CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

sotorasib (Lumakras)

Amgen Canada Inc.

Indication: Treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.

October 20, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0300
Brand name (generic)	Lumakras (sotorasib)
Indication(s)	Treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.
Organization	OH-CCO Lung Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Donna Maziak

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.

The OH-CCO Lung DAC recognizes the limited improvement in progression-free survival and similar overall survival (with 36% crossover) with sotorasib versus docetaxel in the CODEBREAK200 randomized trial. However, as clinicians that routinely administer docetaxel and who also have familiarity with sotorasib use, we disagree with the committee's statement "that sotorasib appeared to be associated with considerable toxicity compared with docetaxel". Treatment-related grade 3 and 4 AEs occurred in 33% of patients that received sotorasib and 40% of patients that received docetaxel. Many sotorasib-related events were asymptomatic transaminitis, common to all approved small molecules and checkpoint inhibitors currently used in the treatment of advanced lung cancer. Serious adverse events were reported for 11% of patients receiving sotorasib and 23% of those receiving docetaxel. This does not suggest a favorable toxicity profile of docetaxel, nor does current clinical experience.

The convenience of oral administration, more than doubling of tumor response (28% versus 13%), reduction in the hazard for disease progression (HR 0.66, 95% CI 0.51 - 0.86), delayed time to deterioration in global health status, physical functioning, and dyspnea all favour sotorasib use over docetaxel. Cough, a key lung cancer symptom, was significantly improved in patients receiving sotorasib versus docetaxel.

While sotorasib is not significantly superior to docetaxel in this study in terms of survival or median PFS gain, it is better tolerated, less toxic, more convenient and associated with better patient reported outcomes. The OH-CCO Lung DAC could not identify a scenario nor patient population for whom we would recommend docetaxel over sotorasib. To the contrary, we would recommend sotorasib as a less toxic, targeted agent for all patients with advanced KRAS G12C mutant lung cancer that are eligible for second-line systemic therapy.

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. 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.

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		
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 a secretariat function to the group.		
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. Peter Ellis • Dr. Andrew Robinson		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Dr. Donna Maziak
Position	OH-CCO Lung Cancer Drug Advisory Committee Lead
Date	12-10-2023
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

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

New or Updated Declaration for Clinician 2	
Name	Dr. Natasha Leighl
Position	OH-CCO Lung Cancer Drug Advisory Committee Member
Date	12-10-2023
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

New or Updated Declaration for Clinician 3	
Name	Dr. Stephanie Brule
Position	OH-CCO Lung Cancer Drug Advisory Committee Member
Date	12-10-2023
☒	**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	Dr. Mihaela Mates
Position	OH-CCO Lung Cancer Drug Advisory Committee Member
Date	12-10-2023
☒	**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	Dr. Sara Kuruvilla
Position	OH-CCO Lung Cancer Drug Advisory Committee Member
Date	17-10-2023
☒	**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	PC0300-000
Brand name (generic)	Sotorasib (Lumakras)
Indication(s)	Treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.
Organization	Lung Cancer Canada – Clinician Group
Contact information[a]	Name: Rosalyn Juergens, MD PhD

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? Our group was not even listed as one of the clinician inputs that was considered (see page 5). Only Ontario Health – CCO is given mention. There was no mention of our submission on page 7 where there is discussion about the clinician group submission either. There was only a single mention of our clinician submission which was on page 15 where we are referenced as having noted that it is unlikely that patients with performance status of 3 or 4 would benefit which suggests you received both our patient and clinician submission.		

