Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

lazertinib and amivantamab (Lazcluze and Rybrevant)

(Janssen Inc.)

Indication: LAZCLUZE® (lazertinib) tablets in combination with RYBREVANT® (amivantamab) for the first-line treatment of adult patients with locally advanced (not amenable to curative therapy) or metastatic non-small lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations.

December 2, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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

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

December 2, 2024

CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: lazertinib (Lazcluze) & amivantamab (Rybrevant)
Indication: Lazcluze (lazertinib) tablets in combination with Rybrevant (amivantamab) for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations.
Name of Patient Group: Joint Submission by Lung Cancer Canada, Lung Health Foundation, and Canadian Cancer Survivor Network
Author of Submission: Winky Yau – Lung Cancer Canada, Lindsay Timm - Canadian Cancer Survivor Network (CCSN), and Riley Sanders - Lung Health Foundation (LHF).

1. About Your Patient Group

This patient input submission is jointly submitted by Lung Cancer Canada (LCC), Canadian Cancer Survivor Network (CCSN), and the Lung Health Foundation (LHF).

Lung Cancer Canada is a registered national charitable organization that serves as Canada's leading resource for lung cancer education, patient support, research and advocacy. Lung Cancer Canada is a member of the Global Lung Cancer Coalition and is the only national organization in Canada focused exclusively on lung cancer. Lung Cancer Canada is registered with CADTH. https://www.lungcancercanada.ca/

The Canadian Cancer Survivor Network (CCSN) is a national network of patients, families, survivors, friends, community partners, funders, and sponsors who have come together to take action to promote the very best standard of care, whether it be early diagnosis, timely treatment and follow-up care, support for cancer patients, or issues related to survivorship or quality of end-of-life care. https://survivornet.ca/

The Lung Health Foundation (previously named the Ontario Lung Association) is registered with the CADTH and pCODR. The Lung Health Foundation (Ontario Lung Association) is a registered charity that assists and empowers people living with or caring for others with lung disease. It is a recognized leader, voice and primary resource in the prevention and control of respiratory illness, tobacco cessation and prevention, and its effects on lung health. The Foundation provides programs and services to patients and health-care providers, invests in lung research and advocates for improved policies in lung health. It is run by a board of directors and has approximately 46 employees, supported by thousands of dedicated volunteers. www.lunghealth.ca

2. Information Gathering

Data Collection:

The information discussed throughout this submission consists of the thoughts and experiences of non-small cell lung cancer patients. They were collected through virtual interviews conducted directly with the patients, or from previous patient input submissions to CADTH. All interviews were conducted in October-November 2024.

Demographic Data:

Amivantamab has been approved by Health Canada for a few indications over the past few years, but LCC, CCSN, and LHF are aware of the limitations of this submission given the small number of patients interviewed with direct

experience within this specific indication. It should be kept in mind that there were limited sites in Canada that were involved in the MARIPOSA clinical trial, so we hope that pERC keeps this into consideration.

We were unable to speak to any patients who had specific experience participating in the MARIPOSA trial, but numerous other patients involved in other trials with amivantamab, including 1 participant ([redacted] on the amivantamab-lazertinib treatment arm of MARIPOSA-2, and others on PALOMA-3 and PAPILLON. Their demographics are summarized in the chart below, and specific treatment experience can be found in section 6.

Name	Patient/ Caregiver	Gender	Age	Diagnosis	Diagnosis Date	Location	Source
[redacted]	Patient	F	42	Stage 4 NSCLC	January 2022	[redacted] AB	Telephone Interview
[redacted]	Patient	F	66	Stage 4 EGFR Exon 20 NSCLC	January 2022	[redacted] ON	Previous Submission
[redacted]	Patient	M	66	Stage 4 d NSCLC	July 2014	[redacted] ON	Previous Submission
[redacted]	Patient	M	70s	Stage 4 EGFR Exon 21 L858R	July 2019	[redacted] AB	Previous Submission

3. Disease Experience

[redacted] had always been a healthy and active woman, going for runs a few times per week. In Spring 2021 she had just given birth to a healthy baby boy, but in the months recovering from it, she noticed an intermittent backache that came and went, but doctors sent her for massage therapy assuming it was from her C-section. By December, the back pain still hadn't resolved and she had become short of breath when walking and pushing the baby stroller. She was sent for an X-ray on New Year's Eve in good spirits, but things changed quickly when doctors immediately sent her to the ER after the scan revealed fluid in her lungs. Further testing confirmed a diagnosis of stage IV lung cancer, which was a total shock to her as her father had passed away of the same disease just two years prior in 2019. She started first-line therapy with osimertinib which only worked for 3 months, then was enrolled into the MARIPOSA-2 trial, which she is still on in November 2024, nearly 2.5 years later.

In early 2014, then 56-year-old [redacted] had some back pain and a cough that didn't seem to go away for months, but simply thought it was due to his other comorbidities. When he suddenly felt breathless walking up one flight of stairs, he knew something was off and decided to head to his primary care doctor. Further tests revealed lesions in his lower back, spine, and bones in addition to the primary tumor in the lung, thus diagnosing [redacted] with stage 4 EGFR Exon 21 NSCLC. He recalls, *"When I was first given this diagnosis, I felt like I had hit a dead end and didn't think I'd even make it to the next Christmas. But then I did make it, and then my next birthday, then more Christmases after that. It has been 8 Christmases and 8 birthdays since I got first diagnosed, and I feel eternally grateful I got this extra time"*. [redacted] found success with two different targeted therapies between 2014 to 2020 and had an incredible quality of life. However after progressing on his 2nd line of treatment, another biopsy showed he was positive for the cMET amplification, so he qualified for the new clinical trial with amivantamab, which [redacted] had done very well on at the time of his most recent interview in May 2022.

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64-year-old [redacted] had always been physically active, was a non-smoker, rarely fell ill, recently retired, and was enjoying her life golfing and travelling with her husband. Around Christmas 2021, she developed a persistent cough that she attributed to a simple cold, but when it hadn't resolved by January, her family insisted she go to the doctor, who ordered x-rays and tests that eventually confirmed she had stage 4 lung cancer with metastases to the L5 vertebrae and lymph nodes. [redacted] was shocked by the diagnosis as she had no symptoms of being unwell when she was diagnosed. When tests confirmed she had the EGFR Exon 20 mutation, her oncologist enrolled her into the PAPILLON trial right away, which she started in March 2022 but unfortunately was randomized to the standard-of-care arm. She received 2 rounds of chemotherapy before a follow-up CAT scan revealed her tumours had grown and spread to the right adrenal gland. [redacted] was offered to switch to treatment with amivantamab monotherapy in May, which she recalls was a "game changer".

