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
Upon consideration of feedback from eligible stakeholders, pERC members considered that criteria for early conversion of an Initial Recommendation to a Final Recommendation were met and reconsideration by pERC was not required.

Drug: Enzalutamide (Xtandi)

Submitted Funding Request:
Treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy who have not received prior chemotherapy

Submitted By: Astellas Pharma Canada, Inc.	**Manufactured By:** Astellas Pharma Canada, Inc.
NOC Date: April 15, 2015	**Submission Date:** October 2, 2014
Initial Recommendation: June 4, 2015	**Final Recommendation:** June 22, 2015

pERC RECOMMENDATION

The pCODR Expert Review Committee (pERC) recommends funding enzalutamide (Xtandi) conditional on the cost effectiveness being improved to an acceptable level. Funding should be for patients with asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer (mCRPC) who have evidence of disease progression following androgen deprivation therapy (ADT), which generally includes an LHRH agonist or orchiectomy, who have not received prior chemotherapy for mCRPC and who have an ECOG performance status of 0 or 1, and no risk factors for seizures. Treatment should be until disease progression or the initiation of chemotherapy.

pERC made this recommendation because it was satisfied that enzalutamide has a net clinical benefit compared with placebo based on a clinically meaningful improvement in overall survival and a manageable toxicity profile. In addition, pERC concluded that treatment with enzalutamide aligns with patient values. However, at the submitted price and the Economic Guidance Panel's range of estimated incremental cost-effectiveness ratios, enzalutamide could not be considered cost-effective compared with placebo.

In the absence of a direct comparison of clinical effectiveness with abiraterone and prednisone, the uncertainty in the economic analyses was too great for the Committee to determine enzalutamide's net clinical benefit or cost-effectiveness relative to abiraterone and prednisone.

POTENTIAL NEXT STEPS FOR STAKEHOLDERS

Pricing Arrangements to Improve Cost-Effectiveness
Given that pERC was satisfied that there is a net clinical benefit of enzalutamide in patients with asymptomatic or mildly symptomatic mCRPC, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of enzalutamide to an acceptable level.

Alignment of Pricing of Enzalutamide with Alternative Treatments
Provinces should be aware that the submitted cost-effectiveness estimates by the manufacturer comparing enzalutamide with abiraterone plus prednisone assumed that the price of abiraterone is the same as the list price in all jurisdictions. Because the economic analysis is very sensitive to drug price, any change in the price of abiraterone would change the cost-effectiveness of enzalutamide compared to abiraterone plus prednisone. pERC recommends that enzalutamide should only be funded if it is costs the same as or less than abiraterone with prednisone.

Optimal Sequencing of Enzalutamide and Abiraterone Unknown
There is currently no evidence available on the effectiveness of enzalutamide in patients with mCRPC who progress after receiving abiraterone and prednisone or vice versa. Therefore, pERC was unable to make an informed recommendation on sequencing.

Consider Restricting the Prescribing to Enhance the Quality of Care
pERC noted that provinces may want to consider additional measures to optimize patient selection for treatment, to optimize the management of toxicity and to limit budget impact by implementing an approved prescriber list. pERC made this suggestion because there is considerable toxicity associated with enzalutamide which may be best managed by clinicians who have experience treating patients with this drug. As well, drug price is the key driver of the incremental cost-effectiveness estimates and the budget impact.

SUMMARY OF pERC DELIBERATIONS

pERC noted that prostate cancer is the most common malignancy in Canadian men. Prostate cancer deaths are commonly the result of metastatic castration-resistant prostate cancer (mCRPC). The median survival for patients with mCRPC has been estimated to be between two and four years. Standard treatment for patients with asymptomatic or mildly symptomatic mCRPC includes abiraterone with prednisone, hormonal therapies or active monitoring for disease progression to determine when chemotherapy is indicated. pERC noted that although abiraterone with prednisone is an effective treatment option in this disease setting, individual patients may experience intolerable side effects, which preclude the use of this drug combination.

