CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

amivantamab (Rybrevant)

Janssen Inc.

Indication: Rybrevant in combination with carboplatin and pemetrexed for the treatment of 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, whose disease has progressed on or after treatment with osimertinib.

December 2, 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH 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.

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Patient Group Input

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: amivantamab (Rybrevant)

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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), 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 and their caregivers. They were collected through virtual interviews directly with the patients, or taken from previous submissions to CADTH. All interviews were conducted in October 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. It should be kept in mind that there were limited sites in Canada that were involved in the MARIPOSA-2 clinical trial, so we hope that pERC keeps this into consideration. Nonetheless, we were able to speak to 2 patients who have direct experience in the MARIPOSA-2 trial, and 3 other patients on other trials involving amivantamab. RG, NB, and LS's interviews were conducted in October-November 2024, while JQ and DK's experiences were taken from previous patient input submissions to CADTH by Lung Cancer Canada – JQ from CHRYSALIS (PC0289-000) and DK from PAPILLON (PC0376-000). 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
RG	Patient	M	Mid-70s	Stage 3 NSCLC	December 2021	Vancouver Island, BC	Telephone Interview
NB	Patient	F	42	Stage 4 NSCLC	January 2022	Calgary, AB	Telephone Interview
LS	Caregiver	F	48	Stage 3 NSCLC (now stage 4)	2017	Ottawa, ON	Telephone Interview
JQ	Patient	M	66	Stage 4 EGFR Exon 19 NSCLC	July 2014	Ottawa, ON	Telephone Interview
DK	Patient	M	70s	Stage 4 EGFR Exon 21 L858R	July 2019	Calgary, AB	Telephone Interview

3. Disease Experience

The December holidays is typically a time of celebration and gathering for many families, but for both **RG** and **NB,** receiving a lung cancer diagnosis on Christmas Eve and New Year's Eve respectively was not at all expected. Earlier in December, **RG'**s lung cancer was discovered incidentally when he had an X-ray done on his left shoulder in preparation for a replacement that he was scheduled to have, and was shocked when further CAT scans showed lesions in his left lower lobe and further spread to his lymph nodes on the right, as he was completely asymptomatic. Prior to his diagnosis, RG had always been a healthy active individual with no other comorbidities, going to exercise classes five times per week and enjoyed spending most of his days outdoors managing his 7.5-acre property in rural Vancouver

Island. He recalls he was totally shocked at the stage III diagnosis and couldn't believe it had spread so far without any symptoms, but after a long career as a family doctor, he knew this was expected for lung cancer. He started first-line treatment in February 2022 with osimertinib, which was only successful for 2 months before he enrolled into the MARIPOSA-2 trial for treatment with amivantamab and chemotherapy, which has continued to be on ever since.

NB 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 had become short of breath when walking and pushing the baby stroller, needing to catch her breath every couple meters. She was sent for an X-ray on New Year's Eve 2021 planning to head straight to a family party afterwards, but 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 in 2019. She started first-line therapy with osimertinib which only worked for 3 months, then enrolled into the MARIPOSA-2 trial, which she is still on today nearly 2.5 years later.

In early 2014, then 56-year-old **JQ** 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 JQ with stage 4 NSCLC. After two decades working as a physician in the army, he was faced with a number of patients with serious conditions, but when it became personal, it was hard to digest for not only himself but also his family. JQ recalls, *"When I was first given a diagnosis with stage 4 lung cancer, 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"*. JQ 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 JQ had done very well ever since at the time of his interview in May 2022.

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 for EGFR Exon 19 and L858R mutations via MARIPOSA-2. The biggest hurdle for patients with these mutations is the resistance mutation of L858R that eventually develops after treatment over an extended period with osimertinib, leaving patients with very limited options aside from standard chemotherapy. LCC, CCSN and LHF strongly urge the CDA for the approval of amivantamab in this indication as it would provide additional treatment options that are desperately-needed for patients in this setting, who currently face a poor prognosis of only months with currently available treatments.

4. Experiences With Currently Available Treatments

Both **NB** and **RG** are on the MARIPOSA-2 trial, which requires patients to have been on osimertinib as a prior line of therapy to be eligible for participation. While not on the specific MARIPOSA-2 trial, **JQ** and **LS** both also have experience on osimertinib prior to treatment with amivantamab.

