CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

DURVALUMAB (IMFINZI)

(AstraZeneca Canada Inc.)

Indication: In combination with gemcitabine-based chemotherapy, for the treatment of patients with locally advanced or metastatic biliary tract cancer

January 19, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0296-000
Brand name (generic)	Imfinzi (durvalumab)
Indication(s)	In combination with chemotherapy for the treatment of patients with locally advanced or metastatic biliary tract cancer.
Organization	The Canadian Gastrointestinal Oncology Evidence Network (CGOEN)
Contact information[a]	Name: Dr. Howard Lim [redacted]

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.

Re: Table 1, Reimbursement Condition #5 - Prescribing: "Durvalumab plus gemcitabine and platinum-based chemotherapy should be prescribed by a clinician with expertise in the management of BTC"

Recognizing that individual jurisdictions have their own guidance for ensuring that appropriate clinicians prescribe treatments for specific conditions, CGOEN recommends that CADTH not make recommendations as to which clinicians should be prescribing treatments for BTC>

Economic Feedback

Re: p. 5

> *"The ICER for durvalumab plus gemcitabine and cisplatin is $665,692 per QALY gained when compared with gemcitabine and cisplatin.*
>
> *A 93% reduction in the price of durvalumab would be required for durvalumab plus gemcitabine and cisplatin to be able to achieve an ICER of $50,000 per QALY gained compared to gemcitabine and cisplatin"*

As a group of physicians with expert knowledge of the clinical factors related to the treatment of BTC, we generally do not comment on issues related to pharmacoeconomics. However, we felt it important to comment on CADTH's recent use of an ICER pegged at $50,000 per QALY as the willingness-to-pay (WTP) threshold for payers. We are aware that previous pERC recommendations included analyses to determine needed price reductions for ICERS of $100,000 and $50,000. We are also aware of ICERS considered that were significantly over $100,000 in situations where there was significant unmet need or where there was considerable therapeutic improvement.

We support the work of Canadian health technology assessment agencies and the pan Canadian Pharmaceutical Alliance (pCPA) in assessing value and achieving value in prescription medications for publicly funded drug programs. However, we are concerned that CADTH is arbitrarily establishing a new (and low) WTP threshold that could ultimately result in Canadian patients with difficult-to-treat cancers being denied access to important new therapies.

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.

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.

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.
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- 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		
1. 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.		
2. 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		
3. 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.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0296-000
Brand name (generic)	Imfinzi (durvalumab)
Indication(s)	In combination with gemcitabine-based chemotherapy is indicated for the treatment of patients with locally advanced or metastatic biliary tract cancer (BTC)
Organization	Ontario Health (Cancer Care Ontario) Gastrointestinal Cancer Drug Advisory Committee (GI DAC)
Contact information[a]	Name: Dr. Erin Kennedy

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. CADTH report over-emphasizes the difference in landmark OS rates throughout the report when in fact the OS difference in landmark times (24 months for example) were driven by less than a dozen patients, and is potentially misleading.		
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.		
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

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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		
1. 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 to the GI DAC.		
2. 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		
3. 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. Erin Kennedy, Dr. Suneil Khanna, Dr. Michael Raphael, Dr. Jim Biagi, Dr. Rachel Goodwin		

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	☐	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0296
Name of the drug and Indication(s)	Durvalumab in combination with gemcitabine-based chemotherapy for biliary tract cancer
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
In Table 2. Responses to Questions from Drug Programs, under the heading "Considerations for Prescribing therapy" PAG is requesting to remove the following text "*There is no evidence to support weight-based dosing or to inform the appropriate dose cap of durvalumab in patients because this was not evaluated in the trial.*" PAG is requesting the addition of the following text "*Jurisdictions use weight-based dosing up to a cap*." In the Cost Effectiveness Table, CADTH reanalysis results component, PAG is seeking clarity whether the ICER and BIA reanalysis is based on flat dosing or weight-based dosing?
b) Reimbursement conditions and related reasons
In Table 1. Reimbursement Conditions and Reasons, under the heading "initiation", first row, PAG is requesting the following revision "*Clinicians think it's reasonable to use durvalumab for patients with good ECOG PS.*"

c) Implementation guidance
None.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0296
Brand name (generic)	IMFINZI (durvalumab)
Indication(s)	Treatment of patients with locally advanced or metastatic biliary tract cancer (BTC)
Organization	AstraZeneca Canada Inc.
Contact information[a]	[redacted]

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

- Overall, AstraZeneca (AZ) agrees with the committee's recommendation and would like to acknowledge CADTH for their clear presentation of the totality of the TOPAZ-1 data (OS, OS landmarks, PFS, safety and HRQoL) as we believe this fully captures the clinical benefit that durvalumab offers in the treatment of BTC.

- From an economic perspective, AZ acknowledges CADTH's standard willingness to pay threshold (WTP) of $50,000 per QALY is convenient in determining the cost-effectiveness across all therapeutic agents. However, AZ believes that the value of treatments, particularly in devastating diseases without treatment options such as BTC, could be better conducted. Durvalumab is the first new treatment for BTC patients in over a decade and AZ believes that applying a 'one-size-fits-all' WTP threshold is overly simplistic and does not truly come to the value of durvalumab in this indication.

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	☐

- AstraZeneca agrees that the recommendation demonstrates that the committee has considered the stakeholder input and has performed a review aligned with the Procedures for CADTH Reimbursement Reviews, specifically recognition of the significantly high unmet need of BTC (pg 5, Discussion Points) as per section 9.3.1 of the procedures document.

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.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
• The final 3-year incremental budget from CADTH's reanalysis was significantly higher than submitted by AZ. Based on the paucity of epidemiology data in Canada for BTC, AZ provided a budget impact model based on the best available evidence and holds the belief that the originally submitted numbers are the best available expected budget impact.		

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