Amivantamab is a therapy used to treat NSCLC, currently approved in Canada for EGFR Exon 20 mutations and has shown promising results in efficacy and progression-free survival in numerous clinical trials, and now as first-line treatment for EGFR Exon 19 and L858R mutations via the MARIPOSA trial. Current standard of care in this setting has been osimertinib, a TKI that has proven to be efficacious for patients between months and years, but progression and treatment resistance remains a critical concern for these patients. The approval of amivantamab and lazertinib would bring a very welcome additional option for treatment-naïve patients in this setting.

4. Experiences With Currently Available Treatments

[redacted] started first-line treatment with osimertinib shortly after receiving the diagnosis in January 2022, which she recalls the only side effects osimertinib had were significantly dry skin and thinning of her hair. But otherwise, she says she felt fine, and only needed to take one pill per day, which was convenient. Unfortunately, osimertinib only worked for 3 months before she progressed with significant symptoms – she could hardly speak more than a couple words and was constantly short of breath, coughing, difficulty going up the stairs, required a wheelchair when she'd go out, and had significant fluid in her lungs. She stopped treatment with osimertinib, and agreed to participate in the MARIPOSA-2 trial, which she started in July 2022 and has been on it ever since.

Once [redacted] was diagnosed with stage 4 EGFR-positive lung cancer, he started on gefitinib right away, which worked well for him for about a year as expected. The only side effect he experienced was diarrhea, but was tolerable and did not have much impact on his lifestyle. When he progressed after a year, another biopsy confirmed he had the L858R mutation, qualifying him for Osimertinib, which he found great success with for about 4.5 years from 2016 to 2020. He had no side effects at all from Osimertinib, and had an incredible quality of life with both of his past treatments, which managed his disease very well, keeping the tumours stable. In fall 2020, scans revealed [redacted] had progressed again with a lesion in his brain and one in his iliac, which was treated with radiation. His physician then suggested the amivantamab clinical trial to him, which he started in January 2021.

[redacted] was diagnosed in August 2019 with Stage 4 EGFR Exon 21 L858R lung cancer, and had previously been on a number of EGFR targeted therapies including afatinib and osimertinib, that kept his disease stable until progression in Fall 2022. He has since been in a few clinical trials involving amivantamab, including PALOMA-3, but was not chosen to receive the intervention, and instead received chemotherapy standard of care, which was ineffective and his cancer spread to the brain with 6 new lesions. After much effort from his oncologist, he was later approved to receive the drug on a compassionate basis by the manufacturer and has been on amivantamab ever since.

5. Improved Outcomes

With osimertinib currently being the standard of care for first-line therapy for EGFR Exon 19 or 21 L858R mutations, the approval of amivantamab in combination with lazertinib will provide an additional treatment option for patients that not only treats their disease successfully and delays further progression, but also gives patients their livelihoods back,

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allows for a good quality of life, and plan further down the line for a possible future going back to work, or enjoying their retirement, or spending time with loved ones. When faced with the decision of enrolling into a clinical trial, they hoped the treatment would provide them with:

- Improved management of their disease symptoms of non-small cell lung cancer
- Delaying further disease progression and potentially be successful at shrinking their tumours
- Allowing patients to have a full and worthwhile quality of life
- Allowing patients to live longer and maintain their independence and functionality to minimize the caregiver burden
- Having manageable side effects

6. Experience With Drug Under Review

Name	Diagnosis Date	Drug access method	Treatment Arm	Period on amivantamab	Line of treatment	Still on trial? (Dec 2024)
[redacted]	January 2022	MARIPOSA-2 clinical trial	Amivantamab + Lazertinib	July 2022 - present	2nd line	Yes
[redacted]	July 2014	Clinical Trial	Amivantamab Monotherapy	January 2021 - April 2024 (or earlier)	3rd line	Deceased
[redacted]	July 2019	Manufacturer's Compassionate Access	Amivantamab Monotherapy	June 2023 - Present	3rd line +	Yes, as of September 2024
[redacted]	January 2022	PAPILLON Clinical Trial	Amivantamab Monotherapy	May 2022 - present	1st line	Yes, as of June 2024

Amivantamab was successful at treating patients' disease while being durable.

Immediately prior to starting the MARIPOSA-2 trial, [redacted] lungs were full of fluid, she could hardly speak a couple words before needing to catch her breath, and her tumours were growing. Now 2.5 years later, she's still doing very well on the trial – her primary lung tumour shrank at first but now all her tumours have been stable for over 2 months, and she's living an excellent quality of life. Being on the amivantamab & lazertinib arm, she takes Lazertinib orally every day at the same time and goes to the cancer center for the amivantamab infusions every 3 weeks.

At diagnosis, [redacted] had mets in her L5 vertebrae and lymph nodes, and after being randomized onto the standard-of-care arm of the PAPILLON trial where she received 2 rounds of chemotherapy, treatment was ineffective and her tumours had spread further to her right adrenal gland in the short period of time. Trial protocol allowed her to stop chemotherapy and receive single agent amivantamab, which she started in May 2022. 2 years later, [redacted] still continues to be on the treatment as of June 2024, and her latest scans showed substantial improvement where amivantamab had shrunk her tumours "down to next to nothing", while her L5 vertebra and adrenal gland mets remain stable.

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By the time [redacted] started his third-line treatment with amivantamab, his disease had metastasized to his brain, bones, and further growth in his primary tumour. At the time of his interview in May 2022 after 14 months on the drug, the mets in his bones and lung have continued to be stable without any additional growth. However, he had developed additional metastases in his brain while on the therapy, compared to the one lesion when he started. Unfortunately, when contacted for an update in October 2024, LCC had been notified that [redacted] had passed away in April 2024.

[redacted] started treatment with amivantamab on June 1, 2023 when he had 6 mets in his brain, which he also had treated with radiation, but his latest CT and brain MRI scans as of September 2024 have been stable, which is promising for him. [redacted] says that because he is currently beyond third-line treatment, there are worries about the next steps after amivantamab when it eventually fails, but is optimistic the drug remains effective on his tumours for as long as possible.