After diagnosis, **RG** had first line treatment with osimertinib starting in February 2022, but this came with many side effects that were hard to manage, and ultimately only was successful for two months before he progressed further. At first, he had no side effects but over the course of two weeks, he started experiencing severe nausea, diarrhea, dizziness and muscle weakness. His oncologist then halved the dose, which resolved the nausea for 18 days but the other side effects, particularly the nausea and weakness, remained. RG says these side effects were incredibly limiting to his day-to-day life, where he couldn't leave the house much as many of his diarrhea episodes would come on very suddenly, almost to the point where he wouldn't make it to the bathroom in time. if he wasn't at home. He couldn't

maintain a healthy lifestyle and his mental health was poor. When his scans in early May showed the tumour had grown to the clavicle area, they made the decision to terminate osimertinib. He was then initially offered standard treatment with chemotherapy (carboplatin and pemetrexed), but his oncologist explained the option of the clinical trial as well, which RG ultimately pursued since his background in medicine knew the chemotherapy wouldn't curtail the growth of the cancer.

Similarly, **NB** 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, the 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 **JQ** 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 while on this therapy was diarrhea, but it was tolerable and did not have much impact on his quality of life. 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 JQ 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 qualified for and started in January 2021.

While living in China, **LS**'s 48-year-old mother, who was otherwise healthy and active, was diagnosed in 2017 with early-stage lung cancer during a routine check-up. She had two surgeries in China, first a lobectomy, but her cancer continued to spread quickly and underwent a 2nd surgery to remove lymph nodes in her underarm. When she moved to Canada in 2019, further genetic testing was done which confirmed the EGFR mutation and she started on osimertinib, which worked well for about 1 year until the cancer spread to numerous areas above her heart, lymph nodes, and spine. LS recalls she didn't have virtually any side effects on Tagrisso – no skin reactions, diarrhea, and her day to day remained pretty normal. However, by the time her disease spread, she was in a lot of pain, so she had chemotherapy and radiation, which came with side effects like low energy levels, hair loss, and nausea, but both treatments didn't help much. She then started on the PALOMA-3 clinical trial in September 2023.

DK 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

There is a serious unmet need for an additional treatment option for patients who have progressed on osimertinib that not only treats their disease successfully and delays further progression, but also gives patients their livelihoods back, 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, patients who were interviewed 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)
RG	December 2021	MARIPOSA-2 clinical trial	Amivantamab + pemetrexed (with carboplatin for cycles 1-4)	June 2022 - present	2nd line	Yes
NB	January 2022	MARIPOSA-2 clinical trial	Amivantamab + Lazertinib	July 2022 - present	2nd line	Yes
LS	2017	PALOMA-3 clinical trial	IV amivantamab	Sept 2023 – Oct 2024	2nd line	No
JQ	July 2014	Clinical Trial	Monotherapy	January 2021 - April 2024 (or earlier)	3rd line	Deceased
DK	July 2019	Manufacturer's Compassionate Access	Monotherapy	June 2023 - Present	3rd line +	Yes, as of September 2024

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

By the end of the first 4 cycles with triplet therapy, **RG**'s disease showed a dramatic reduction in size of his primary lesion by half – down from 4cm to 2cm. Afterwards, he stayed on amivantamab and pemetrexed for 1.5 years, when scans continued to be stable, with no spread to his brain or lymph nodes. At the time of his interview in Oct 2024, his most recent scan two weeks prior showed there was still no change in his tumours, which is promising.

Immediately prior to starting the MARIPOSA-2 trial, **NB's** 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 like RG, goes to the cancer center for the amivantamab infusions every 3 weeks.

By the time **JQ** started this 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 JQ had passed away in April 2024.

DK 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 have been stable, which is promising for him. DK 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.

LS says his mother's CT scans while she was on the PALOMA-3 trial on amivantamab showed a little bit of shrinkage at the beginning, but has primarily remained stable for the last year.