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 one randomized controlled trial (PREVAIL, 2014) which compared enzalutamide (n=872) to placebo (n=845) in patients with asymptomatic or mildly symptomatic mCRPC who had not received prior chemotherapy. pERC deliberated upon the results of the PREVAIL study and agreed with the Clinical Guidance Panel's (CGP) conclusion that there is a net clinical benefit of enzalutamide, based on a statistically significant and clinically meaningful improvement in overall survival (OS) in patients receiving enzalutamide compared to placebo. pERC also noted that PREVAIL demonstrated statistically significant improvements in radiographic progression-free survival (rPFS) and quality of life. pERC discussed the toxicity profile of enzalutamide based on the PREVAIL study and concluded that the side effects associated with enzalutamide were manageable. Therefore, pERC concluded that there is a net clinical benefit compared to placebo, as enzalutamide demonstrated a statistically significant and clinically meaningful improvement in OS, statistically significant improvement in rPFS and quality of life, and had a manageable toxicity profile.

pERC noted that in the absence of a head-to-head trial comparing enzalutamide to abiraterone and prednisone, the relative efficacy and safety of enzalutamide compared with abiraterone and prednisone is uncertain. pERC discussed the results of an indirect comparison of enzalutamide and abiraterone and prednisone conducted by the manufacturer but noted that there were several limitations to the indirect comparison. The methodological rigour of the indirect comparison was questionable due to several factors including the lack of a common comparator arm and differences in the patient populations in the included studies. pERC did not consider the evidence to be sufficient to assume that the two therapies have similar efficacy and harms. pERC was, therefore, unable to draw any conclusions from the results of the indirect comparison between enzalutamide and abiraterone and prednisone. However, pERC noted that enzalutamide may provide another treatment option for those patients who cannot tolerate abiraterone and prednisone.

pERC deliberated on the potential alignment of enzalutamide with patient values based on input provided by two patient advocacy groups. pERC noted that patients valued access to new effective treatments that would prolong their survival with fewer side effects. pERC noted that enzalutamide does provide an effective treatment option that prolongs survival in patients with mCRPC. However, enzalutamide is associated with substantial, albeit manageable, side effects and adverse events. pERC discussed whether or not treatment with enzalutamide aligns with patient values since it offers patients and their clinicians an opportunity to assess the toxicity profile of the treatment options and make an informed decision based on the patient's specific circumstances. pERC concluded that enzalutamide aligns with patient values because it improves survival and has a different profile of side effects and adverse events than alternative treatments.

pERC deliberated on the cost-effectiveness of enzalutamide. The submitter provided two economic models in their submission. The first model compared the cost-effectiveness of enzalutamide followed by treatment with docetaxel then abiraterone to best supportive care (BSC) followed by docetaxel and then treatment with enzalutamide. The second model compared enzalutamide followed by docetaxel and then treatment with abiraterone to abiraterone followed by docetaxel then treatment with enzalutamide. The

estimates used in the second model were derived from the indirect comparison. pERC considered that the estimates of clinical effectiveness used in the second model comparing enzalutamide to abiraterone were highly uncertain, and questioned the modelled 2 extra months of survival for enzalutamide compared to abiraterone modelled based on indirect comparison. Therefore, pERC relied on the first economic model comparing enzalutamide to best supportive care in making their recommendation. pERC agreed with the Economic Guidance Panel's (EGP) reanalysis of the submitted model comparing enzalutamide to BSC. The EGP's estimates of incremental cost-effectiveness for the comparison of enzalutamide with BSC were higher than the submitter's estimate based on a number of structural limitations of the economic model and clinical assumptions that led to overestimations of clinical benefit. Based on the reanalysis of the submitted economic model by the EGP, pERC concluded that enzalutamide is not cost-effective at the submitted price compared to best supportive care.

