CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

OSIMERTINIB (TAGRISSO)

(AstraZeneca Canada Inc.)

Indication: Non-small cell lung cancer

September 17, 2021

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0246-000
Brand name (generic)	Osimertinib
Indication(s)	Reimbursement of osimertinib in the adjuvant setting for resected Stage IB-IIIA EGFR-mutated (exon 19 deletion/L858R) NSCLC
Organization	Lung Cancer Canada
Contact information[a]	Name:

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

While we agree with the recommendation for reimbursement of osimertinib in the adjuvant setting for resected Stage IB-IIIA EGFR-mutated (exon 19 deletion/L858R) NSCLCs we disagree with the assessment in the following areas:

1) Lung Cancer Canada disagrees with CADTH's QALY threshold of $50K. This threshold is aligned with non-cancer drugs and is not appropriate for cancer. The original threshold which uses a range that includes $150K, acknowledges the life-threatening nature of cancer. PCODR was established in recognition of cancer's unique needs. This change undermines JODR, and then PCODR's, premise and places cancer treatment in the same model as one used to evaluate treatments for common ailments.

2) Lung Cancer Canada disagrees with the wording in regards to clinical efficacy. Within the summary CADTH recognizes that there appears to be clinical benefit. It also highlights that there is uncertainty in the data and that the data is immature. Lung Cancer Canada agrees with this assessment. However we disagree with the following statement.

   "Cannot be concluded that osimertinib confers and OS benefit compared to placebo."

   Lung Cancer Canada questions this wording as this does not acknowledge the efficacy shown in the preliminary data. We would prefer to see wording such as,

   "…uncertain level of benefit that Osimertinib confers on OS benefit compared to placebo."

   The change is significant as this wording has implications on the modeling and scenarios used by CADTH in their economic evaluation. Within this wording, ANY scenarios, ranging from patients receiving an OS benefit, to no OS benefit, to less OS benefit compared to placebo may be considered. While all these scenarios are valid within an academic sense, economic modeling should be grounded with clinical validity.

   Our suggested wording acknowledges both the early efficacy and safety of the treatment, while recognizing the uncertainty. This wording places reasonable clinical parameters upon the economic analysis.

Lung Cancer Canada is highlighting this as we are unable to determine which scenarios were used in the economic evaluation - CADTH no longer releases the draft clinical and economic reports at the same time as the initial recommendation. We are therefore, guessing and projecting different scenarios in a fashion similar to asking reviewers of a manuscript to decide on publication by only looking at an abstract and not the full paper. It is undermining the original principles of transparency and engagement that CADTH is anchored in.

Cancer is a quickly evolving field and many new treatment types, paradigms and treatment stages are being researched and coming to market. This submission is one such case – it is the first adjuvant treatment for early-stage disease. All stakeholders need to be careful in their review and conclusions. It is with this oversight and care in mind that we make our comments and it is with this care in mind that we ask CADTH to reconsider the decision to withhold the draft economic and clinical guidance reports. We ask that you release them to us and give us an opportunity to meaningfully comment on the draft recommendation after review.

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	☒

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. We cannot know if the reasons for the recommendations are clearly stated without the drafts of the full economic and clinical guidance reports.		
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. Cannot determine unless you have the whole reports		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
The inability to see the full reports prevents us from reasonably commenting on this.		

[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.

A. Patient Group Information	
Name	*Lung Cancer Canada, Christina Sit*
Position	*Director, Programs Stakeholder Relations*
Date	*Please add the date form was completed (17, 09, 2021)*
☒	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.		
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

- 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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- 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.		
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				
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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

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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

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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	
Brand name (generic)	Osimertinib/ Tagrisso
Indication(s)	Non-small cell lung cancer
Organization	Lung Health Foundation
Contact information[a]	[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.

While we agree with the decision to recommend the reimbursement of Osimertinib, we are concerned about the comments regarding Overall Survival and the long-term benefits of Osimertinib as a first-line treatment.

"Due to the immaturity of the ADAURA trial data, pERC could not draw any conclusions on the effect of osimertinib on OS, PFS, and time to next treatment. Therefore, based on the available trial evidence, there is uncertainty whether the significant DFS benefit observed will translate to a clinically meaningful improvement in OS in this patient population."

Given that the clinical data clearly shows the reductions in disease recurrence, we do not believe this statement provides an accurate representation of the treatment results. For early stage lung cancer patients, comprehensive data on overall survival will take several years to gather. Delaying access to treatment in the interim when a sufficient level of data exists that shows its benefits is unethical to patients. As an organization that advocates heavily for early screening in lung cancer, patients must have access to treatment options once disease is detected.

We are concerned about the precedent this decision may set for future first-line therapies for lung cancer patients and hope that the language used can be reconsidered.

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?

We were pleased to see that DFS has been accepted as an endpoint.

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.

See comments in question#1		
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. See comments in question #1		

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

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A. Patient Group Information	
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 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.		
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.