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 have great concerns about this statement on page 3. "pERC also considered that sotorasib appeared to be associated with considerable toxicity compared with docetaxel as the comparative safety from the CodeBreak 200 trial indicated that Grade 3 and 4 AEs were more common in patients treated with sotorasib compared with docetaxel." Our group has 2 main concerns with this statement. 1) While numerically there are more grade 3 and 4 toxicities with sotorasib, this does not account for time bias with the patients on the sotorasib arm continuing on treatment for a longer duration. Docetaxel is not a therapy that can be continued indefinitely and generally stops after 4-6 cycles due to toxicity / lack of efficacy. Sotorasib is a treatment that is continuous. As per the code break 200 study, patients remained on treatment 2 months longer with sotorasib in contrast to docetaxel. When patients remain on drug, they continue to have risk for toxicity. The manuscript in the Lancet speaks to this issue and when you take into account the time bias, there is no increase in toxicity. Second, the character of the toxicity is also important. The grade 3 and 4 toxicities of docetaxel are things like neutropenia and febrile neutropenia, pneumonia, etc. These are toxicities that lead to hospitalizations, and increased health care usage. The grade 3 and 4 toxicities of sotorasib are		

elevated transaminases and diarrhea – things that are common to the majority of the tyrosine kinase inhibitors that lung cancer oncologists are used to managing and generally do not require hospitalization.

Our Lung Cancer Canada clinician group is also concerned about how the HRQoL was discounted by the CADTH team. “pERC could not reach definitive conclusions regarding the effects of sotorasib compared to docetaxel on health-related quality of life (HRQoL) and disease symptoms due to a significant decline in the number of patients available to provide assessments over time and the open-label and descriptive nature of the analyses.” “pERC acknowledged that there was a high degree of uncertainty regarding the magnitude of clinical benefit due to the non-comparative, open-label study design, and the small sample size.” When a trial compares an IV versus an oral agent in a relapsed refractory setting, it would be unethical to have anything but an open label study. Doing an IV placebo adds an undue burden to patients and the health care system. Sotorasib was able to delay the time to deterioration in global health status, physical functioning, and the cancer-related symptoms dyspnoea and cough. These items are of critical importance to lung cancer patients. The descriptive nature of the analyses was a by-product of the statistical design.

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.

This recommendation does not acknowledge the system impacts of implementing sotorasib. This patient population is in their last year of life. Sotorasib offers an oral option that can be taken in the comfort of the patient’s homes. Docetaxel must be administered in a chemotherapy suite. Patients need to take steroids to reduce the risk of edema and allergic reaction as well as anti-emetics, increasing their pill burden. Patients on docetaxel definitely spend more of their time physically present within the health care system with lab visits every 3 weeks and treatment visits every 3 weeks which takes up many hours of the patient’s limited remaining time. Sotorasib patients only require physician assessments but no chemotherapy suite time. These assessments can even be done with local labs and telemedicine assessments allowing patients in all jurisdictions of Canada to equally benefit as they are not limited by the need to travel.

Sotorasib has a better response rate and a longer PFS with toxicities that are manageable in an outpatient setting even when grade 3 or 4. While we acknowledge that a clear overall survival benefit wasn’t seen in this patient population, with all the other benefits of the agent, the Lung Cancer Canada physician group recommends a positive recommendation with pricing considerations to allow a dialogue around price, that could lead to reduced health care utilization and definitely aligns with patient values.

Please see our Canadian Consensus Guidelines that have been published in Current Oncology about managing K-ras G12C with implications for the implementation of sotorasib in Canada.

Cheema, P et al. Curr Oncol. 2023 Jul 6;30(7):6473-6496.
https://pubmed.ncbi.nlm.nih.gov/37504336/

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.

Not applicable

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

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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  - 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		
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	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: • *Dr. Rosalyn Juergens (lead)* • *Dr. Geoffery Liu* • *Dr. Quincy Chu* • *Dr. Mahmoud Abdelsalam* • *Dr. Kevin Jao* • *Dr. Dorothy Lo* • *Dr. Ron Burkes* • *Dr. Lacey Pitre* • *Dr. Randeep Sangha* • *Dr. David Stewart* • *Dr. David Dawe* • *Dr. Brandon Sheffield* • *Dr. Normand Blais* • *Dr. Nathalie Daaboul* • *Dr. Sunil Yadav* • *Dr. Barb Melosky* • *Dr. Catherine Labbé*		

- *Dr. Stephanie Snow*
- *Dr. Paul Wheatley-Price*
- *Dr. Jefferey Rothenstein*
- *Dr. Mark Vincent*
- *Dr. Parneet Cheema*
- *Dr. Shaqil Kassam*
- *Dr. Jawaid Younus*
- *Dr. Diana Ionescu*
- *Dr. Silvana Spadafora*
- *Dr. Michela Febbraro*