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

When **RG** first started the triplet therapy (amivantamab, pemetrexed, and carboplatin) for the first 4 cycles, his initial side effects included mouth ulcers (which he says was the one of the worst side effects), loss of taste, dizziness, significant skin issues, constipation, tinnitus, and overall weakness (muscle weakness and fatigue). However, his dosage of amivantamab was then reduced in half which helped the side effects become milder compared to the first cycle. RG also struggled with low energy levels for the first year of treatment and wasn't happy with where he was. In early 2024, he saw an endocrinologist, who confirmed his testosterone levels were very low, so RG was prescribed to take testosterone by injection every two weeks, and he felt much better rather quickly; "this was the best I've been feeling for a long time, especially since I started the trial". Skin issues were a significant problem for RG at the very beginning of amivantamab, but after seeing a dermatologist who prescribed Epuris (isotretinoin), it made a "phenomenal difference" to his skin and dried up his scalp, and dramatically reduced the rashes on his face, chest, and shoulder. Hypoalbuminemia is another side effect that RG noted is the primary cause of his current muscle weakness in his legs, but is manageable day-to-day with lots of breaks in between. As of October 2024, RG says the two major side effects he experiences now are the skin issues and edema.

NB 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, NB 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, NB 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, NB 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".*

Similarly, **LS**'s mother also dealt with the dryness and tingling/numbness in her fingers and toes, bleeding and 3-4 ingrown toenails which had to be removed, and infections around her toenails. She still can walk but couldn't really feel her feet very well, however ever since she stopped the amivantamab treatment, these have improved. At the beginning of the trial, she also developed a blood clot in the lung area because she didn't receive blood thinners, but this was immediately resolved and did not progress further. Additionally, she has grown facial hair (upper lip/mustache and eyebrows) in which hair removal cream helps, and developed some rashes at the beginning of the trial around her eye, scalp, and forehead, but these only showed up once and have resolved since.

Patients were able to return to a good quality of life, enjoying their hobbies, being active, and spending time with loved ones.

Prior to diagnosis, **RG** used to be able to walk an easy 2 miles, but when he first started the clinical trial with amivantamab, he could barely walk half a mile, or a few laps around the track on his property. When he started cycle 5 without carboplatin, he slowly started regaining his energy and could walk 4 laps around the track. Although he noted one of the side effects, hypoalbuminemia, causes the muscle weakness he struggles with in his legs, it is still manageable and he can get up and continue to go for his 1.5-mile walks, and work on the property in two-hour increments with rest in between. He has no issues going grocery shopping, cleaning and vacuuming the house, cooking, and doing everyday chores. RG hadn't gone swimming ever since he started the trial, but over the summer recently he swam for the first time in the lake while on vacation, which he says made him happy since he loves being in the water.

Being diagnosed with stage IV lung cancer less than a year after having her second child has really changed **NB**'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".* NB 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 about 2.5 years ago 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, NB 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.

The primary reason **LS** terminated treatment with the amivantamab was due to the impact on her energy levels and quality of life. Even while on prior treatments, she would walk a lot, but during amivantamab, her energy significantly diminished where she'd get shortness of breath even just walking to the washroom at home. She was still able to care for herself and perform basic activities of daily living, but at one point she had no interest in leaving the house, she'd just eat and go back to bed, and had to force herself to perform chores around the house like cleaning and bathing. Ever since she stopped treatment in October 2024, she has slowly been resting and recovering from the trial effects, and has been regaining her energy to leave the house even for grocery shopping or short walks in the neighborhood. She says her cancer "doesn't bother her nowadays".

Most patients agreed that they would strongly prefer their experience on amivantamab over previous therapies.

One of the biggest highlights that **RG** was able to do while on the trial was travel to Ireland to visit friends and family, which he hadn't done in nearly a decade, and it brought him so much happiness and joy. Being able to travel internationally again. He has a great support system through his wife, 4 children and 11 grandchildren, and will be 60 years married in July 2025, so he's hoping to do more travelling with his wife next summer when possible. He says although the skin side effects were a nuisance, it's no longer impacting him mentally to see people. He continues to meet friends for coffee once a week, spending time with his grandchildren, and enjoying his retirement. RG says the trial has given him so much hope and is hoping it'll continue to be successful until the trial ends in 2026.