pERC discussed the feasibility of implementing a funding recommendation for enzalutamide. It was noted that there is no direct comparison between enzalutamide and abiraterone with prednisone, and the indirect comparison of the two regimens is not reliable. Without direct comparative evidence, pERC considered that enzalutamide is an alternative to abiraterone and prednisone. pERC also noted that there is no evidence on whether there is a preferred sequence of enzalutamide and abiraterone with prednisone, and thus could not make an informed conclusion regarding the sequencing of these treatments. Finally, pERC noted that the provinces may want to consider additional measures to optimize the management of toxicity and limit budget impact by implementing an approved prescriber list. pERC made this suggestion because there is considerable toxicity associated with the use of enzalutamide, but can best be managed by clinicians who have experience treating patients with this drug. As well, and because drug price is the key driver of the incremental cost-effectiveness estimates and budget impact.

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 (Prostate Cancer Canada [PCC] & Canadian Cancer Survivor Network [CCSN])
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- input from pCODR's Provincial Advisory Group.
- one patient advocacy group (Prostate Cancer Canada)
- the Submitter (Astellas Pharma Canada Inc.)

The pERC initial recommendation was to fund enzalutamide (Xtandi) conditional on the cost effectiveness being improved to an acceptable level.

Feedback on the pERC Initial Recommendation indicated that the manufacturer, patient advocacy group and pCODR's Provincial Advisory Group agreed with the initial recommendation.

The pERC Chair and pERC members reviewed the feedback and it was determined that the pERC Initial recommendation was eligible for early conversion to a pERC Final Recommendation without reconsideration by pERC because there was unanimous consensus from stakeholders on the recommended clinical population outlined in the pERC Initial Recommendation.

OVERALL CLINICAL BENEFIT

pCODR review scope

The purpose of the review is to evaluate the effectiveness and safety of enzalutamide compared with standard therapies or placebo in patients with asymptomatic or mildly symptomatic mCRPC who have not received prior chemotherapy for mCRPC.

Studies included: One RCT comparing enzalutamide to placebo

The pCODR systematic review included one international, multicenter, double-blind, placebo-controlled randomized phase 3 trial, the PREVAIL study (Beer et al, 2014). This study included patients with mCRPC who had not received prior chemotherapy and were randomized to receive either enzalutamide 160 mg orally once daily (n=872) or matching placebo (n=845) until unacceptable side effects, or confirmed radiographic progression. The study used two co-primary endpoints; overall survival (OS) and radiographic progression-free survival (rPFS). Secondary endpoints included time to prostate specific antigen (PSA) progression, time to initiation of cytotoxic chemotherapy (TTC), quality of life (QoL) and safety.

pERC noted that there were no trials comparing enzalutamide to abiraterone and prednisone in patients with mCRPC who had not received prior chemotherapy for mCRPC identified by the pCODR systematic review. Abiraterone and prednisone has recently become the standard of care in most Canadian jurisdictions.

Patient populations: Median age >70 years, ECOG PS 0-1

Overall, baseline patient characteristic were balanced between both study arms in the PREVAIL study. The median age was 72 years (range 43-93) in the enzalutamide arm and 71 years (range 42-93) in the placebo arm. The majority of patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 (67% in the enzalutamide arm and 69% in the placebo arm). The rest of the patients had an ECOG performance status of 1 as patients with an ECOG performance status of 2 or higher were excluded from the study. In addition, patients with brain metastases, a history of seizure, or any condition that might predispose them to seizure, were also excluded.

Key efficacy results: Clinically meaningful improvement in overall survival

pERC noted that a statistically significant and clinically meaningful difference in OS was demonstrated in favour of the enzalutamide group (median 32.4 months) compared with the placebo group (median 30.2 months; hazard ratio [HR] 0.71, 95% confidence interval [CI] 0.60 to 0.84; p<0.001). In addition, a statistically significant difference in rPFS was demonstrated in favour of enzalutamide (median not reached) compared with placebo (median 3.9 months; HR 0.19, 95% CI 0.15 to 0.23; p<0.001), after a median follow-up time of 12 months. Statistically significant differences in favour of enzalutamide compared with placebo were also demonstrated for time to PSA progression (median 11.2 months versus [vs.] 2.8 months, respectively; HR 0.17, 95% CI 0.15 to 0.20; p<0.001) and time to initiation of cytotoxic chemotherapy (median 28.0 months vs. 10.8 months; HR 0.35, 95% CI 0.30 to 0.40; p<0.001).