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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.		
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.		
B. Previously Disclosed Conflict of Interest		
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	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	

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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				
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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)*
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Conflict of Interest Declaration				
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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

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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

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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	PC0246-000
Brand name (generic)	Tagrisso (Osimertinib)
Indication(s)	Reimbursement of osimertinib for stage IB-IIIA EGFR exon 19 deletions or exon 21 (L858R) substitution mutations for non-small cell lung cancer
Organization	Lung Cancer Canada - Medical Advisory Committee and Supporters, including: Dr. Geoffrey Liu, Dr. Paul Wheatley-Price, Dr. Stephanie Snow, Dr. Rosalyn Juergens, Dr. David Stewart, Dr. Barb Melosky, Dr. Parneet Cheema, Dr. Mahmoud Abdelsalam, Dr. Kevin Jao, Dr. Ron Burkes, Dr. Catherine Labbé, Dr. Quincy Chu, Dr. Nicole Bouchard, Dr. Jeffrey Rothenstein, Dr. David Dawe, Dr. Donna Maziak, Dr. Sunil Yadev, Dr. Silvana Spadafora, Dr. Randeep Sangha
Contact information[a]	Name: Christina Sit

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

Overall, we agree with the recommendation for reimbursement of osimertinib in the adjuvant setting for resected Stage IB-IIIA EGFR-mutated (exon 19 deletion/L858R) NSCLCs.

However, we note several issues with the committee's recommendation that we are in disagreement with.

(1) The reduction in price of at least 82% required by the committee brings into question the assumptions used in the pharmacoeconomic models that serve as the base model. That these models and assumptions are not released as part of this committee's recommendations, but only alluded to in the draft recommendation are inappropriate and undermines CADTH's drive for transparency of process. In the past, there was opportunity for feedback prior to a final recommendation. As clinicians, we reserve the right to ensure that these models represent the most likely clinical scenarios. Currently, we as clinicians are unable to see the rationale or logic taken by the committee to reach the economic conclusions. We only know that CADTH's re-analysis changed the manufacturer's assumptions around transitions to local recurrence and metastatic disease, lengthened time to establish cure, changed type of treatment used and costs for that treatment in local recurrence, adjusted utility values, and adjusted RDI to 100%. The lack of transparency to changes in assumptions around survival and utility values are important because they have large impacts on modelled cost-effectiveness/cost-utility.

The risk of this lack of transparency is five-fold:

(i) as this is the first CADTH submission for adjuvant therapy for resected early stage lung cancer, it sets a new standard for all the upcoming submissions of other drugs. As such, the base models and assumptions made for the experimental and control arms will also set a precedent. It is incumbent on CADTH to ensure they have gotten this right, and be transparent in this process;

(ii) This clinician community feels that a minimum expected reduction in price of 82% for a product that has a DFS hazard ratio of 0.20 (Stage IB-IIIA) leads us to assume that the set of assumptions and base model utilized in the modeling does not capture the true clinical benefit of osimertinib. It appears that the economic assessment may have interpreted longer term clinical uncertainty as equivalent to lack of clinical benefit; we disagree with this assessment. Our clinician knowledge and opinion are backed up by other groups: Project Orbis is a US FDA Oncology Center of Excellence initiative established in 2019 to support concurrent submission and review of oncology drugs by multiple international health agencies, including Health Canada. It provided a published summary that states that: "Therefore, it is unlikely that any remaining information gained from these [future] analyses will change the assessment of effectiveness of osimertinib as adjuvant treatment for early-stage EGFR-mutated NSCLC which is based on a robust clinically meaningful and statistically significant improvement in DFS without a detriment in OS. DFS as a regulatory endpoint has supported approvals of adjuvant therapies for multiple tumor types (e.g., breast cancer, colorectal cancer) and represents direct clinical benefit."[1]

(iii) Our oncology clinician group has significant concerns that if the precedent is set for an 82% reduction in price for a drug that yields a hazard ratio of 0.20, then other drugs in the lung cancer adjuvant setting that benefit patients with clinically and statistically significant hazard ratios of lesser magnitude (i.e. hazard ratios of 0.25-0.80, for instance) will have to endure discounts of greater magnitude. If it is perceived by pharmaceutical companies that the health technology process used in Canada is not based on the use of most clinically-reasonable models, our oncology clinician group fears that pharmaceutical companies may come to see Canada as an outlier in health economic and outcome research that may drive them away from even starting price negotiations – not only in the lung cancer adjuvant setting, but in other settings (both cancer and non-cancer settings). A major assumption in all negotiations is that all parties arrive at the table in good faith; that can only happen if the base models and assumptions underlying these models are released publicly and appropriately scrutinized;

(iv) Lack of access to medications due to extreme price reduction may also potentially limit clinical trials access in the future; early access to life-saving agents through clinical trials has been shown in the Canadian literature to improve patient outcomes.