For **NB**, 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 + amivantamab combination arm, and says the ease of Lazertinib is similar to when she was on osimertinib. NB 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."

Although **LS** decided to stop treatment with amivantamab because of the side effects, she agreed that for the purposes of treating the cancer and keeping her disease from worsening, it did its job so they'd take it. They ranked it at about a 7 or 8 out of 10 in terms of preferring amivantamab over previous treatments, because the drug controlled her disease. However, if there were any other choices available to her, they would prefer that over amivantamab.

While **JQ** was on Osimertinib for nearly 5 years progression-free, it was hard to accept when he had progressed afterwards in late 2020. JQ mentions that amivantamab was a genuine lifesaver for himself and other patients who have no other option left.

DK 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, DK 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 while on afatinib 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 DK has no issues helping out with chores around the house whenever he can.

7. Companion Diagnostic Test

Patients with EGFR Exon 19 or 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?

N/A

Appendix: Patient Group Conflict of Interest Declaration

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.

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

No

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

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 Reimbursement Review
Clinician Group Input Template
CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0393-000

Generic Drug Name (Brand Name): Amivantamab (Rybrevant)

Indication: Rybrevant in combination with carboplatin and pemetrexed for the treatment of 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, whose disease has progressed on or after treatment with osimertinib

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

Current treatment of patients with advanced non-small lung cancer with common EGFR mutations (exon 19del and exon L858R substitution) after progression on osimertinib includes platinum pemetrexed chemotherapy followed by pemetrexed maintenance chemotherapy for those without contraindications.

Palliative chemotherapy showed median PFS of 5-6 months and median OS of 12-14 months. A regimen combining chemotherapy and immune therapy (platinum doublet chemotherapy + bevacizumab + atezolizumab) post osimertinib progression was compared to platinum chemotherapy alone and showed modest PFS benefit, no OS benefit and is not a funded regimen in Ontario in the second line setting.

Patients not eligible for platinum doublet treatment will be managed with symptomatic care alone. Ultimately all patients will progress and die of their disease.

There are no other targeted therapies available at this time post progression on osimertinib.

Some patients may undergo repeat biopsy and molecular testing. Those patients with a new molecular abnormality may be candidates for participation in a clinical trial. A small proportion of patients' cancers may transform into small cell lung cancer and require alternate 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.

Despite initial efficacy, nearly all patients treated with osimertinib develop resistance. Mechanisms of resistance to osimertinib are diverse with the most common being alterations in the MET gene (e.g. up to 51% by FISH) and EGFR pathways. There is no targeted therapy currently available post progression on osimertinib that targets mechanism of resistance.

Current second line treatment with platinum chemotherapy is less effective with shorter PFS. In particular many patients have disease progression in the brain where chemotherapy has lower response and disease control.

5. Place in Therapy

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

Amivantamab is an EGFR-MET bispecific antibody with immune cell-directing activity. By binding extracellularly, amivantamab bypasses intracellular mutations, and its bispecific nature addresses MET as a mechanism of resistance. Clinically, amivantamab has shown activity against a wide range of activating and resistance mutations in EGFR-mutated NSCLC and in patients with MET alterations. Amivantamab in combination with platinum based chemotherapy could address osimertinib-based resistance and would be used as second line treatment post progression on osimertinib. In the MARIPOSA2 trial there was significant PFS benefit including intracranial PFS benefit. OS data is immature.

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?

Best suited for treatment: Patients with sensitizing EGFR mutated (Ex19del or L858R) advanced non-small cell lung cancer after progression on osimertinib, with ECOG 0-2 and no contraindications to chemotherapy, including patients with treated or untreated brain metastases.

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?

Clinical and radiological assessments. Patients are generally assessed for clinical response and tolerability of treatment before each cycle of systemic treatment. Radiologic assessment is performed roughly every 3 months while on treatment. A clinical meaningful response is improvement in symptoms/quality of life, delay in progression and improvement in overall survival.

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

Patients generally continue treatment until disease progression or intolerable side effects occur.

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]?

This is an outpatient treatment under the supervision of a Medical Oncologist.