Quality of life: Delay in deterioration of QoL in favour of enzalutamide

Quality of life was assessed in the PREVAIL study using the time to a 10-point decrease in the Functional Assessment of Cancer Therapy-Prostate (FACT-P) global score compared to baseline. The time to decline in FACT-P was statistically significantly longer in the enzalutamide group (median 11.3 months) compared with the placebo group (median 5.6 months; HR 0.63, 95% CI 0.54 to 0.72; p<0.001).

Pain was assessed using the Brief Pain Inventory-Short Form (BPI-SF). At 6 months, fewer enzalutamide-treated patients (32% of 698 patients) reported severe pain (≥30% increase in BPI-SF score from baseline) compared with those treated with placebo (37% of 358 patients); however, the difference was not statistically significant (p=0.092).

Safety: Similar frequency of adverse events for enzalutamide group and placebo group

The proportion of patients who experienced an adverse event was similar between the enzalutamide group (97%) and the placebo group (93%). Fatigue, back pain, constipation, and arthralgia were more commonly reported in the enzalutamide group than in the placebo group. More patients who received enzalutamide reported Grade 3 or higher adverse events (43%) than those who received placebo (37%). pERC noted that the proportion of patients who withdrew due to adverse events was 6% in both groups.

Comparator information: Abiraterone plus prednisone is the current standard therapy

pERC noted that for patients with asymptomatic or minimally symptomatic mCRPC, the standard treatment includes abiraterone in combination with prednisone. This is based on the result of the COU-AA-302 study comparing abiraterone plus prednisone to prednisone plus placebo in patients with mCRPC who had not received chemotherapy. pERC acknowledged that the PREVAIL study was conducted before abiraterone plus prednisone became standard therapy in this setting. pERC also noted that the pCODR Clinical Guidance Panel (CGP) and Methods Team indicated that there is substantial heterogeneity between the PREVAIL and COU-AA-302 studies that precludes a formal indirect treatment comparison. In conclusion, pERC noted that the results of the PREVAIL study comparing enzalutamide to placebo were compelling, but evidence to compare enzalutamide to abiraterone and prednisone would have been preferred.

Need: Additional treatment option for individual patient circumstances

pERC acknowledged that enzalutamide represents an option to abiraterone with prednisone for patients and clinicians to consider in the management of mCRPC especially considering those patients who may have relative contraindications to the use of abiraterone and prednisone.

PATIENT-BASED VALUES

Values of patients with mCRPC: Treatment options that prolong survival and reduce disease symptoms

Input from two patient advocacy groups (Canadian Cancer Survivor Network [CCSN] and Prostate Cancer Canada [PCC]) indicated that patients with mCRPC value prolongation of life expectancy and reduction in the symptoms of their disease without a significant increase in the side effects of treatment. pERC noted that the most common symptoms that patients wanted to manage better were fatigue, pain, sleepless and/or restless nights, fractures (or fear of fracture), depression, living with the uncertainty of the disease, urinary incontinence and sexual dysfunction.

pERC noted that the respondents to the CCSN survey reported that the most common side effects of current therapies included diarrhea (42%), nausea and vomiting (42%), anemia (47%) and infection (28%). Half of the respondents indicated that nausea and vomiting were the most difficult side effects to manage, while one-third reported that diarrhea, anemia and risk of infection were the most difficult to manage.

pERC also noted that there is a considerable impact on caregivers as they often shoulder an additional financial burden by taking time off work and covering costs associated with the disease that are not covered under public or private health benefits. Caregivers often experience increased burdens in family and household responsibilities. In addition to the above, caregivers report increased anxiety and stress due to the impact on the family of the diagnosis of an incurable disease.