Side effects are significant at onset, but ultimately improve in severity with dose reduction and prescription medications.

[redacted] also had many side effects during the first few weeks of starting the trial – her scalp often bled due to the dryness, but after a year, the scabs got infected and her scalp was full of wounds. After her dermatologist prescribed her creams, it significantly decreased the severity and although she still currently struggles with the dry scalp and scabbing, [redacted] says it's not as bad as before. She also struggled with paronychia on her toe and fingernails, to the point where she couldn't wear any closed-toe shoes for two years since starting the trial, until very recently when prescriptions finally worked where she's now looking forward to being able to wear winter boots and shoes again. Furthermore, [redacted] struggles with acne on her face, which she says is painful and stings – lots of bumps and discoloration on her back and chest, but was recently prescribed Accutane last month, which completely faded away her acne. Nonetheless, [redacted] says she feels well aside from these side effects, which are slowly healing too, and feels stronger every day – she says, *"I'm doing OK and I'm grateful to be part of the trial. I don't mind the side effects if it means I get to live".*

[redacted] had to pause her treatment with amivantamab for 2 cycles about a year into treatment due to the severity of the rashes on her scalp, back and chest, and was happy to hear the dose interruption had no impact on her tumours. She has since returned to regular treatments every 3 weeks, with no issues. Her rashes are now controlled with an antibiotic cream, and reiterates she'd prefer these side effects over what she experienced when on chemotherapy.

Patients were able to return to a good quality of life, enjoy their hobbies, and spend time with loved ones.

Being diagnosed with stage IV lung cancer less than a year after having her second child has really changed [redacted]'s perspective on life. 2.5 years later, she's currently feeling well on treatment, is able to take care of her kids, who are now 8 and 3 years old (at diagnosis, they were around 5 and 1), and is always out and about with them. She cooks at home, plays with her kids at the park, looks after her family, and *"just doing all the mommy stuff with my husband, who's such a trooper".* [redacted] still drives herself, goes on road trips with her family to see the mountains in British Columbia, and overall living a quality of life that is a complete-180 from before she started the trial, when she could barely speak a full sentence without feeling out of breath, relied on a wheelchair to get around, and even going upstairs was hard. But now, she's able to go on long walks with her family and even jumping on the trampoline with her kids, and although her hips felt sore afterwards, [redacted] is taking it very positively and remaining strong, believing it's a really great sign she's tired from jumping around rather than being due to the cancer.

With the stability [redacted] found on amivantamab, she continues to live a good quality of life while pursuing her hobbies of golf, gardening, and socializing in her book club. She continues to travel as much as she can, and even flew to Ireland the day after one of her infusion treatments, and was also looking to downsize her home. When asked about her goals for the future, she wanted to just remain healthy and active, and be able to enjoy life with her friends. In the first few

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months of amivantamab treatment, [redacted] also was the primary caregiver for her elderly parents who were in their nineties, so she was able to simultaneously care for them as well.

Patients agreed that amivantamab and lazertinib was worth accessing and they'd prefer it to other therapies.

For [redacted], she says it was absolutely worth accessing the trial, despite the significant side effects at first. She does admit that if the osimertinib pills had worked for her cancer, she would have preferred it because of the ease of taking it everyday at home, rather than needing to go to the hospital for long infusions every few weeks. However, she is on the Lazertinib and amivantamab combination arm, and says the ease of Lazertinib is similar to when she was on osimertinib. [redacted] says that as long as the treatment is working, that's what matters the most, not the side effects or her appearance. She says, *"It's worth it to have access to the trial, and every time my kids yell "mom" and I'm there to answer them, it makes me so happy and grateful. I'm so glad I'm alive and I just want to see my kids grow up. Tomorrow isn't promised anyways, so I'm just savoring the moment that the drugs work, because I know there'll be a day when it doesn't."*

[redacted] noted there were pros and cons associated with his previous targeted therapies versus amivantamab. In terms of side effects, amivantamab was much more preferable as the targeted therapies had much more intense and dramatic side effects, notably GI issues that were unpredictable, but skin issues with amivantamab were manageable with creams and lotions. However in terms of quality of life, [redacted] preferred the ease and convenience of oral targeted therapies that he could take at home as a pill, versus long infusion times in the hospital every 3 weeks with amivantamab. He was also able to take part in weekly exercise programs while on TKIs, starting in November 2019 until the end of 2023, 6 months into amivantamab, as his strength had diminished and energy levels were low due to progression in his brain. He has since stopped running errands and is not allowed to drive due to the brain mets, so his wife takes care of most daily tasks like grocery shopping and driving him into the city for his infusion appointments, but [redacted] has no issues helping out with chores around the house whenever he can.

[redacted] says *"100% I'd rank it a 10 - ami is 100 times better than chemotherapy. I can go about my day-to-day with no issues and don't need to worry about feeling or getting sick, or being around people as I did with the weakened immunity during chemo. The side effects are manageable, and I can do everything on my own. As long as the drug keeps working, I will absolutely advocate staying on it."*

7. Companion Diagnostic Test

Patients with EGFR Exon 19 or 21 L858R mutations are identified using Next Generation Sequencing, which is routinely conducted in all patients diagnosed with advanced NSCLC with a non-squamous and squamous histology, without a smoking history.

8. Anything Else?

LCC, CCSN, and LHF recognize that in this submission, [redacted] is the only patient with direct relevant experience with both amivantamab and Lazertinib treatments per the submission indication, though this was not her first-line therapy. As a result, [redacted]'s experience on the PAPILLON clinical trial was included as her experience with amivantamab was in the first-line setting, and similarly for [redacted] and [redacted] who were treated with amivantamab for their EGFR Exon 21 and 19 mutations respectively, which are in line with this submission's indication.

Appendix: Patient Group Conflict of Interest Declaration

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To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Janssen - LCC 2023			X	
Janssen - LCC 2024				X
Janssen - LHF 2023				X
Janssen - LHF 2024				X
Janssen - CCSN 2023				X
Janssen - CCSN 2024				X

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.