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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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

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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Canada's Drug and Health Technology Agency

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0300
Name of the drug and Indication(s)	Sotorasib for the treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.
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	☐
	No requested revisions	X

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

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons

Version: 1.0
Publication Date: TBC
Report Length: 2 Pages

Please provide details regarding the information that requires clarification.
c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

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

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

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0300-000
Brand name (generic)	Sotorasib (Lumakras)
Indication(s)	Treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.
Organization	Lung Cancer Canada - Patient Group
Contact information[a]	Name: Shem Singh, Executive Director, Lung Cancer Canada [redacted]

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

LCC is disappointed with CADTH's recommendation to not reimburse sotorasib as indicated for KRAS G12C NSCLC patients. In the rationale for recommendation, pERC noted it was uncertain whether a clinically meaningful improvement in PFS was notable, as well there were more severe adverse effects in the sotorasib arm compared to docetaxel, and uncertainty in the quality of life for patients on sotorasib. From a patient perspective, these points on QoL and PFS were discussed in our initial patient submission (a joint submission with Canadian Cancer Survivor Network and Lung Health Foundation) made to CADTH.

Firstly, numerous patients interviewed in our initial submission noted how effective sotorasib was in maintaining stable disease. One patient progressed from stage 2B to 4A while on chemotherapy prior to starting sotorasib. After 6 weeks on sotorasib, her primary lung tumour shrunk by 65% with further reduction afterwards. She remained progression-free on the treatment for over 1.5 years. Another patient with metastatic disease had significant reduction within the first 5.5 weeks and by the 3rd scan, she had a complete response and was NED. A third patient's tumour had shrunk by 50% after 1.5 years on the treatment, which was her 3rd line of therapy. All three patients noted how successful sotorasib was in maintaining PFS for over a year, which is a significant feat for not only them in their disease management, but also for loved ones and care partners who have seen these patients gain an extra year together, when the initial diagnosis of "metastatic disease" seems almost to be a death sentence for many.

Secondly, pERC could not conclude that the health-related quality of life and disease symptoms on sotorasib for patients was better than docetaxel, which is untrue. As discussed in our patient submission, patients were able to maintain or improve their QoL, and disease symptoms were much more manageable with sotorasib in comparison to other systemic treatments. One patient, for example, had a very poor QoL prior to treatment where she could barely eat or shower without caregiver assistance, and required supplemental oxygen 24/7. After 2 weeks on sotorasib, her symptoms resolved and QoL skyrocketed – she moved back to her home state, returned to work, travelled to new countries, and took on being a caregiver for her father. She has since regained her independence and no longer depends on others for activities of daily living. Another patient has luckily never had a significant drop in quality of life, independence, or functionality since diagnosis because of the success they have seen with sotorasib. She went about her life as normal with minimal disease symptoms, and frequently flew across the country to visit family. LCC has seen, first-

hand, the drastic differences in quality of life that sotorasib has had on patients and decreasing the burden on care partners. It is crucial for these patients to be able to access treatments that are effective, and the real-world evidence provided has clearly shown improved outcomes for numerous individuals.

In terms of toxicity, pERC stated that the toxicity was higher for sotorasib and numerically that may be true with treatment emergent events. However, patients in the CodeBreak 200 clinical trial stayed on sotorasib over a month longer than the control arm, so it makes sense there will be more treatment emergent events due to time bias. Additionally, the treatment-related AEs for sotorasib were relatively minor, the most common grade 3 or higher AEs were diarrhea, ALT and AST elevations, which are relatively manageable as outpatients. However for docetaxel, the most common grade 3+ AEs were pneumonia, febrile neutropenia, and neutropenia, which are comparatively more severe and can lead to hospitalization.

There is currently a large unmet need in the treatment paradigm for patients with KRAS G12C non-small cell lung cancer. First-line treatment with immune-checkpoint inhibitors are being incorporated into standard of care more frequently, but once patients progress on these treatments, there are limited second-line options available to them. Sotorasib has induced rapid and durable responses and allowed patients to enjoy a quality of life that is worthwhile and fulfilling while decreasing the caregiver burden. LCC hopes that CADTH takes these patient values into consideration in re-evaluating the draft recommendation, as patients are ultimately bearing the brunt of the decisions regarding treatment reimbursement.