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: 15-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

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				

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

Declaration for Clinician 2

Name: Dr. Mihaela Mates

Position: Member, OH-CCO Lung DAC

Date: 22-Oct-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

* 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: 14-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			

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

Declaration for Clinician 4

Name: Dr. Michela Febbraro

Position: Member, OH-CCO Lung DAC

Date: 14-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. Andrew Robinson

Position: Member, OH-CCO Lung DAC

Date: 14-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.

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0393-000

Generic Drug Name (Brand Name): Amivantamab (Rybrevant)

Indication: Rybrevant in combination with carboplatin and pemetrexed for the treatment of 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, whose disease has progressed on or after treatment with Osimertinib.

Name of Clinician Group: Lung Cancer Canada – Medical Advisory Committee

Author of Submission: Dr. David Dawe (lead), Dr. Abhenil Mittal, Dr. Rosalyn Juergens, Dr. Shantanu Banerji, Dr. Vishal Navani, Dr. Geoffrey Liu, Dr. Kevin Jao, Dr. Ron Burkes, Dr. Jeffrey Rothenstein, Dr. Normand Blais, Dr. Shaqil Kassam, Dr. David Stewart, Dr. Nicolas Meti, Dr. Quincy Chu, Dr. Randeep Sangha, Dr. Catherine Labbé, Dr. Stephanie Snow, Dr. Kirstin Perdrizet, Dr. Sunil Yadav

1. About Your Clinician Group

Lung Cancer Canada (LCC) is a national charity committed to increasing awareness about lung cancer, providing support and education to lung cancer patients and their families, supporting lung cancer research, and advocating 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 consists of clinicians and key opinion leaders in the field of lung cancer across the country.

Homepage | Lung Cancer Canada

2. Information Gathering

The information provided in this submission is from publicly available sources, primarily published manuscripts and conference presentations, together with clinical experience of members from the MAC. This Submission is independent of the manufacturer (Johnson & Johnson/Janssen).

3. Current Treatments and Treatment Goals

In Canada, lung cancer is the most commonly diagnosed invasive cancer and, by far, the leading cause of cancer death[1]. Non-small cell lung cancer (NSCLC) accounts for approximately 88% of lung cancer diagnoses and at diagnosis, approximately half of NSCLC patients have incurable, stage IV disease[2]. Surgery does not play a significant role in the management of stage IV NSCLC and radiotherapy is primarily provided for symptom control, though there is growing evidence for its use in patients with either oligo-metastatic or oligo-progressing disease[3,4]. The primary treatment for incurable NSCLC is systemic therapy, with the aim of extending life and delaying worsening of quality of life. In the last 15 years, there has been a dramatic increase in our understanding of lung cancer biology and improvements in available treatment[5]. The initial shift in biological understanding was the discovery of driver

mutations, the first and most commonly targetable with systemic therapy being the epidermal growth factor receptor (EGFR)[6]. The two most commonly found EGFR mutations are an exon 19 deletion and an L858 substitution mutation. EGFR mutations are found in approximately 10-15% of non-squamous NSCLC, with the highest rates in the adenocarcinoma subtype[5]. EGFR mutations can be found in any patient with non-squamous NSCLC, but are most common in patients dealing with NSCLC who are younger, East Asian, female, and non-smokers[5]. Driver mutations can be targeted using tyrosine kinase inhibitors (TKIs), which have become the standard first line treatment option for EGFR mutated NSCLC.

A third generation, EGFR TKI, osimertinib, is the most commonly used first line treatment option for EGFR mutated NSCLC. It results in an overall response rate of 80%, median progression-free survival (PFS) of 18.9 months, and a median overall survival (OS) of 38.6 months[7,8]. Progression of the cancer while receiving this drug may be driven by the development of another driver/resistance mutation, transformation to small cell lung cancer, and is unknown in 30-40% of patients[9–12]. The most common targetable resistance mechanisms are secondary EGFR and MET alterations, occurring in 25-50% of tumour resistance. If progression is only in a small number of sites (oligo-progression), radiotherapy is often provided and osimertinib is continued until there is further confirmed progression. At the point of broader progression, some jurisdictions in Canada are not able to access either repeat biopsy in a timely enough manner and/or are unable to access funded circulating tumour DNA testing to evaluate targetable resistance mechanism. Therefore, when a patient's cancer progresses more substantially than oligo-progression on osimertinib in Canada, the primary standard of care is a platinum-doublet chemotherapy regimen, usually cisplatin or carboplatin plus pemetrexed. In a real-world cohort, this regimen led to an objective response in 27.6% of patients and a median PFS of 7.4 months[13,14].