Name: Winky Yau
Position: Coordinator, Medical Affairs
Patient Group: Lung Cancer Canada
Date: December 2, 2024

CADTH

CADTH Reimbursement Review
Clinician Group Input Template
CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0392-000
Generic Drug Name (Brand Name): Amivantamab-lazertinib (Rybrevant-Lazcluze)
Indication: Lazertinib (tablets) in combination with amivantamab (IV) for the first line treatment of adult patients with advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations
Name of Clinician Group: OH (CCO) Lung Cancer Drug Advisory Committee
Author of Submission: Dr. Donna Maziak and members of OH (CCO) Lung Cancer Drug Advisory Committee

1. About Your Clinician Group

OH(CCO)'s Cancer Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate.

2. Information Gathering

Information was gathered by email.

3. Current Treatments and Treatment Goals

Treatment for patients with advanced EGFR mutated lung cancer is palliative and aimed at prolonging life, improving symptoms and delaying cancer progression. The current standard is osimertinib, an oral - once daily - targeted therapy with a median progression-free survival of 18.9 months, median survival of 38.6 months and overall response rate of 80% [Soria et al NEJM 2018; Ramalingam et al NEJM 2020]. Osimertinib treatment also leads to rapid symptom improvement, regression in brain metastases and longer time to cancer progression in brain, and a low rate of side effects. Many patients are able to maintain independence while treatment is effective, reducing burden on caregivers and in some cases allowing patients to continue to work. This treatment has been considered ideal for many patients, except for the inevitable development of resistance.

In order to overcome the inevitable resistance to osimertinib, intensified regimens have been tested in the first-line setting including the recently Health Canada approved (not yet publicly funded) "FLAURA2" regimen, adding pemetrexed/platinum chemotherapy to osimertinib first-line. This improves progression-free survival significantly compared to osimertinib (HR 0.62, p=0.0002) with a median PFS of 29.9 months (versus 19.9 with osimertinib alone). Response rates are similar but the duration of response is longer (24 months versus 15 months). The intracranial response rate is the same but the depth and duration of response are improved with the addition of chemotherapy. There is a trend for overall survival improvement (HR 0.80, 95% CI 0.64-1.00), median 28.6 versus 31.8 months. This new standard option is offered to patients considered at higher risk of disease progression on osimertinib alone, such as those with liver or brain metastases, and also based on patient preference and ability to tolerate chemotherapy. In the FLAURA2 study, 6% of patients receiving osimertinib discontinued treatment for toxicity, while 11% of patients in the osimertinib/chemotherapy arm discontinued all treatment and 48% discontinued at least one of 3 drugs.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Despite a high response rate initially, not all patients respond to standard therapy with osimertinib, or even osimertinib plus chemotherapy. All patients develop treatment resistance, usually in year 2 of treatment.

Additional treatments that improve survival, symptoms, progression-free survival, and protect the brain from cancer growth to a greater degree than the current standard are all needed.

Intensified regimens beyond osimertinib alone need greater convenience and more manageable toxicity. The DAC notes that the amivantamab and lazertinib regimen does not fulfil the need for greater convenience nor manageable toxicity.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The combination of amivantamab/lazertinib would be used as a first-line treatment in patients with advanced EGFR mutated NSCLC. It would be considered alongside single agent osimertinib or the intensified regimen of osimertinib plus chemotherapy.

In the MARIPOSA study, progression free survival was significantly longer with the combination than with osimertinib alone (HR 0.70, p<0.001; median 23.7 versus 16.6 months). Response rates are similar but the duration of response is longer (25.8 months versus 16.8 months). The intracranial response rate is the same but the depth and duration of response are improved with the addition of chemotherapy. There is a trend for overall survival improvement (HR 0.80, 95% CI 0.61-1.05, median survival not yet reached), and patients had longer time to progression of cancer in brain as well.

This new option would be offered to patients considered at higher risk of disease progression on osimertinib alone, such as those with liver metastases and genetic co-alterations in TP53 (shown to be associated with adverse prognosis) [Felip et al Ann Oncol 2024]. Patient preference for intensified therapy and their ability to tolerate the combination (weekly infusions of amivantamab x 4 weeks and then every two weeks, plus oral daily lazertinib) will also be key factors in treatment decision making. This would also allow platinum chemotherapy to be used as second-line treatment after cancer progression, similar to the option of osimertinib alone currently. Osimertinib + chemotherapy as initial treatment would lead to docetaxel as second-line therapy (third line for the others).

With respect to treatment tolerance in the MARIPOSA study, 14% of patients receiving osimertinib discontinued drug for toxicity while 10% receiving the combination discontinued all treatment and 35% discontinued at least one of the two drugs.

Distinct from osimertinib and osimertinib plus chemotherapy, this novel combination appears to suppress the 3 most common mechanisms of resistance, i.e. driven by *MET* and *EGFR*-signaling, and transformation to small cell carcinoma [presented at ESMO 2024 by Besse et al]. By contrast, resistance mechanisms after osimertinib alone or with chemotherapy are similar, driven by MET and EGFR-signaling and histologic transformation [presented by Ahn et al ESMO Asia 2023]. How to overcome resistance with this novel treatment is not yet known, but platinum chemotherapy would be standard second-line treatment for these patients.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

This treatment is best suited for patients with advanced EGFR-mutated NSCLC. The treatment improves outcomes (survival data not yet mature) in all subgroups. However, this comes at the cost of greater treatment burden (more visits, need for IV therapy) and more side effects (rash, infusion reactions on first treatment day with IV therapy). To balance this, providers and patients will need to discuss risks – those patients with greater disease burden and with co-mutations such as TP53 should all be considered for intensified therapy with the combination (although TP53 mutations are not routinely tested for). In addition, all patients that are interested in intensified therapy and able to withstand side effects (performance status 0, 1) and able to manage the increased visit

schedule would be good candidates for this therapy. At present, it is unknown which patients should receive osimertinib plus chemotherapy versus amivantamab plus lazertinib.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

In practice, as in the trial, we would use regular clinical assessment and imaging to assess response or disease stabilization and symptom improvement. Benefits will need to be balanced against toxicity and treatment burden (visits for IV therapy).