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	☒

We thank CADTH for receiving, respecting, and thoughtfully considering our patient input submission. However, LCC's Medical Advisory Committee ("Clinician Group") input submission was not acknowledged or referenced by CADTH in the draft recommendation as published, although we have confirmed our submission of the file prior to the deadline of September 12h, 2022. We have contacted CADTH on this issue but have yet to hear back. We would like clarification on behalf of CADTH whether our clinician input was received, acknowledged, and honestly considered by pERC during the decision-making process.

We applaud CADTH for holding external stakeholder feedback in high regard during the decision-making process as these recommendations hold heavy weight for those patients and their care givers impacted first-hand by these drug recommendations. However at the same time, these submissions require valuable time and effort by our volunteers. To have reassurance that our feedback will consistently be respected and considered by CADTH is an integral part of the process. LCC is looking forward to receiving clarification on the status of our Clinician Group input to CADTH on this file. Please do not hesitate to contact Lung Cancer Canada if you have any further questions or need clarification on this aspect.

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	☒
Sotorasib offers patients a treatment option that can be taken orally from anywhere that is convenient for them, without having to go to clinics or hospital centers for administration. Docetaxel must be administered in hospitals, and this has implications and barriers for patients and family members in terms of travel time, accessibility and logistics of travel. Patients value treatment options that give them the flexibility and freedom to administer care anywhere that works for them, including in the comfort of their homes. CADTH's draft recommendation document doesn't highlight this key value for patients and caregivers.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

[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	*Shem Singh*
Position	*Executive Director*
Date	*October 19, 2023*
☒	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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0300
Brand name (generic)	LUMAKRAS™ (sotorasib)
Indication(s)	Adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy
Organization	Amgen Canada Inc. (Amgen)
Contact information[a]	[redacted]

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

Amgen strongly disagrees with the pERC committee's "Do Not Reimburse" category of recommendation.

The recommendation is contrary to, and not in full consideration of, the clinical evidence submitted to CADTH which demonstrates a favorable benefit/risk profile for sotorasib over docetaxel. Further, the recommendation is not aligned to input received from various stakeholders who more directly represent NSCLC patients, as well as the latest Canadian Consensus Recommendations on the management of KRAS G12C-mutated NSCLC, which states: "*Sotorasib, the only approved KRAS G12C inhibitor in Canada, is recommended for patients with advanced KRAS G12C-mutated NSCLC who progressed on guideline-recommended first-line standard of care for advanced NSCLC without driver alterations (immune-checkpoint inhibitor(s) [ICIs] +/− chemotherapy). Sotorasib could also be offered as second-line therapy to patients who progressed on ICI monotherapy that are not candidates for a platinum doublet and those that received first-line chemotherapy with a contraindication to ICIs." This recommendation was made for "sotorasib over docetaxel based on improved progression-free survival, response rates, patient-reported outcomes, and improved tolerability profile."*[1]

Additionally, the conclusions of pERC are not aligned to the totality of evidence presented in the CADTH review reports. Most notably, pERC appears to have overlooked the following:

- Clinical benefit of sotorasib consistently demonstrated across the clinical development program and real world studies. Such clinical benefits in CodeBreaK 200 (CB200) favoured sotorasib across several endpoints, including objective response rate, time to response, durability/duration of response, disease control, tumor shrinkage, progression free survival, health-related quality of life, symptom scores and an established safety profile.[2,3]
- Patient reported outcome measures, assessed by multiple instruments, are clearly in favour of sotorasib, demonstrating the potential for meaningful improvements in quality of life for patients and their loved ones.[2,3]
- Clinicians have stated that *"sotorasib has superior efficacy and quality of life, and reduced side effects, when compared to docetaxel. It… should become the second-line standard of care for patients with advanced KRAS G12C NSCLC."*[4]
- Patient group insights from patients who had experiences taking sotorasib, as well as their caregivers, included the following:

- versus other treatments, side effects with sotorasib were more manageable and there were better opportunities to live an improved quality of life (QoL) as well as have a second chance at enjoying life and spending their time in meaningful ways,[4]
- treatments that can be taken at home, reducing the need for travel to infusion clinics, are important for maintaining patient QoL and decreasing caregiver burden.

- CodeBreaK 100 (CB100) demonstrates that 32% of patients are still alive at 2 years.[5,6] This is in stark contrast to historical data with docetaxel.[4,7]

There are additional benefits of having an oral therapy in these NSCLC patients who are actively dying, which could markedly impact individuals living in more rural geographies and/or patients who seek to limit travel and healthcare contact days for themselves and their caregivers. Given the open-label nature of the CodeBreaK 200 trial, it is evident that many patients did not want to be on docetaxel and that comparatively those patients who remained on sotorasib did much better than those patients who remained on docetaxel. There is merit in consideration of these facts which should not be overlooked.
Not recommending reimbursement for this group of Canadian NSCLC patients will create ongoing inequity on multiple levels:

- Only patients with other avenues for reimbursement, such as those with private insurance or who can pay out-of-pocket, would be able to access sotorasib,
- Patients with other actionable oncogenic alterations (i.e., EGFR, ALK, ROS-1, etc.) would have access to targeted treatments, while patients with KRAS G12C mutations would remain disadvantaged,
- NSCLC patients in other international jurisdictions have been able to access sotorasib through early access schemes and a broad range of countries having already granted full reimbursement from public funds, based on HTA and pricing reviews. Full access to sotorasib was granted in UK, Germany, Sweden , Poland, Slovenia, the Czech Republic and Bulgaria as well as in USA and Japan. In several other jurisdictions, patients can benefit from sotorasib treatment through specific individual case requests, covered also from public funds, like Austria, Hungary, Slovakia, Bahrain, Kuwait, Qatar, United Arab Emirates.[8-15]

As the Sponsor, given the large unmet need in NSCLC, Amgen believes that all relevant patients should be given the opportunity to access sotorasib.[1,16,17]

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	☒

Amgen strongly disagrees. The pERC committee appears to have disregarded much of the stakeholder information provided from our organization. The lack of consideration for stakeholder input does not appear to have been limited to Amgen's input. It also appears that a crucial submission, from Clinician Group Input #2 representing 26 NSCLC experts from across Canada, may have been overlooked.

In particular, regarding the submission provided by the Sponsor, the recommendation from pERC contains content about efficacy and safety that is in direct opposition to the clinical interpretation of the CB200 trial: *"Sotorasib significantly increased progression-free survival and had a more favourable safety profile, compared with docetaxel, in patients with advanced NSCLC with the KRAS G12C mutation and who had been previously treated with other anticancer drugs."*[2]

Additional evidence that was submitted by the Sponsor, including real-world data and some CodeBreaK study (both CB100 and CB200) outcomes inclusive of a publication on patient-reported outcomes, were not fully considered.[3,4]

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☒
While the reasons are stated, they are not clear or based on the totality of evidence or the lived experiences of patients and the physicians that treat them, nor are they congruent with the content of the CADTH review report(s). pERC appears to have misunderstood and/or misinterpreted the totality of evidence, taking a narrow perspective rather than what would be overwhelmingly best for this group of patients. Some main areas that have been overlooked in the rationale: • Recognition by clinician groups and guidelines of sotorasib as the new standard of care for these patients which is clinically meaningful. • Contextualization of the safety profile for sotorasib and implications of AEs in terms of the impact to patients and on health-care resource use.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
No. Implementation issues are not presented and are therefore not adequately addressed. We would like to see a positive reimbursement recommendation with guidance for implementation stated.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
No. We believe this is applicable as per the input of various stakeholders, "we strongly support the funding of sotorasib for this indication", as well as published guidelines for KRAS G12C-mutated NSCLC in Canada,[1] the US (NCCN)[17] and Europe (ESMO)[16] which also support the use of sotorasib. Therefore, the recommendation should have stated reimbursement conditions.		

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

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