The options for first line treatment in incurable EGFR mutated NSCLC are likely to expand in the near future due to the results of the FLAURA2 and MARIPOSA trials[8,15]. FLAURA2 tested the potential advantage of giving osimertinib plus platinum-pemetrexed simultaneously[8]. The trial found improvements in disease control, which may translate into improvements in OS. However, the trial does not yet show statistically significant improvements in OS and there is concern that adding chemotherapy up front increases toxicity and the number of visits patients must attend in the cancer centre for ongoing intravenous therapy. There are similar concerns for the MARIPOSA trial, which assessed amivantamab (an EGFR-MET bispecific antibody) added to lazertinib (an EGFR TKI similar to osimertinib)[15]. This trial also showed better PFS when compared to osimertinib, but has not yet demonstrated a statistically significant improvement in OS, increases toxicity, and requires ongoing visits for intravenous therapy. Therefore, due to the additional visits and toxicity seen with these new regimens compared to osimertinib alone, even if they are adopted more permanently into our standard of care, a significant proportion of patients will likely continue to receive osimertinib alone up front.

The most important goals in the setting of progression on osimertinib of EGFR mutated NSCLC are to maximize quality of life and prolong life. Secondary goals are to minimize toxicity, and prolong control of disease.

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 current standard of care of platinum-pemetrexed after progression on osimertinib creates a significant unmet need because most patients do not respond, all become refractory to this treatment, , and even chemotherapy alone has a roughly 65% risk of grade 3+ adverse events[16]. Patients dealing with EGFR mutated NSCLC need options that are more effective and where benefit lasts longer than seen with chemotherapy alone.

MARIPOSA2 was a large, multinational randomized trial of 657 patients whose EGFR mutated (exon 19 deletion or L858R mutation) lung cancer had progressed on osimertinib, comparing three arms – chemotherapy alone (n=263), chemotherapy plus amivantamab (n=131), and chemotherapy plus amivantamab plus lazertinib (n=263)[17]. Amivantamab is an EGFR-MET bispecific antibody with immune cell-directing activity. It is active against a wide range of EGFR and MET alterations. Lazertinib is a highly selective, 3rd generation EGFR TKI that penetrates the central nervous system. Amivantamab was administered intravenously at 1400 mg (1750 mg for body weight ≥80 kg) weekly for the first 4 weeks, and then 1750 mg (2100 mg for body weight ≥80 kg) every 3 weeks starting at cycle 3 (week 7). Lazertinib was administered orally at 240 mg daily. Chemotherapy was administered intravenously at the beginning of every cycle, with pemetrexed at 500 mg/m2 administered every cycle and carboplatin at area under the curve 5 for the first four cycles[17]. Amivantamab, lazertinib, and pemetrexed treatments were to be continued until disease progression or lack of clinical benefit as deemed by the investigator.

The dual primary endpoints evaluated was PFS by blinded independent central review (BICR) for amivantamab + chemotherapy versus chemotherapy and amivatamab + lazertinib + chemotherapy versus chemotherapy. The median PFS by BICR was 6.3 months (95% CI 5.6-8.4 months) for patients treated with amivantamab-chemotherapy, 8.3 months (95% CI 6.8-9.1 months) with amivantamab-lazertinib-chemotherapy, and 4.2 months (95% CI 4.0-4.4 months) with chemotherapy. PFS was significantly longer in the amivantamab-chemotherapy arm compared to the chemotherapy arm (HR for disease progression or death 0.48, 95% CI 0.36-0.64, P < 0.001). The benefit in PFS was seen across subgroup analyses of age, sex, race, weight, ECOG, smoking history, history of brain metastases, and for both types of EGFR mutation. The objective response rate was also higher with amivantamab-chemotherapy (64%) versus chemotherapy (36%). For both PFS and response rate, adding lazertinib did not appear to improve outcomes. OS has also been reported, with the most mature analysis reported at ESMO 2024[18]. At a median follow-up of 18.1 months, the median OS for amivantamab-chemotherapy was 17.7 months versus 15.3 months with chemotherapy alone (HR 0.73, 95% CI 0.54-0.99, P=0.039). A statistical analysis was not done on specific time points, but 12-month OS was 70% versus 63% and 18-month OS 50% versus 40% for amivantamab-chemotherapy versus chemotherapy. Similar trends were seen for time to treatment discontinuation, time to symptomatic progression, time to subsequent treatment, and PFS after first subsequent therapy (PFS2).