There is an assessment every one to two cycles for benefit and toxicity, with a history and physical typically supplemented by periodic diagnostic tests such as diagnostic imaging like CT and MRI, depending on where disease is known, and patient characteristics. Imaging, laboratory work, and clinical assessment are all combined by clinicians to determine when the therapy is no longer beneficial. In terms of frequency of imaging, this may be done on a symptom directed basis, and also at a regular time interval, typically every two to three months initially, but intervals may be increased the longer the patient is on therapy.

The improvement in progression-free survival is important for patients, as are the emerging data on survival. If the survival data demonstrate a significant improvement for patients, this will lead to more providers and patients pursuing this combination.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Patients with progressive disease should stop treatment. For patients with focal progression in the CNS but well controlled disease extracranially, SRS or surgery to the brain and continuation of systemic therapy is widely considered (demonstrated safety of this approach). Patients with intolerable toxicity which cannot be managed with supportive care should also stop treatment, as well as those who wish to withdraw.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Amivantamab should be administered in hospital (outpatient chemotherapy units) or specialty clinics with expertise in managing side effects and preparation of biologics. Patients will take lazertinib daily at home. Medical oncologists would oversee the patient's care but trained experts (e.g. nurses) can deliver the IV treatment.

6. Additional Information

NA

7. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? 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? If yes, please detail the help and who provided it.

   No

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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Donna Maziak
Position: Lead, OH-CCO Lung/Thoracic Cancers Drug Advisory Committee (OH-CCO Lung DAC)
Date: 25-Nov-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Natasha Leighl
Position: Member, OH-CCO Lung DAC
Date: 19-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen	x			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Peter Ellis
Position: Member, OH-CCO Lung DAC
Date: 21-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen	x			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Andrew Robinson
Position: Member, OH-CCO Lung DAC
Date: 21-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Stephanie Brule
Position: Member, OH-CCO Lung DAC
Date: 22-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr. Michela Febbraro
Position: Member, OH-CCO Lung DAC
Date: 24-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 6: Conflict of Interest Declaration for Clinician 6

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 7

Name: Dr. Mihaela Mates
Position: Member, OH-CCO Lung DAC
Date: 24-Nov-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 7: Conflict of Interest Declaration for Clinician 7

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

* Place an X in the appropriate dollar range cells for each company.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0392-000
Generic Drug Name (Brand Name): Amivantamab and lazertinib
Indication: Locally advanced or metastatic non-small cell lung cancer (NSCLC)
Name of Clinician Group: Lung Cancer Canada – Medical Advisory Committee
Author of Submission: Dr. Stephanie Snow (lead), Dr. Catherine Labbé, Dr. Jeffrey Rothenstein, Dr. Abhenil Mittal, Dr. Sunil Yadav, Dr. Nicole Bouchard, Dr. Ron Burkes, Dr. Alison Wallace, Dr. Paul Wheatley-Price, Dr. David Dawe, Dr. Normand Blais, Dr. Shaqil Kassam, Dr. Quincy Chu, Dr. Mahmoud Abdelsalam, Dr. Lacey Pitre, Dr. Randeep Sangha, Dr. Callista Phillips, Dr. Rosalyn Juergens, Dr. Geoffrey Liu, Dr. Mark Vincent, Dr. Biniam Kidane, Dr. Susanna Cheng, Dr. Barbara Melosky, Dr. Vishal Navani

1. About Your Clinician Group

Lung Cancer Canada (LCC) https://lungcancercanada.ca is a national charity with the purpose of increasing awareness about lung cancer, providing support and education to lung cancer patients and their families, to support research and to advocate for access to the best care for all lung cancer patients in all provinces and territories.

Through the LCC Medical Advisory Committee (MAC), we have been providing clinician input for submissions of new lung cancer drugs to the HTA process for many years. The LCC MAC is made up of clinicians and key opinion leaders in the field of lung cancer across the country.

2. Information Gathering

Information is from publicly available sources, primarily published manuscripts and conference presentations, together with experience of the members of the clinician group. This submission is entirely independent of the manufacturer (**Janssen**)**.**

3. Current Treatments and Treatment Goals

The goals when treating patients with non-small cell lung cancer (NSCLC) are stage dependent. In patients with stage 4 disease, the goal is palliation. The primary goals are to prolong a patient's lifespan (improve survival) while maintaining a high quality of life.

When developing a treatment plan for stage 4 NSCLC, one of the first steps is to determine if there is a driver mutation. If a driver mutation is found, the goal is to inhibit that drive for as long possible. In *EGFR* mutated NSCLC, the standard first line treatment in the common mutations (Deletion 19 and L858R) is osimertinib, an oral tyrosine kinase inhibitor which is widely funded and available throughout Canada. The FLAURA trial showed a benefit with osimertinib versus first generation EGFR TKI with a PFS of 18.9 months vs. 10.2 months.[1] The overall survival was significantly improved

at 38.6 months.[2] Unfortunately, this is still not curative and all patients with a diagnosis of stage 4 NSCLC are expected to die from their disease.

The FLAURA2 trial was a randomized Phase III trial that produced results showing that the combination of osimertinib with platinum and pemetrexed doublet chemotherapy in the first line improved progression-free survival (PFS) compared to single agent osimertinib. Specifically, the primary endpoint of investigator assessed PFS in FLAURA2 was 25.5 months versus 16.7 months (HR 0.62; P<0.001).[3] These results have led to a CDA recommendation for reimbursement with conditions for osimertinib with pemetrexed and platinum-based chemotherapy, however, this combination yet to be funded by Canadian health jurisdictions. There is an active industry sponsored patient support program in Canada to support access to the combination at present.

Non drug treatments may include radiation or other local therapies to palliative symptoms or address areas of oligo-progression with the goal of extending time on targeted therapy.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

The standard of care in patients diagnosed with EGFR mutations is single agent osimertinib. The response rate by RECIST criteria from the first line FLAURA trial was over 80%. In practice, it is rare for patients to have primary resistance. The problem is that all patients progress. In the FLAURA trial, the PFS was 18.7 months. Upon progression, most patients who are fit are given chemotherapy with a pemetrexed and platinum doublet. Response rates for chemotherapy in the setting of progression on EGFR TKI first line therapy are approximately 30% and median progression is short 4.4 months and most have progressed by 6 months.[4]

The goal is to keep patients on targeted therapy for as long as possible.

There are a variety of mechanisms of resistance to osimertinib that have been identified, with secondary EGFR and MET alterations accounting for up to 25%–50% of tumour resistance[5-7]. There are no publicly funded targeted therapies available for patients progressing on osimertinib in Canada.