(v) Other Canadian stakeholders (patients, clinicians) will lose faith in the CADTH process, and the group vulnerable to bear the brunt of the consequences in this process will be non-small cell lung cancer patients.

(2) It should also be noted that in 2019, CADTH recommended reimbursement of trastuzumab-emtansine in the adjuvant breast cancer setting, including an economic model that presumed dominance over use of trastuzumab beyond a 10 year-period, despite the lack of mature overall survival (OS) data. Why was the assumption that DFS benefit would translate into OS benefit felt to be reasonable in that setting, but not seemingly in the setting of NSCLC?

(3) The threshold for cost-effectiveness using a QALY of $50,000 appears to be a moving target over the last 1-2 years in CADTH/pCODR analyses. Lung cancer is a particularly lethal disease, and the subgroup of patients eligible for this indication, the resectable EGFR-positive patient, is a small subgroup of this disease, akin to an orphan disease indication.

[1]Koch AL, Vellanki PJ, Drezner N, Li X, Mishra-Kalyani PS, Shen YL, Xia H, Li Y, Liu J, Fourie Zirkelbach J, Palazov E, Gamarian A, Choo Q, Girčys A, Rohr UP, Fesenko N, Spillman D, Pazdur R, Beaver JA, Singh H. FDA Approval Summary: Osimertinib for adjuvant treatment of surgically resected non-small cell lung cancer, a collaborative Project Orbis review. Clin Cancer Res. 2021 Jul 22:clincanres.1034.2021. doi: 10.1158/1078-0432.CCR-21-1034. Epub ahead of print. PMID: 34301748.

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	☒

In our clinician input, we provided data and opinion that support the concept that DFS will likely be maintained for some time beyond the current trial data, along the most likely scenario of an OS benefit over time, and that the very significant hazard ratios of high magnitude observed would likely be preserved at least partially over many years. Given the reimbursement conditions recommended by the committee, it is unlikely that the committee chose a base scenario that considered DFS and OS benefits for any length of time beyond what was reported by the trial.

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 rationale for reimbursement conditions are not clearly provided. The specific details are outlined in our response to Questions 1 and 2.

[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.

A. Patient Group Information	
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 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.		
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

- 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.		
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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0246-000
Brand name (generic)	Tagrisso (osimertinib) AstraZeneca Canada Inc.
Indication(s)	Manufacturer requested reimbursement criteria: Tagrisso (osimertinib) is indicated as adjuvant therapy after tumour resection in patients with stage IB-IIIA non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
Organization	Ontario Health (Cancer Care Ontario) Lung and Thoracic Cancers Drug Advisory Committee
Contact information[a]	Name: Dr. Gail Darling [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. In table 1 point 3 it says patients should have no comorbidities. This is not consistent with the subsequent rationale where they give examples of QT prolongation and interstitial lung disease. This population of patients mostly have some other comorbidities mostly which do not interfere with administration of osimertinib. The Lung DAC would suggest this should be 'no relevant comorbidities'.		
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.		
	Yes	☒

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	No	☐
If not, please provide details regarding the information that requires clarification.		

[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.
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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.

A. Patient Group Information	
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 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.		
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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- 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.
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- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
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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. OH-CCO provided secretariat support to the DAC.		
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.		
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. Gail Darling • Dr. Peter Ellis • Dr. Natasha Leighl • Dr. Andrew Robinson • Pamela Ng (Pharmacist) – DAC term completed June 2021.		

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

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0246
Name of the drug and Indication(s)	Osimertinib for NSCLC
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
In Table 1 Reimbursement Conditions and Reasons, under the heading initiation, 3. states *"Osimertinib should be reimbursed for a total duration of 3 years in patients who continue to receive clinical benefit from treatment and do not have intolerable toxicity."* PAG is seeking clarity on the total duration of 3 years and whether this includes dose reductions and dose interruptions.
c) Implementation guidance
In the Discussion Points section of the recommendation, the seventh bullet states "*pERC acknowledged that there is substantial uncertainty regarding the appropriate osimertinib free*

interval for re-treatment of osimertinib in the first-line distant metastatic setting." PAG is requesting the removal of the word 'distant.'

In the Implementation Guidance section of the recommendation, 4. states *"pERC also agreed with the clinical experts that rechallenge with osimertinib after a 6-month off-treatment interval is reasonable unless the patient experiences a recurrence. Retreatment with osimertinib in the metastatic setting would not be indicated in patients who progressed on osimertinib in the adjuvant treatment setting*." PAG is suggesting the following editorial revision, "Retreatment with osimertinib in the metastatic setting would not be indicated in patients who progressed while on osimeritnib or progressed within 6 months of their last dose of osimertinib in the adjuvant treatment setting."

In Appendix 1: CADTH pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC) Responses to Drug Program Implementation Questions under the Generalizability heading, PAG is asking for alignment with the revisions requested in the Implementation Guidance section of the recommendation under the 4th point.