Patient values on treatment: Adverse events persist, but preferred over prednisone

pERC noted that of the six respondents to the CCSN survey who had experience with enzalutamide, the most common side effects of enzalutamide were fatigue (75%), diarrhea (50%), and hot flashes (50%). In total, 20% of respondents said that fatigue was acceptable, whereas no respondents reported that diarrhea or hot flashes were acceptable side effects. Of the three respondents to the PCC survey who had experience with enzalutamide, two respondents each experienced decreased sexual desire, erectile dysfunction, and fatigue, while one respondent each experienced anemia, breast swelling or tenderness, depression, hot flashes, loss of bone density, or weight gain/muscle loss. pERC noted that respondents in the both surveys reported that while they seek an effective treatment with fewer side effects, they also would be willing to tolerate the side effects of therapy to halt disease progression. In addition, pERC noted that respondents in both surveys reported that taking enzalutamide was easier as it avoided having to take prednisone with its known adverse effect profile.

ECONOMIC EVALUATION

Economic model submitted: Cost-utility (QALY) and cost-effectiveness (Life-years [LY]) analyses

The pCODR Economic Guidance Panel (EGP) assessed two cost-utility analyses of enzalutamide in patients with mCRPC after failure of androgen deprivation therapy prior to cytotoxic chemotherapy: the first analysis compared enzalutamide with watchful waiting (best supportive care [BSC]) followed by docetaxel based on the results of the PREVAIL study; and the second analysis compared enzalutamide with abiraterone plus prednisone based on an indirect comparison of enzalutamide (PREVAIL study) with abiraterone plus prednisone (COU-AA-302 study). The estimates used in the second analysis were derived from an indirect comparison which compared enzalutamide to abiraterone. The methodological rigour of the indirect comparison was questionable due to several factors including the lack of a common comparator arm in the PREVAIL and COU-AA-302 studies and differences in the included patient populations in the studies. In addition, pERC questioned the results of the indirect comparison which claimed two extra months of survival for enzalutamide compared to abiraterone. Thus, pERC considered that the estimates of clinical effectiveness used in the second model comparing enzalutamide to abiraterone were highly uncertain, and instead relied on the first analysis comparing enzalutamide to best supportive care to make their funding recommendation.

Basis of the economic model: clinical and economic inputs

Costs considered in the analysis included hospitalization costs, medication costs, test and procedure costs, and costs of treatment for adverse events and severe adverse events.

The key clinical outcomes considered in the cost-effectiveness analyses using life-years gained (LYs) as the measure of effect, were OS and rPFS, based on data from the PREVAIL study for the comparison of enzalutamide with BSC. The key clinical outcomes considered in the cost-utility analysis using quality-adjusted life years gained (QALYs) were also used OS and rPFS data as above, as well as utility data from the PREVAIL study.

Key drivers: Drug cost, OS extrapolation, and time horizon

pERC noted the similarity in the list prices for enzalutamide and abiraterone and prednisone. At the list price, enzalutamide costs $28.34 per 40mg tablet. At the recommended dose of 160 mg daily, the average cost per day in a 28-day course of enzalutamide is $113.38 and the average cost per 28-day course is $3,174.64.

At the list price, abiraterone costs $28.33 per 250mg tablet. At the recommended dose of 1,000 mg daily, the average cost per day in a 28-day course of abiraterone is $113.33 and the average cost per 28-day course is $3,173.33. The additional cost of prednisone is low with an average cost per day of $0.04, and an average 28-day course costing $1.23.

Clinical effect estimates: Key drivers for enzalutamide compared with BSC include OS extrapolation, time horizon, and utility values

The EGP's best estimate of the extra clinical effect of enzalutamide compared with BSC was between 0.269 to 0.519 QALYs and 0.226 to 0.391 life-years. The factors that most influenced the incremental cost effectiveness of enzalutamide were OS extrapolation, the time horizon, and the utility values.

Cost-effectiveness estimates: EGP's range of estimates for enzalutamide compared with BSC was higher than manufacturer's estimate

pERC noted that the estimates of incremental cost-effectiveness for the comparison of enzalutamide with BSC provided by the EGP were higher than the manufacturer's estimate. The EGP's best estimate of the incremental cost-utility ranged from $125,424/QALY gained (based on reducing the time horizon to 5 years) to $224,266/QALY gained (based on using the September 2014 data cutoff for OS, rPFS, and time to initiation of cytotoxic chemotherapy and extrapolating with a Weibull distribution, reducing the stable disease utility value by 10%, adjusting the utility values of post-progression states 1 and 2, and removing on-treatment utility gain). The EGP's best estimate of the cost-effectiveness ranged from $166,517/life-year gained (based on reducing the economic model's time horizon to 5 years) to $267,402/life-year gained (based on the September 2014 data cutoff for OS, rPFS, and time to initiation of cytotoxic chemotherapy and extrapolating with a Weibull distribution). pERC concluded that at the EGP's estimated incremental cost-utility ratios, enzalutamide could not be considered cost-effective.

ADOPTION FEASIBILITY

Considerations for implementation: No evidence on sequencing

pERC discussed the feasibility of implementing a funding recommendation for enzalutamide. It was noted that there is no direct comparison between enzalutamide and abiraterone with prednisone, and that the submitter's indirect comparison of the two regimens could not be considered reliable. Without direct comparative evidence, pERC considered enzalutamide to be an alternative to abiraterone with prednisone. pERC also noted that there is no evidence on which to base a recommendation on the sequencing of enzalutamide and abiraterone, and therefore could not make an informed conclusion regarding the sequencing of the treatments. Finally, pERC noted that provinces may want to consider additional measures to optimize the management of toxicity and limit budget impact by implementing an approved prescriber list. pERC made this suggestion because there is considerable toxicity associated with enzalutamide, which can best be managed by clinicians who have experience treating patients with this drug, and because drug price is the key driver of the incremental cost-effectiveness estimates and budget impact.

DRUG AND CONDITION INFORMATION

Drug Information	• Hormonal therapy, androgen receptor antagonist • 40 mg capsule • Recommended dosage of160 mg administered daily as a single oral dose
Cancer Treated	• Asymptomatic or mildly symptomatic metastatic castration resistant prostate cancer (mCRPC)
Burden of Illness	• Prostate cancer is the most common cancer diagnosed in Canadian men (excluding non-melanoma skin cancers) • It is the third leading cause of cancer related death with 4,000 deaths expected in 2014
Current Standard Treatment	• Docetaxel based chemotherapy, given with prednisone • Abiraterone, given with prednisone
Limitations of Current Therapy	• No direct comparative study with abiraterone/prednisone • Patient experience with prednisone related side-effects

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. Scott Berry, Oncologist
Bryson Brown, Patient Member
Dr. Matthew Cheung, Oncologist
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 Wasney, Pharmacist
Carole McMahon, Patient Member Alternate
Jo Nanson, Patient Member
Dr. Tallal Younis, Oncologist
Dr. Kelvin Chan, Oncologist

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

- Scott Berry who was not present for the meeting
- Bill Evans who was excluded from voting due to a conflict of interest
- Carole McMahon who did not vote due to her role as a patient member alternate

Because the pERC Initial Recommendation met the criteria for early conversion to a pERC Final Recommendation, reconsideration by pERC was not required and deliberations and voting on the pERC Final Recommendation did not occur.

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 enzalutamide (Xtandi) for first-line metastatic castration-resistant prostate cancer (mCRPC) through their declarations, four members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, and two of these members were excluded from voting.

Information sources used

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

Consulting publicly disclosed information

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

Use of this recommendation

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

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