The MARIPOSA trial tested the hypothesis that adding amivantamab to lazertinib would prolong the time before progression compared to single agent osimertinib, possibly by suppressing the emergence of common resistance secondary EGFR and/or MET alterations. Lazertinib is a highly selective, CNS-penetrant, 3rd-generation EGFR TKI[8,9] comparable to osimertinib, while amivantamab is an EGFR-MET bispecific antibody with immune cell directing activity[10-12] and activity against a wide range of EGFR and MET alterations[13,14].

MARIPOSA was a large global phase that confirmed the superiority of amivantamab and lazertinib compared to osimertinib alone. It was a very well designed trial from an academic research perspective, including using blinded independent central review to determine primary outcomes, and including serial CNS surveillance scans every 8 weeks for all patients regardless of whether they had brain metastases at the time of trial enrollment. This allowed for the most precise determination of true time of progression, as CNS metastatic lesions when they first develop may be asymptomatic and only detectable with imaging. This trial design distinguishes MARIPOSA from other trials done in this space; for instance, the FLAURA2 trial only required regular serial CNS imaging in those patients with pre-existent CNS disease on trial entry[3], potentially leading to an overestimate of the true PFS with the osimertinib-chemotherapy combination.

The primary endpoint of the MARIPOSA trial, PFS as assessed by blinded independent central review, was significantly longer in the amivantamab-lazertinib group than in the osimertinib group (HR 0.70; P<0.001).[15] The median PFS was 23.7 months vs 16.6 months), representing a 7.1 month difference in median PFS or time on first line targeted therapy.

The objective response rate was similar at 86% in patients in the amivantamab and lazertinib combination arm compared to 85% of those in the single agent osimertinib group. More importantly, however, responses were more durable with the amivantamab and lazertinib combination. Specifically, the duration of response was 25.8 months compared to 16.8 months with osimertinib alone.[15] This translated into a longer time to subsequent therapy, in keeping with the goal of having patients remain on targeted therapy as long as possible. Specifically, the time to subsequent therapy for patients who received amivantamab and lazertinib in the MARIPOSA study was 30 months vs 24 months for those who received single agent osimertinib (HR 0.77, P=0.005).[16]

At the time of the initial publication of results from the MARIPOSA trial, the initial planned interim analysis of overall survival after a median follow up of 22.0 months revealed a statistically insignificant trend favouring the amivantamab and lazertinib combination (HR 0.80, 95%CI 0.61-1.05, p=0.11).[15] Updated results from the MARIPOSA trial were presented recently at the WCLC 2024 congress, including an updated OS analysis. After a median follow up of 31.1 months, the OS trend suggesting benefit with the amivantamab and lazertinib combination has strengthened (HR 0.77, 95% CI 0.61-0.96 p=0.019).[16] This is also seen in a greater difference in proportion of subjects alive at key landmark analysis time points; 75% of patient treated with amivantamab and lazertinib were alive at the 24 month point compared to 70% treated with single agent osimertinib (delta 5% at 24 months) while 61% of amivantamab and lazertinib patients were alive at the 36 month mark compared to just 53% of those treated with osimertinib (delta 8% at 36 months).

Brain metastases in EGFR driven lung cancer are an urgent unmet need. These patients often receive radiation which impacts their quality of life. They as well are unlikely to receive subsequent lines of therapy. Both amivantamab and lazertinib have CNS activity. On subset analysis, there was a consistent PFS benefit by blinded independent central review for patients receiving amivantamab and lazertinib both with and without brain metastases (HR 0.69 for both groups).[15]

Intracranial PFS results were reported at WCLC 2024; there was a favourable trend in intracranial PFS supportive of the use of amivantamab and lazertinib which was durable and increased over time culminating in a 38% intracranial PFS rate for amivantamab and lazertinib patients vs 18% for those treated with osimertinib at the 36 month landmark.[16] Finally, the duration of intracranial response is longer with amivantamab and lazertinib.[16]

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

The combination of amivantamab and lazertinib would be an option in patients with sensitizing EGFR mutations who are treatment naïve in the stage 4 setting.

Single agent osimertinib will also remain an option. There will be patients who do not want to receive intravenous systemic therapy or prefer the logistics involved with an oral agent alone. Single agent osimertinib is an oral drug which is well tolerated.

In the event there is access to the combination of osimertinib with pemetrexed and platinum (FLAURA2 regimen) in the future, this regimen would add an additional front-line therapeutic option.

Of note, after amivantamab and lazertinib, treatment with pemetrexed and platinum doublet chemotherapy would remain a treatment option in second line, as there would be no expectation that treatment with amivantamab and lazertinib would confer resistance to chemotherapy.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Young patients are the ones that are most likely going to want and choose osimertinib with chemotherapy.

Patients with brain metastases are important subgroup to consider as per the data from the MARIPOSA trial suggesting improved outcomes with amivantamab and lazertinib compared to single agent osimertinib.

Patients with common EGFR alterations are identified using Next Generation Sequencing (NGS). NGS is routinely conducted as standard of care in all patients with advanced NSCLC with a non-squamous and squamous histology (without a smoking history).

At this time, it is not yet possible to identify those specific patients who are more likely to respond to this therapy. As with all targeted therapies, studies will be conducted to identify potential biomarkers. That being said, the combination of amivantamab and lazertinib has specific potential for those who are known to have other molecular alterations identified at initial diagnosis concurrent with the common sensitizing exon 19 del or exon 21 L858R EGFR mutations, such as concurrent rare EGFR co-mutations, or de novo concurrent MET mutations/amplifications, given the broad spectrum of activity of amivantamab against those alterations specifically.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

The outcomes used in clinical practice are aligned with the outcomes typically used in clinical trials and include safety/side effect profiles, treatment response and clinical response which are evaluated at regular intervals. The intervals of evaluation in clinical practice are usually not as frequent as in clinical trials, where trials protocols need to be strictly adhered to.

When starting on amivantamab and lazertinib, patients will need to be seen more frequently for adverse effect and tolerance assessments, especially for potential dermatologic adverse effects. Once stable on therapy, and adverse effects have been managed, most patients will not need to be seen in person as often. In general patients in clinical practice are often evaluated every 2-4 months for evidence of response status with radiographic studies including CTs +/- MRIs/bone scans depending on the sites of metastatic disease.