It should be noted that treatment duration for amivantamab-chemotherapy was 6.3 months versus 3.7 months with chemotherapy alone, allowing more time for adverse events to occur. Reporting of treatment-related toxicity shows grade 3+ adverse events (measured using National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0) were experienced by 72% of patients with amivantamab-chemotherapy versus 48% of patients with chemotherapy alone[17]. Adding amivantamab appeared to increase the risk of grade 3+ neutropenia (45% v 21%), infusion-related reaction (5% v 0%), rash (10% v 0%), but similar rates for many other toxicities. Of special interest, any grade of infusion-related reaction occurred in 58% of patients with amivantamab-chemotherapy versus 0.4% with chemotherapy, the risk of any grade thromboembolism was 10% versus 5%, and pneumonitis risk was 2% vs 0%. There have been attempts to reduce the risk of infusion-related reactions and venous thromboembolism by administering amivantamab subcutaneously[19]. In a trial assessing Lazertinib combined with either subcutaneous or intravenous amivantamab, subcutaneous administration reduced the risk of infusion-related reactions from 66% to 13% and the risk of venous thromboembolism from 14% to 9%, with no negative impact on PFS or OS[19]. Subcutaneous administration may become the standard option for amivantamab.

From a patient reported outcomes perspective, using the EORTC-QLQ-C30 (European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire) at 6 months, a commonly used quality of life measure, amivantamab-chemotherapy resulted in a higher proportion of patients reporting stable or improving global health status (49% vs 26%, P=0.0001) and physical functioning (45% vs 29%, P=0.006) when compared to chemotherapy alone[20]. The amivantamab-chemotherapy group also experienced a longer time to sustained deterioration in total symptom score of median 11.6 months versus 8.5 months with chemotherapy (HR 0.62, 95% CI 0.43-0.88, P=0.0057) by NSCLC-SAQ (Non-Small Cell Lung Cancer Symptom Assessment Questionnaire).

Therefore, the analyses for MARIPOSA2 to date show statistically significant improvements in disease control, quality of life measures, and a trend towards improved OS. While adding amivantamab to standard of care chemotherapy increased the risk of treatment-related adverse events, that increase does not appear to have translated into meaningful reductions in quality of life, since those measures were equal to superior with the addition of amivantamab.

5. Place in Therapy

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

The regimen of amivantamab-chemotherapy investigated in MARIPOSA2 is an iteration on the existing standard of care chemotherapy. This regimen would, therefore, replace chemotherapy with platinum-doublet after progression on osimertinib of EGFR mutated NSCLC. When patients progress on amivantamab-chemotherapy, the most frequent next line of treatment would be either a clinical trial, docetaxel, or possibly datopotamab deruxtecan (if approved or available through an access program).

As alluded to above, adding amivantamab to chemotherapy helps target secondary EGFR and MET alterations that develop during treatment with osimertinib in 25-50% of resistance mechanisms[9–12]. The improvements seen in median PFS, multiple surrogate survival endpoints, and the trend to improved OS all suggest that targeting these mechanisms and adding an immune cell-directing mechanism component are intervening in the underlying disease process. Through targeting these processes, the MARIPOSA2 regimen shifts the current treatment paradigm of chemotherapy alone after EGFR mutated NSCLC progresses on osimertinib to an approach that continues to include targeted therapy, while also applying the benefits that chemotherapy provides. The MARIPOSA2

trial data only provides evidence applicable to patients who have incurable, EGFR mutated NSCLC that has progressed on osimertinib.

