The main drivers of incremental cost in the analysis were the cost of olaparib, the time horizon, and the treatment duration. pERC noted a number of other inputs explored by the EGP that had an impact on the ICER, including: reducing the time horizon from 15 years to 10 years, seven years, and five years, as the CGP felt that a shorter time horizon was clinically more plausible in a relapsed ovarian population; the use of alternative extrapolation methods; including the cost of BRCA mutation testing; the use of PFS instead of time to discontinuing treatment to represent the duration that patients would receive olaparib since the CGP felt that patients would not continue treatment with olaparib beyond progression; the source of utility data; the mean dosage of olaparib; and the use of equal OS benefit between arms at the end of the trial period. The Committee agreed that the lack of OS data from the SOLO-2 trial and limitations in the clinical data from Study 19 increased the uncertainty in the incremental cost-effectiveness estimates for olaparib. pERC also noted that, although the submitter's ICER was included in the EGP's best estimate range of the ICER, pERC agreed that the ICER is likely towards the upper range and likely even higher given a more clinically plausible time horizon of 5 to 7 years, more plausible health utility state values, and the lack of evidence of survival beyond 78 months. pERC noted that at the submitted price, olaparib is not cost-effective. Overall, pERC concluded that a substantial price reduction would be required in order to improve the cost-effectiveness of olaparib to an acceptable level.

The submitted BIA was based on the Study 19 which used the 50mg capsule formulation and a target daily dose of 800 mg per day. The SOLO-2 trial used 150 mg tablets with an apparent higher bioavailability that allowed an equivalent dosing of 600 mg per day (800 mg capsules = 600 mg tablets). While the BIA used olaparib capsules at a cost of $0.33/mg and the cost-effectiveness analysis uses olaparib tablets at a cost of $0.45/mg, the daily costs are roughly equivalent (800 mg per day capsules, $267.84 per day; 600 mg per day tablets, $267.86 per day). The submitter used the mean daily dose of 687.60 mg per day in the base-case analysis. This dosage was 86% of the planned dose of 800 mg in Study 19. This is higher than the 568.2 mg or 94.7% of the planned dose of 600 mg in the SOLO-2 trial. pERC noted that the submitted pharmacoeconomic and BIA models are based on different dosage forms (tablets versus capsules) that use different but apparently equivalent daily dosages (600 mg versus 800 mg) and equivalent daily costs. Therefore, the use of different dosage and formulations complicates the interpretation of the BIA.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: BRCA testing, alternative formulation with lower oral medication burden

pERC discussed factors affecting the feasibility of implementing a reimbursement recommendation for olaparib for patients with platinum-sensitive BRCAm ovarian cancer including, but not limited to: the costs associated with BRCA mutation testing, monitoring AEs and drug–drug interactions, especially for grade 3 or 4 anemia and the risk of developing MDS, AML, and pneumonitis; and the availability of olaparib tablets pending Health Canada regulatory approval.

pERC noted that olaparib is an oral drug, which can be administered more easily than an intravenous drug. However, the dose requirement of eight capsules twice per day (a total of 16 capsules per day) is a large burden for patients. pERC noted that alternative dose formulation (e.g., a 150 mg tablet) may lower the oral medication burden and may be available in the future. The Committee discussed that information from the manufacturer is required on when the 150 mg tablets will be available in Canada. pERC noted that it is reasonable for patients to be treated with olaparib capsules until olaparib tablets are available in Canada. Jurisdictions may want to consider developing processes or plans to transition patients who are currently taking capsules to tablets in the future.

pERC discussed the feasibility of implementing a reimbursement recommendation for olaparib for the treatment of patients with relapsed BRCAm ovarian cancer who are in response to platinum-based chemotherapy. pERC acknowledged that, in accordance with the EGP analysis, that the number of eligible patients, the inclusion of BRCAm testing, and the drug cost have the largest impact on the BIA. Given that the number of eligible patients with BRCAm is between 20% and 30% and is expected to increase, if testing for *de novo* tumoural mutations becomes available, pERC considered that the submitter's estimates and the reanalysis estimates provided by the EGP likely underestimate the BIA as related to BRCAm testing. Therefore, pERC considered that the submitter's analysis, and likely the reanalysis provided by the EGP, underestimated the BIA as related to BRCAm testing. In addition, pERC discussed the need for BRCA mutation testing to implement a reimbursement recommendation for olaparib. pERC noted that the BRCA mutation is not routinely tested at this time. Input from the pCODR Provincial Advisory group (PAG) noted that BRCA mutation test results can take a long time, which could lead to a delay in the initiation of treatment from completion of platinum-based chemotherapy. Given that BRCA mutation (somatic and germline) testing is essential to determine susceptibility to PARP inhibition and, thus, response to treatment with olaparib, pERC discussed that jurisdictions will need to ensure BRCA mutation testing is available. pERC agreed that it would be ideal for jurisdictions to have BRCA mutation reflex testing at the time of diagnosis to manage both the patient population and the budget impact of a reimbursement recommendation.