A clinically meaningful endpoint to treatment is either stable or improved radiological response, especially if it is durable. In most patients, a radiological response to treatment is reflected by a clinical response (i.e. symptom improvement) which is also durable.

Treatment with amivantamab and lazertinib combination therapy in the MARIPOSA study significantly delayed symptomatic progression compared to osimertinib (HR 0.72, P=0.005).[17] Further, while the combination of

amivantamab and lazertinib had a higher rate of specifically EGFR and MET related adverse effects, the patient reported outcomes collected during the study indicated that this did not translate into a meaningful impact on patients' functioning or health related quality of life over time. Specifically, for all patients treated in the MARIPOSA study, regardless of treatment arm, patient-reported functioning was stable throughout treatment compared to baseline, total symptom scores based on NSCLC-SAQ were comparable throughout treatment and individual lung cancer-associated symptoms were similar throughout treatment in both arms.[17]

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Treatment with amivantamab and lazertinib should be continued until symptomatic progression, unacceptable toxicity or patient choice.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Lazertinib as an oral medication is administered at home. The appropriate setting for amivantamab treatment includes systemic therapy outpatient units both in academic and community settings either at cancer centres or in a hospital setting, by personnel experienced in administering these agents.

6. Additional Information

The MARIPOSA trial showed an improvement in PFS with amivantamab and lazertinib compared to single agent osimertinib with a longer duration of response among those who respond. Maturing overall survival data show a strong trend towards superiority for the combination, and amivantamab and lazertinib patients enjoyed a longer period of time before deterioration of their lung cancer symptoms.

In younger patients especially with brain metastases, the combination is important with significant activity.

The MARIPOSA data represents a new option in first line therapy, along with single agent osimertinib (FLAURA) and osimertinib in combination with pemetrexed and platinum chemotherapy (FLAURA2). We need to discuss the results of all trials to appropriate patients. This is a time for shared decision making.

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1. Soria J-C, et al. Osimertinib in untreated EGFR-mutated advanced non–small-cell lung cancer. N Engl J Med 2018;378:113-125.
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4. Mok T et al. Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer. N Engl J Med 2017 Feb 16;376(7):629-640.

5. Leonetti A, et al. Resistance mechanisms to osimertinib in EGFR-mutated non-small cell lung cancer. Br J Cancer. 2019;121(9):725-737.

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8. Ahn M-J, et al. Lazertinib in patients with EGFR mutation-positive advanced non-small-cell lung cancer: results from the dose escalation and dose expansion parts of a first-in-human, open-label, multicentre, phase 1-2 study. Lancet Oncol. 2019;20(12):1681-1690.

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14. Haura EB, et al. JNJ-61186372, an EGFR-cMet bispecific antibody, in EGFR-driven advanced non-small cell lung cancer. J Clin Oncol. 2019;37(15 suppl). Abstract 9009.

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16. Gadgeel SM et al. Amivantamab plus lazertinib vs osimertinb in first-line *EGFR*-mutant advanced NSCLC: Longer follow-up of the MARIPOSA study. Presented at WCLC 2024, abstract OA.02.03.

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7. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

No

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No

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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Stephanie Snow
Position: Professor Dalhousie University, Medical Oncologist QEII Health Sciences Centre, Halifax, NS
Date: December 2, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AstraZeneca			X	
Astellas	X			
BMS		X		
Taiho	X			
Roche			X	
Merck		X		
GSK	X			
Janssen	X			
Pfizer	X			
Sanofi	X			
Knight	X			
Lilly	X			
Takeda	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Shaqil Kassam
Position: Medical Oncologist, Southlake Regional Hospital
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	x			
Merck	x			
BMS	x			
Takeda	x			
Novartis	x			
Ipsen	x			
Sanofi	x			
Pfizer	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Quincy Chu
Position: Medical Oncologist, Cross Cancer Institute, Edmonton, AB
Date: December 2, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Abbvie	X			
Amgen	X			
AnHeart	X			
Astellas	X			
Astra Zeneca		X		

Boehringer Ingelheim	X			
BMS	X			
Daichii Sankyo	X			
Eli Lilly	X			
GSK	X			
Janssen	X			
Meck	X			
Novartis	X			
Ocellaris	X			
Pfizer	X			
Roche		X		
Takeda	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 4

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
BMS	Advisory role, Honoraria and travel grants	☐	☒	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Biniam Kidane*
Position	*Associate Professor, Dept of Surgery, University of Manitoba*
Date	December 2, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AstraZeneca	☐	☐	☒	☐
Merck	☒	☐	☐	☐
Roche	☐	☒	☐	☐
Bristol Myers Squibb	☒	☐	☐	☐
Medtronic	☒	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	*Dr. Alison Wallace*
Position	*Assistant Professor Department of Surgery, Division of Thoracic Surgery and Department of Pathology, Dalhousie University. Thoracic Surgeon QEII HSC, Halifax. NS.*
Date	December 2, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Confli-ct 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**
Merck	☒	☐	☐	☐
Bristol Myers Squibb	☒	☐	☐	☐
AstraZeneca	☒	☐	☐	☐

New or Updated Declaration for Clinician 7	
Name	*Ronald Burkes*
Position	*Medical Oncologist Mount Sinai Hospital*
Date	December 2, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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

Conflict of Interest Declaration for Clinician 8

Name: Dr. Abhenil Mittal
Position: Medical Oncologist, Health Sciences North, Assistant Professor, Northern Ontario School of Medicine
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Gilead	X			
Knight Therapeutics	X			
Janssen	X			
Roche	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 9

Name: Dr. Rosalyn Juergens
Position: Chair, LCC Medical Advisory Committee; Medical Oncologist, Juravinski Cancer Center
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 9

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bristol Myers Squibb	x			
Astra Zeneca		x		
Merck Sharp and Dohme	x			
Roche	x			

Declaration for Clinician 10

Name: Dr. Paul Wheatley-Price
Position: Medical Oncologist, The Ottawa Hospital. Associate Professor, Department of Medicine, University of Ottawa
Date December 2, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 10

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Sanofi	X			
Astra Zeneca	X			
Jazz Pharmaceuticals	X			
Amgen	X			
Janssen	X			
Novartis	X			
Merck	X			
BMS	X			
Roche	X			
EMD Serono	X			
Pfizer	X			
Bayer	X			
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