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?

The evidence from MARIPOSA2 appears to apply to any patient dealing with incurable, NSCLC with a common EGFR mutation (exon 19 deletion or L858R mutation) that has experienced cancer progression on osimertinib. Patients would need to be fit since there is a significant risk of toxicity with amivantamab-chemotherapy and the trial was limited to patients with ECOG performance status 0-1. All evaluated subgroups appeared to benefit from the addition of amivantamab. Therefore, there are no other patient or disease characteristics that would limit provision of this treatment.

Patients eligible for this regimen would be identified through previous EGFR mutation testing (already required for receipt of osimertinib), previous receipt of osimertinib to treat the cancer, and evidence of progression on osimertinib. Evidence of progression would typically be through growth of disease identified via serial computed tomography scans. There is no new companion diagnostic required since the companion diagnostic of EGFR mutation testing is already required to identify patients eligible for osimertinib. There are also no test or characteristic that can identify those most likely to benefit from the addition of amivantamab to standard of care chemotherapy.

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-chemotherapy, patients will need to be seen more frequently for adverse event and tolerance assessments. 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 evaluated before each cycle with blood work and clinical evaluation, as well as 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. This approach to evaluation is essentially the same as how physicians evaluate any intravenous regimen.

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

Treatment with amivantamab and chemotherapy 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]?

The appropriate setting for amivantamab and chemotherapy 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. The risk of infusion-related reactions with the current mode of administration is high, but is manageable and may improve in future with consideration of subcutaneous administration.

6. Additional Information

References

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2. Canadian Cancer Statistics Advisory Committee. *Canadian Cancer Statistics: A 2020 Special Report on Lung Cancer*. (2020).

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16. Garassino, M. C. *et al.* Pembrolizumab Plus Pemetrexed and Platinum in Nonsquamous Non-Small-Cell Lung Cancer: 5-Year Outcomes From the Phase 3 KEYNOTE-189 Study. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **41**, 1992–1998 (2023).

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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.

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

   No

5. 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

6. 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. 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 1: Conflict of Interest Declaration for Clinician 1

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 2

Name: 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 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**
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 3

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 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
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 4

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 4

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

	$5,000	$10,000		
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.

New or Updated Declaration for Clinician 5	
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 6

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 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**
Gilead	X			
Knight Therapeutics	X			
Janssen	X			
Roche	X			

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

Declaration for Clinician 7

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 7

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			

New or Updated Declaration for Clinician 8	
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 9

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 9

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 10

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 10: 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

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

Declaration for Clinician 11

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 11: Conflict of Interest Declaration for Clinician 11

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 12	
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 13

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 13: Conflict of Interest Declaration for Clinician 13

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

Declaration for Clinician 14

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 14

	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 15

Name: Dr. Kirsten Perdrizet

Position: Medical Oncologist, Princess Margaret 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 5: Conflict of Interest Declaration for Clinician 15

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
		☐	☐	☐	☐
		☐	☐	☐	☐

Conflict of Interest Declaration for Clinician 16

Name: Dr. Kevin Jao

Position: Medical Oncologist, Hôpital Sacré-Cœur, Montreal; Co-Chair, LCC Medical Advisory Committee

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.

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
Bristol-Myers Squibb	Advisory Role	☒	☐	☐	☐

New or Updated Declaration for Clinician 17	
Name	*David J. Stewart*
Position	Professor of Medicine, University of Ottawa and The Ottawa 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
Merck Canada 2021, 2023	☒	☐	☐	☐
AstraZeneca Canada 2021, 2023	☒	☐	☐	☐
Abbvie Canada 2021, 2022, 2023	☒	☐	☐	☐
Canadian Agency for Drugs and Technologies in Health 2021	x			
Amgen Canada 2022	x			

Declaration for Clinician 18

Name	*Shantanu Banerji*
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.

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	☐	☒	☐	☐
Roche	☐	☒	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Declaration for Clinician 19

Name: Nicholas Meti
Position: Medical Oncologist, St Mary's Hospital & Lakeshore General Hospital (CIUSSS ODIM); Assistant Professor, McGill University
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	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000