The PAG requested input on the use of olaparib for patients who have received more than two lines of platinum-based therapy. The Committee agreed that there would be a time-limited need for patients who have received more than two lines of platinum-based therapy. PAG is also seeking guidance on whether olaparib could be considered for patients who completed platinum-based chemotherapy for longer than eight weeks. pERC noted that patients in the SOLO-2 trial were required to complete platinum-based chemotherapy within eight weeks of completing the final dose of the last platinum-containing regimen. However, the Committee considered the CGP's recommendation, and agreed that if there is a delay in initiating treatment with olaparib beyond eight weeks, in rare circumstances beyond the control of the patient and physician, it is reasonable that olaparib be initiated as long as there is no evidence of disease progression at the start of olaparib.

Furthermore, the Committee discussed whether re-treatment with olaparib would be an option following periods of planned treatment interruption due to patient preference during maintenance treatment. pERC noted that if olaparib treatment were temporarily stopped, clinicians would have to confirm no evidence of progression before re-starting treatment. The Committee noted that if there was evidence of progression as determined by the clinician, treatment with olaparib would be permanently discontinued. Finally, pERC discussed the fact that there will be a small number of patients who may be allergic to or unable to tolerate platinum-based chemotherapy, and therefore would be substituted with non-platinum therapy for up to four cycles. pERC noted that jurisdictions will have to assess such situations on a case-by-case basis to determine if a patient who is unable to tolerate platinum-based chemotherapy can receive olaparib.

DRUG AND CONDITION INFORMATION

Drug Information	• Olaparib is a PARP inhibitor. • Olaparib is available as a 50 mg capsule. • The recommended dose is eight 50 mg capsules twice per day.
Cancer Treated	• Platinum-sensitive relapsed BRCA mutation-positive (germline or somatic) ovarian cancer in response to platinum-based chemotherapy
Burden of Illness	• 2,800 new cases and 1,750 deaths from ovarian cancer in Canada in 2015 • 75% to 85% of ovarian cancer recurs (high grade) • 20% to 30% of high-grade serous ovarian cancer patients are BRCA mutation-positive • Shortened progression-free survival intervals during subsequent lines of chemotherapy
Current Standard Treatment	• "Watch and wait" after response is observed following a fixed number of cycles of platinum-based regimen until further disease progression occurs
Limitations of Current Therapy	• No maintenance therapy

ABOUT THIS RECOMMENDATION

The pCODR Expert Review Committee

Recommendations are made by the CADTH pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC) following the pERC *Deliberative Framework*. pERC members and their roles are as follows:

Dr. Maureen Trudeau, Oncologist (Chair)
Dr. Paul Hoskins, Oncologist (Vice-Chair)
Dr. Scott Berry, Oncologist
Dr. Kelvin Chan, Oncologist
Dr. Matthew Cheung, Oncologist
Dr. Craig Earle, Oncologist
Dr. Allan Grill, Family Physician
Don Husereau, Health Economist
Dr. Anil Abraham Joy, Oncologist
Karen MacCurdy Thompson, Pharmacist
Valerie McDonald, Patient Member Alternate
Carole McMahon, Patient Member
Dr. Catherine Moltzan, Oncologist
Jo Nanson, Patient Member
Dr. Marianne Taylor, Oncologist
Danica Wasney, Pharmacist

Dr. Catherine Moltzan chaired the meeting due to the Chair's and Vice-Chair's conflicts of interest. All members participated in deliberations and voting on the Initial Recommendation, except:

- Dr. Maureen Trudeau, who was excluded from chairing and voting due to a conflict of interest
- Dr. Paul Hoskins, who did not participate in the information-gathering, deliberations, or voting due to a conflict of interest
- Dr. Anil Abraham Joy, Dr. Kelvin Chan, Danica Wasney, and Jo Nanson, 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 olaparib (Lynparza) for platinum-sensitive relapsed BRCA mutation-positive (germline or somatic) ovarian cancer in response to platinum-based chemotherapy, through their declarations, two members had a real, potential, or perceived conflict, and based on application of the *pCODR Conflict of Interest Guidelines*, two of these members were excluded from voting.

Information sources used

pERC 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 its 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 base its recommendations 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*. All information provided to pERC for its deliberations was handled in accordance with the *pCODR Disclosure of Information Guidelines*.

Use of this Recommendation

This Recommendation from pERC is not intended as a substitute for professional advice, but rather to help Canadian health systems leaders and policy-makers 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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