CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

darolutamide (Nubeqa)

(Bayer Inc.)

Indication: Metastatic castration-sensitive prostate cancer

December 15, 2022

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CADTH and do not necessarily represent or reflect the view of CADTH. No endorsement by CADTH is intended or should be inferred.

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CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting stakeholder group and all conflicts of interest information from individuals who contributed to the content are included in the posted submission.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0294-000
Brand name (generic)	Darolutamide (Nubeqa)
Indication(s)	in combination with docetaxel for mCSPC patients who are chemotherapy-eligible
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.		

Generalizability	
Should patients who recently initiated docetaxel + ADT for mCSPC be eligible to add on darolutamide? If so, what is the appropriate time frame?	pERC and the clinical experts noted there is currently no clinical evidence to inform the addition of darolutamide in patients who recently initiated docetaxel + ADT. The clinical experts indicated that the addition of darolutamide to docetaxel + ADT would be reasonable if done within the first 6 months of therapy .

The GU DAC recommends that the addition of darolutamide to docetaxel + ADT be allowed not just for a time-limited basis.

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.		

[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 secretariat support.		
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: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**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	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**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	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**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 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**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 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**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	☐	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0294
Name of the drug and Indication(s)	Darolutamide for the treatment of patients with metastatic castration-sensitive prostate cancer (mCSPC) in combination with docetaxel
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
None.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
None.
b) Reimbursement conditions and related reasons
None.
c) Implementation guidance
In Table 2. Responses to questions from the drug programs, under the heading "*Considerations for discontinuation therapy*' row 2, PAG is seeking clarity whether pERC members agreed with the clinical experts. Under the heading, "G*eneralizability*" row 1, PAG is seeking clarity whether pERC members agreed with the clinical experts.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0287-000
Brand name (generic)	Darolutamide
Indication(s)	In combination with docetaxel for the treatment of metastatic castration-sensitive prostate cancer (mCSPC) in patients who are chemotherapy-eligible.
Organization	Canadian Cancer Society with Dr Urban Emmenegger (clinician submission lead)
Contact information[a]	Name: Sasha Frost Email: [redacted] Phone: [redacted]

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

Overall, the recommendation reflects the needs of the patient group as identified in the patient submission.

The lead clinician for the clinician submission coordinated by the Canadian Cancer Society, Dr Urban Emmenegger, stated in response to this draft recommendation *"The draft recommendations capture the findings of the ARASENS study and put them into the Canadian treatment context for metastatic castration-sensitive prostate cancer."*

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, the recommendation reflected patient needs as described in the patient submission. More clarity on the weight placed on the patient submission in decision making would be helpful in determining the degree to which patient submissions are considered.

Information about the experience of the patient that tried darolutamide that CCS interviewed was absent from the draft. Overall, Patient A believed darolutamide had been effective at controlling his cancer, reduced his time in the clinic, was easy to use and indicated he would strongly recommend this drug for others with mCSPC. The recommendation to reimburse this drug with conditions meets the needs as described by this patient.

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.
N/A

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. N/A		
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. N/A		

[a] CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.

Appendix 1. Conflict of Interest Declarations for Patient 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.

A. Patient Group Information	
Name	*Sasha Frost*
Position	*Senior Advocacy Specialist, Public Engagement*
Date	*Please add the date form was completed (14-12-2022)*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it. Dr Urban Emmenegger provided clinician feedback within this submission but did not assist in feedback related to the patient submission.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. 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	☐	☐	☐	☐

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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- CADTH may contact your group with further questions, as needed.
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  - 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. N/A		
3. Did you receive help from outside your clincian group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it. N/A		
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	☒
Conflict of interests were declared and have not change since the initial submission.		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**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**			
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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0294
Brand name (generic)	Nubeqa (darolutamide)
Indication(s)	Metastatic castration-sensitive prostate cancer (mCSPC)
Organization	Bayer
Contact information[a]	[redacted]

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

Bayer agrees with CADTH's recommendation for NUBEQA in mCSPC, and the supporting rationale, which includes the clinical evidence that demonstrated the "statistically significant and clinically meaningful improvements in overall survival" of NUBEQA + ADT with docetaxel, and its efficacy in "delaying progression to metastatic castration-resistant prostate cancer (mCRPC), the need for subsequent antineoplastic therapy, worsening of pain, and symptomatic skeletal events, compared with docetaxel plus ADT." Bayer is in agreement with CADTH's conclusion that the safety profile of NUBEQA + ADT with docetaxel was "overall similar to that of docetaxel and ADT in the ARASENS trial, with no additional serious safety concerns".

As described further in section 5 below, Bayer disagrees with the price reduction cited in the reimbursement conditions.

Overall, Bayer agrees that NUBEQA + ADT with docetaxel should be reimbursed for mCSPC treatment.

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, the committee has considered the input provided by Bayer.

Outside of Bayer, clinical experts consulted by CADTH and clinician groups that provided input have respectively stated that "triplet therapy with darolutamide, docetaxel and ADT should be available to all men with mCSPC who are candidates for cytotoxic chemotherapy" and "darolutamide would be used as a first-line treatment for mCSPC in combination with ADT and docetaxel in patients who are fit for chemotherapy". The CADTH recommendation reflects an understanding and consideration of this input.

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

The reasons for the recommendation are generally clearly stated.

Bayer notes that in the rationale for the recommendation section, CADTH indicated that "the comparator in the clinical trial does not reflect the current standard of care". This is not aligned with CADTH-consulted clinicians who have stated that the comparator regimen in ARASENS, docetaxel + ADT, "is an appropriate and relevant comparator" (even though "it accounts for a small proportion of treatment regimens prescribed"). Clinician groups that provided input to CADTH have also noted that "current treatment for mCSPC includes either chemotherapy (docetaxel) or a second-generation androgen receptor inhibitor (i.e., abiraterone acetate plus prednisone, enzalutamide, or apalutamide) in combination with ADT". Such input from prostate cancer experts demonstrates that docetaxel + ADT is a relevant standard of care treatment option and an appropriate comparator in mCSPC for patients who are chemotherapy-eligible.

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

N/A

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

Bayer acknowledges the clarity of the reimbursement conditions but does not agree with the pricing condition and the rationale provided. A recommended "price reduction of at least 58%" was based on the uncertainty of the ITC results and CADTH's application of more conservative assumptions in the economic evaluation, including a higher cost of docetaxel, which does not reflect a provincial drug plan price list.[1]

Lastly, in the prescribing conditions, Bayer agrees that an oncologist with expertise in the management of prostate cancer should prescribe, or be part of the multidisciplinary consultations, when initiating treatment with NUBEQA + ADT with docetaxel. This approach would take into account the multitude of oncology care models across the country and reflect Canadian treatment guidelines.

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

References

1. Beca J, Majeed H, Chan KKW, Hotte SJ, Loblaw A, Hoch JS. Cost-effectiveness of docetaxel in high-volume hormone-sensitive metastatic prostate cancer. *Can Urol Assoc J*. 2019:396-403.