## CADTH REIMBURSEMENT REVIEW

# Patient and Clinician Group Input

**amivantamab (Rybrevant)**

(Janssen Inc.)

**Indication:** Rybrevant in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) exon 20 insertion mutations.

**July 8, 2024**

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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CADTH

# Patient Group Input

**Name of Drug:** Amivantamab (Rybrevant)

**Indication:** Rybrevant in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) exon 20 insertion mutations.

**Name of Patient Group:** Joint Submission by Lung Cancer Canada (lead), Canadian Cancer Survivor Network, and Lung Health Foundation

**Author of Submission:** Winky Yau – Lung Cancer Canada (lead), Lindsay Timm - Canadian Cancer Survivor Network and Riley Sanders – Lung Health Foundation

## 1. About Your Patient Group

**This patient input submission is jointly submitted by Lung Cancer Canada (LCC), the 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 9 non-small cell lung cancer patients, conducted mainly through virtual interviews by LCC and CCSN. 7 patients are Canadian, 1 from the United States, and 1 from the United Kingdom. All data was collected between May-July 2024.

1 patient, SP, was interviewed by LCC in April 2022 for the previous amivantamab patient input submission (Project # PC0289-000) as she had experience on the PAPILLON trial, but when contacted for an update, LCC was notified she had unfortunately passed away in February 2024.

**Demographic Data:**

EGFR-positive non-small cell lung cancer (NSCLC) is a relatively common mutation; however, exon 20 insertion mutations as per this indication are very rare within this biomarker subset, making up between 0.1 – 4% of all NSCLC cases. All but 1 patient interviewed for this submission are positive for the EGFR exon 20 mutation, and 3 patients accessed

amivantamab via the PAPILLON clinical trial in Canada. Full demographic data is summarized in the chart below, and specific treatment experience can be found in section 6.

| Name | Gender | Patient/Caregiver | Age | Diagnosis | Diagnosis Date | Location | Source |
|---|---|---|---|---|---|---|---|
| LC | M | Patient | 57 | Stage 4 EGFR Exon 20 NSCLC | June 2020 | Canada (BC) | Video Interview |
| IN | F | Patient | 66 | Stage 4 EGFR Exon 20 NSCLC | January 2022 | Canada (ON) | Phone Interview |
| VE | F | Patient | 70s | Stage 1 in 2017, now stage 4 EGFR Exon 20 | 2017, progression in 2021 | Canada (ON) | Phone Interview |
| DK | M | Patient | 70s | Stage 4 EGFR Exon 21 L858R | July 2019 | Canada (AB) | Phone Interview |
| SP | F | Patient | 65 | Stage 4 EGFR Exon 20 | October 2021 | Canada (ON) | Phone Interview |
| KL | F | Patient | 58-60 | Stage 4 EGFR Exon 20 | November 2022 | Canada (ON) | Video Interview |
| JZ | M | Patient | 50s | Stage 4 EGFR Exon 20 | May 2022 | Canada (ON) | Phone Interview |
| JG | F | Patient | 40-50s | Stage 4 EGFR Exon 20 | April 2022 | USA (Kansas) | Video Interview |
| SJ | M | Patient | Unknown | EGFR Exon 20 | Unknown | United Kingdom | Environmental Scan |

## 3. Disease Experience

64-year-old **IN** 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. IN was shocked by the diagnosis as she had no symptoms of being unwell when she was diagnosed; she never felt unusually tired, had no problems breathing, her lungs and heart were clear, and the persistent cough was the only indication that led to the unexpected diagnosis. IN recalls in her interview that the first physician she saw was a radiologist, who mentioned her prognosis without treatment would be about 6 months. 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. IN was offered to switch to treatment with amivantamab monotherapy (no chemotherapy) in May, which she recalls was a "game changer", and has remained on it ever since.

**JG** had always been very active throughout her life, played numerous different sports each week and worked out nearly every day. One day in April 2022, the sudden onset of severe back and chest pain brought her to the hospital as she thought she'd been having a heart attack, but instead, was shocked to hear she had stage 4 lung cancer. Like IN, JG had no symptoms of the disease or any indication she'd been unwell, but further testing showed she had numerous tiny lesions

in her chest across both lungs, and was positive for the EGFR Exon 20 mutation. She had first-line therapy with pembrolizumab in combination with chemotherapy for about 1.5 years until progression, then started second-line amivantamab monotherapy treatment in February 2024, and has remained on it ever since. JG says that she has been "incredibly grateful" her treatments have allowed her to maintain an excellent quality of life, and even continues to play tennis and pickleball each week throughout treatment.

Lung cancer is the most commonly diagnosed type of cancer in Canada, with an estimated 32,100 new cases in 2024. Non-small cell lung cancer (NSCLC) represents 85% of these cases, and mutations in the epidermal growth factor receptor (EGFR) gene are among the most common targetable genomic drivers of NSCLC. The most common subsets of EGFR mutations include exon 19 deletion and exon 21 L858R mutations, while EGFR exon 20 mutations are much less common, with a frequency of roughly 0.1 - 4% in NSCLC. Patients with Exon 20 mutations face a unique challenge as the mutation is insensitive to conventional TKIs and thus, face a poorer prognosis and necessitating different treatment options. In Canada, chemotherapy remains the current standard of care for advanced NSCLC patients with this mutation, but has been well-documented to come with toxic side effects and limited long-term success. Without approved targeted treatment options for this patient population, there is an urgent unmet need for novel treatment options for patients with the EGFR-positive exon 20 non-small cell lung cancer.

Amivantamab is a therapy used to treat NSCLC for EGFR Exon 20 mutations and has shown promising results in efficacy and progression-free survival through the CHRYSALIS and MARIPOSA studies, and now in combination with chemotherapy with the most recent phase 3 PAPILLON clinical trial. The available targeted treatment options for patients with this uncommon EGFR subtype are limited, and patients deserve treatment options that are effective beyond the current standard of care that is specific to their mutation. LCC, CCSN and LHF strongly encourage the CDA to take this into consideration as it would lead the pathway to new developments, new treatments, improvements in accessibility, and better affordability for lung cancer patients across the country.

## 4. Experiences With Currently Available Treatments

**Chemotherapy:**

The current standard of care for patients with NSCLC driven by EGFR exon 20 mutations remains platinum doublet chemotherapy followed by single agent docetaxel. Chemotherapy has been a long-standing and well-documented standard of care for lung cancer patients and has seen some benefits. However, it is limited as a viable long-term treatment option due to its nature as a systemic treatment with harsh and toxic side effects, which often creates additional burden on patients, leading to decreased functionality, poorer quality of life, and increased dependence on caregivers for daily activities. It should be noted that patients treated with adjuvant chemotherapy still relapse, showing this form of standalone treatment is not effective at preventing recurrence or keeping patients disease-free. Because patients on the PAPILLON trial are on treatment with amivantamab in combination with chemotherapy, patients who received the combination noted it was difficult to isolate which side effects were due to chemotherapy vs amivantamab. As such, the side effects from their treatment experience overall are detailed in Section 6.

In late spring of 2022, **KL** felt something was off when a persistent cough hadn't gone away for a few months and urged her GP for a chest x-ray that came back "all clear". However, when symptoms still hadn't resolved after 5 months and a trip to the respirologist who gave her medication for heartburn, she knew something was wrong. In November, she had new x-rays done that showed a mass visible in her lungs. Further tests confirmed KL had stage 4 non-small cell lung cancer that presented with pleural effusion. She was shocked by the diagnosis yet frustrated as she got a second opinion and in hindsight, radiologists potentially had misread the initial scan back in the spring until it had already grown and spread by November. Nonetheless, testing confirmed she had the EGFR exon 20 mutation, but because there were no targeted treatments available to her at the time, she started first line therapy in January 2023 with chemotherapy (carboplatin & pemetrexed), which was initially quite successful. Scans showed her 6 rounds of carboplatin shrunk her disease by 50%, but then she switched to maintenance pemetrexed which did not yield significant results. KL remained on chemotherapy for about 15 months at three-week cycles until April 2024, after which she started amivantamab monotherapy and has been on it ever since.

While on chemotherapy, **KL** noted that side effects at onset of treatment were much worse before becoming more manageable overtime. Nausea and epigastric pain were the main AEs she experienced in the first week after treatment. She felt well in the first 3 days immediately following infusions, but days 4-6 were the worst - she constantly felt nauseous and had the epigastric pain that also affected her appetite, in addition to weakness and tiredness. During those days, she agrees the severity of the side effects did impede her quality of life where she couldn't leave the house, ate a special diet, would only have enough energy to do the bare minimum of tasks like getting out of bed, getting changed, and brushing her teeth. However, day 7 and onwards, she felt better and had no issues going about her regular activities like grocery shopping, going for walks outside, and running errands. KL says that because she knew the carboplatin was effective in treating her disease, it was worth it to put up with the side effects.

**JG's** first line of treatment was pembrolizumab in combination with chemotherapy, which she was on for 19 months between June 2022 until January 2024. She recalls that although constipation and nausea were the only consistent side effects during this treatment, it kept her in a *"weird state where I'd never felt 100% any day, but still felt strong enough to push it all down and carry on with my activities*". However, she was able to stay active and work out nearly as often as she did prior to diagnosis, and also had no issues with daily activities of living.

After his diagnosis with stage 4 EGFR Exon 20 NCLC in May 2022, **JZ** had his first 2 lines of therapy treated with TKIs (explained below), before moving onto his third line treatment with numerous cycles of chemotherapy beginning on May/June 2023 - firstly pemetrexed + carboplatin combination for 6 cycles over 3 weeks, then 7 rounds of pemetrexed only, but after progression, he had 7-8 more rounds of carboplatin over 3 months in March 2024 until June, when he was approved for compassionate access to amivantamab by the manufacturer. Overall, JZ was on chemotherapy for roughly 1 year, noting the first week after infusions he was constantly fatigued, but slowly felt better over the next 2 weeks, before restarting the cycle again every 3 weeks.

**Other targeted therapies:**

A key challenge that EGFR exon 20 patients face is the insensitivity to other EGFR-specific TKIs and limited benefit from immunotherapies. Thus, it is imperative that targeted treatments like amivantamab be approved and publicly accessible for these patients, who otherwise have no other viable treatment option specific to their cancer.

When **LC** was diagnosed with stage 4 EGFR Exon 20 NSCLC in June 2020, his disease had already metastasized to his bone, liver and lymph nodes. He started initial treatment with chemotherapy in August and his first CT scan in October showed further progression. He then was able to access mobocertinib through manufacturer's expanded access program, which worked well for a year between Dec 2020 until Dec 2021, when his doctor switched him onto amivantamab monotherapy in January 2022, which was very successful for LC and he was on it for 13 months before further disease progression in his lungs by early Feb 2023. Since amivantamab, LC has been treated with a few novel targeted therapies: zipalertinib between May 2023-March 2024, and is now currently on furmonertinib.

**LC** noted in his interview that of the TKIs he's been on (mobocertinib, zipalertinib, and furmonertinib), the most prominent side effects experienced by all were caused gastrointestinal issues such as diarrhea, and also altered his taste, which made it difficult to eat and drink. In terms of diarrhea, LC says *"mobocertinib has been the most challenging, then comes furmonertinib with mild and infrequent diarrhea, and the best was zipalertinib with no diarrhea. With amivantamab, the treatment came with no diarrhea and less altered taste. Although the infusion time was long, it had the advantage of freeing the patient from taking multiple pills daily, as in the case of the TKIs"*.

**JZ** started his first two lines of treatment with TKIs - first on afatinib immediately after diagnosis in May 2022, which was successful for 10 months until he progressed in March 2023. He then was on osimertinib for 2-3 months but had no response, before switching to third-line treatment with chemotherapy. In regards to the TKIS he's been on, JZ recalls that afatinib by far had the worst side effects - gastrointestinal issues, dehydration, and significant impacts on his skin. He had to completely change his diet and manage the skin issues constantly, which were only mitigated with dose reduction.

**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, such as 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.

**Radiotherapy:**

When **LC** was diagnosed with stage 4 EGFR Exon 20 NSCLC in June 2020, his disease had already metastasized to his bone, liver and lymph nodes. He started primary treatments with chemotherapy and TKIs before amivantamab. In the meantime, he received an initial brain MRI nearly 10 months after diagnosis in April 2021, which revealed that LC had about 100 very tiny brain lesions that were not present at diagnosis. He opted to travel to the United States for gamma knife radiation treatments, paying 100% out of pocket and a 7-hour drive from his home, and has had 9 sessions scattered throughout his journey since April 2021. LC says the gamma knife radiation was very successful in treating the lesions and had no side effects from it. He also notes that he was able to do the radiation in conjunction with his other primary treatments including while on amivantamab, which was a "huge advantage" to whole brain radiation (WBR), which was his only option offered to him through the provincial healthcare system, as he would have had to stop his other systemic or targeted therapies while undergoing WBR.

After his first lines of treatment with EGFR targeted therapies, **DK** was enrolled into a clinical trial but was randomized to standard of care, and completed 4 cycles before it was clear it had failed and he now had 6 new mets to his brain. He has since been involved in a few clinical trials, including radiation trials to treat these brain mets. One of the SBRT trials were unsuccessful, and he completed WBR in 2023 while on amivantamab, which caused some memory loss but his brain mets have been stable so far.

**KL** also had 1 treatment with cyber knife radiation in March 2024 while undergoing chemotherapy to treat the brain metastases. Because her treatment was short, she didn't recall having any side effects like dizziness or headaches, aside from the fatigue mainly associated with her chemotherapy treatment. According to her oncologist, the radiation treatment was successful in treating the lesions.

## 5. