CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

olaparib (Lynparza PC)

(AstraZeneca Canada Inc.)

Indication: Olaparib in combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC).

January 18, 2024

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0319
Brand name (generic)	Lynparza (olaparib)
Indication(s)	In combination with abiraterone and prednisone or prednisolone is indicated for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) for whom chemotherapy is not clinically indicated
Organization	Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee ("GU DAC")
Contact information[a]	Name: Dr. Girish Kulkarni

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. Patients should be eligible for this treatment if they have received docetaxel in the mCSPC setting. In very high-risk patients who have received adjuvant abiraterone for 2 years, then discontinued treatment then encounter disease recurrence, should be eligible to receive abiraterone and olaparib. The question "Does BRCA mutation need to be confirmed before olaparib therapy is initiated to align with Health Canada NOC?" needs to be explicitly answered in the response. As per the indication, "BRCA mutation must be confirmed before Olaparib treatment is initiated."		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

If not, please provide details regarding the information that requires clarification. In condition #5, the statement needs to clarify that “other anticancer drugs” does not include LHRH therapy. The DAC is requesting to clarify the % price reduction applied for olaparib and abiraterone to be cost-effective at a $50,000 per QALY gained threshold.

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
If yes, please detail the help and who provided it. OH-CCO provided a secretariat function to the group.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Girish Kulkarni • Dr. Reeta Barua		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Dr. Akmal Ghafoor
Position	Ontario Health CCO Genitourinary Cancer Drug Advisory Committee member
Date	10-01-2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Dr. Sebastien Hotte
Position	Ontario Health CCO Genitourinary Cancer Drug Advisory Committee member
Date	10-01-2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	Dr. Christina Canil
Position	Ontario Health CCO Genitourinary Cancer Drug Advisory Committee member
Date	10-01-2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Janssen	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	Dr. Urban Emmenegger
Position	Ontario Health CCO Genitourinary Cancer Drug Advisory Committee member
Date	10-01-2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Janssen	☐	☒	☐	☐
AstraZeneca	☐	☐	☒	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	Dr. Aly-Khan Lalani
Position	Ontario Health CCO Genitourinary Cancer Drug Advisory Committee member
Date	10-01-2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Janssen	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0319
Name of the drug and Indication(s)	Olaparib and abiraterone for mCRPC
Organization Providing Feedback	PAG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. An algorithm update is needed (rapid algorithm). 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0319
Brand name (generic)	Lynparza (olaparib)
Indication(s)	In combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious germline and/or somatic BRCA mutated metastatic castration resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated.
Organization	AstraZeneca Canada
Contact information[a]	Name: [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

AstraZeneca would like to thank the CADTH staff and the pERC committee for their thorough review. Overall AstraZeneca agrees with the CADTH recommendation and reimbursement conditions.

Although AstraZeneca is not making nor suggesting the need for a request for reconsideration, we would like to flag one concern regarding the initiation criteria. The committee stipulated that to initiate treatment with olaparib in combination with abiraterone, patients should "*have not received prior treatment with an ARPi in the mCSPC or nmCRPC setting*."

AstraZeneca agrees that treatment with olaparib in combination with abiraterone should generally be for patients who are NHA-naïve, given that the PROpel trial studied NHA-naïve patients.

There are however a very small number of Canadian patients who may have received an ARPi (i.e. an NHA such abiraterone or enzalutamide) in the mCSPC or nmCRPC setting without progressing on that treatment. With the current wording of the initiation criteria, such patients would not be eligible for olaparib in combination with abiraterone. Such patients however would not be eligible for treatment with olaparib monotherapy either as it is only approved for the treatment of adult patients with mCRPC with a BRCA or ATM mutation and who have progressed following prior treatment with a NHA (as assessed in the PROfound trial).

In the PROpel trial, patients were allowed to have been treated with second-generation antiandrogen agents (except abiraterone) without PSA progression/clinical progression/radiological progression during treatment provided the treatment was stopped at least 12 months before randomisation. As CADTH noted, we recognize that only one such patient was recruited (having received enzalutamide) but believe that this small subset of NHA-experienced patients may still benefit from treatment with olaparib in combination with abiraterone. As such, AstraZeneca would like to request that CADTH consider rewording the following initiation criteria without incurring a request for reconsideration:

*"have not **received** prior treatment with an ARPi in the mCSPC or nmCRPC setting"*

to

*"have not **failed on** prior treatment with an ARPi in the mCSPC or nmCRPC setting"*

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Overall AstraZeneca agrees that input from both clinician and patient groups was addressed adequately. However, on page 7 in the 2nd paragraph of the Clinician Input section, the following is stated:

"The clinical experts indicated that among the current treatment options for adult patients with mCRPC, ARPIs (e.g., abiraterone or enzalutamide) or docetaxel can be used as first-line therapy, while ARPIs, docetaxel or radium-223 may be considered as the second-line therapies, depending on what the first-line therapy is. Lutetium vipivotide tetraxetan, olaparib monotherapy (in patients with BRCA/ATM mutation), radium-223 or cabazitaxel can be used as later lines of treatment thereafter."

The above text implies that olaparib monotherapy is not suitable as a 1st line treatment for mCRPC. CADTH has, however, recommended the reimbursement of olaparib as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) and deleterious or suspected deleterious germline and/or somatic mutations in the homologous recombination repair (HRR) genes BRCA or ATM who have progressed following prior treatment with a new hormonal agent/ androgen receptor axis-targeted therapy (ARAT). Please see PC0223-000 for further information (https://www.cadth.ca/olaparib-lynparza-metastatic-castration-resistant-prostate-cancer-details).

Currently a majority of 1st line mCRPC patients have already received treatment with an NHA prior to having mCRPC and would be eligible for treatment with olaparib monotherapy if they had progressed on that prior NHA. AstraZeneca would like to request that the text be modified as follows to make it clear that olaparib monotherapy is a suitable 1st line therapy for the treatment of mCRPC.

*"The clinical experts indicated that among the current treatment options for adult patients with mCRPC, ARPIs (e.g., abiraterone or enzalutamide) or docetaxel can be used as first-line therapy, while ARPIs, docetaxel or radium-223 may be considered as the second-line therapies, depending on what the first-line therapy is. Lutetium vipivotide tetraxetan, **~~olaparib monotherapy (in patients with BRCA/ATM mutation)~~**, radium-223 or cabazitaxel can be used as later lines of treatment thereafter. **Olaparib monotherapy can be used at any line in patients with a BRCA/ATM mutation who have progressed following prior treatment with a NHA**"*

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

In Table 2 in the relevant comparators section, the following response is noted to questions from the Drug programs:

"The clinical experts indicated that currently, olaparib monotherapy is not a standard of care for patients with mCRPC in the first-line setting. There is a lack of direct evidence to explore the relative efficacy of olaparib and abiraterone versus olaparib monotherapy in the first-line setting."

AstraZeneca believes that the responses to these questions are somewhat redundant because olaparib monotherapy could not be considered the standard of care for the 1st line treatment of mCRPC in general because its regulatory label is restricted to patients with a BRCA or ATM mutation and who have progressed following prior treatment with an NHA. Additionally, it does not make sense to compare olaparib in combination with abiraterone to olaparib monotherapy because they are intended for different populations (i.e. NHA-naïve and NHA-experienced populations respectively).

In Table 2 in the Considerations for the Initiation of Therapy section, CADTH notes that:
"Based on feedback from the clinical experts consulted by CADTH, pERC concluded that if patients have progressed from mCSPC to mCRPC while on abiraterone, they should not be eligible for olaparib and abiraterone in the mCRPC setting."

AstraZeneca would like to request that a special exception be made for patients that have received an NHA but who did not progress on that treatment (see comments above in section 1).

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

[a] CADTH may contact this person if comments require clarification.