New or Updated Declaration for Clinician 11

Name	*Vishal Navani*
Position	*Medical Oncologist, University of Calgary*
Date	December 2, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Janssen	☐	☐	☒	☐
Consulting - Novotech Pty, Pfizer, Sanofi, Astra Zeneca, EMD Serono, Oncology Education, Sanofi, Janssen, Roche, MSD, Bristol Meyers Squibb, Takeda	☐	☐	☒	☐
Speaking – Ipsen, Astra Zeneca, MSD, Bristol Meyers Squibb	☐	☐	☒	☐
Research – Astra Zeneca (Inst), Janssen (Inst)			X	
Travel – EMD Serono, Pfizer, Sanofi			X	

Declaration for Clinician 12

Name: Normand Blais
Position: Medical Oncologist, CHUM Cancer Center, Montreal
Date: December 2, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 12

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Abbvie	Advisory Board and Honoraria	☒	☐	☐	☐
Amgen	Advisory Board and Honoraria	☒	☐	☐	☐

Astra Zeneca	Advisory Board and Honoraria	☒	☐	☐	☐
Beigene	Advisory Board and Honoraria	☒	☐	☐	☐
Bristol-Myers Squibb	Advisory Board and Honoraria	☒	☐	☐	☐
EMD Serono	Advisory Board and Honoraria	☒	☐	☐	☐
Merck	Advisory Board and Honoraria	☒	☐	☐	☐
Novartis	Advisory Board and Honoraria	☒	☐	☐	☐
Pfizer	Advisory Board and Honoraria	☒	☐	☐	☐
Roche	Advisory Board and Honoraria	☒	☐	☐	☐
Sanofi	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Research Funding to institution	☐	☐	☐	☒

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 13

Name: Dr Randeep Sangha
Position: Medical Oncologist, Cross Cancer Institute
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 9: Conflict of Interest Declaration for Clinician 13

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 14

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 14: Conflict of Interest Declaration for Clinician 14

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	
Bristol-Myers Squibb	Advisory Board	☒	☐	☐	
Astra Zeneca	Advisory Board and Speaking	☒	☐	☐	☐
Merck	Advisory Board and Speaking	☐	☐	☒	☐
Roche	Advisory Board and Speaking	☐	☒	☐	☐
Takeda	Advisory Board and Speaking	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

New or Updated Declaration for Clinician 15	
Name	*Dr. Geoffrey Liu*
Position	*Medical Oncologist*
Date	December 2, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Pfizer	☐	☒	☐	☐
Novartis	☒	☐	☐	☐
Anheart	☒	☐	☐	☐
Takeda	X			
AstraZeneca		X		
Jazz	X			
Roche	X			
Johnson & Johnson	X			
EMD Seron	X			
Merck	X			

Declaration for Clinician 16

Name: Dr. David Dawe
Position: Medical Oncologist, CancerCare Manitoba
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 8: Conflict of Interest Declaration for Clinician 16

Name of Organization	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AstraZeneca	Advisory boards	☒	☐	☐	☐
Merck	Advisory Boards	☒	☐	☐	☐
AstraZeneca	Research Grant	☐	☐	☒	☐
Boehringer-Ingelheim	Honoraria	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 17

Name: Dr Nicole Bouchard
Position: Respirologist, Sherbrooke University Hospital
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 17

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Astra Zeneca	Advisory Role/Conference	☒	☐	☐	☐
Bristol-Myers Squibb	Advisory Role/Research	☒	☐	☐	☐
Merck	Advisory Role /Research/Conference	☒	☐	☐	☐
Bayer	Advisory Role	☒	☐	☐	☐
Pfizer	Conference/Research	☒	☐	☐	☐

Roche	Advisory Role	☒	☐	☐	☐

Declaration for Clinician 18

Name: Callista Phillips
Position: Medical Oncologist and Clinical Lead, Oncology Clinic, Joseph Brant Hospital
Date: December 2, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 18

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
AstraZeneca	X			
Bayer	X			
Roche	X			

Declaration for Clinician 19

Name: Dr. Mark Vincent
Position: Medical Oncologist, London Regional Cancer Centre
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 19

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
			☐	☐	☐

Declaration for Clinician 20

Name: Dr Jeffrey Rothenstein
Position: Medical Oncologist, Lakeridge Health
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 20

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	x			

Declaration for Clinician 21

Name: Dr Catherine Labbé
Position: Head of Respiratory Medicine Service, Université de Laval
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 12: Conflict of Interest Declaration for Clinician 21

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Amgen	X			
Astra Zeneca		X		
Brystol-Myers Squibb	X			
Jazz Pharmaceuticals	X			
LEO Pharma	X			
Merck	X			
Pfizer	X			
Roche	X			
Sanofi Genzyme	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 22

Name: Dr. Barbara Melosky
Position: Medical Oncologist, BC Cancer
Date: December 2, 2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 7: Conflict of Interest Declaration for Clinician 22

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	Advisory Board	☒	☐	☐	☐
Roche	Advisory Board	☒	☐	☐	☐
Merck	Advisory Board	☒	☐	☐	☐

Declaration for Clinician 23

Name: Lacey Pitre
Position: Medical Oncologist, Systemic Therapy Lead - Northeast Region, CCO/Ontario Health
Date: December 2, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 23

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis Ribbon Program 2018	X			
MERCK Oncology Speaker's honoraria 2017	X			
EMD Serono Speaker's honoraria 2018	X			
MERCK Oncology Speaker's honoraria 2021	X			
Astra Zeneca Speaker's honoraria 2021	X			
Astra Zeneca Speaker's honoraria 2022	X			
Fuse Health Advisory Board 2017	X			
Novartis Advisory Board 2018	X			
Astella's Oncology Advisory Board 2016	X			

* Place an X in the appropriate dollar range cells for each company.

New or Updated Declaration for Clinician 24

Name	*Dr. Susanna Cheng*
Position	*Medical Oncologist, Associate Professor, Sunnybrook Health Sciences Centre, University of Toronto*
Date	December 2, 2024
X	**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**
Merck	X	☐	☐	☐
BMS	X	☐	☐	☐
Janssen	X	☐	☐	☐
Roche	X			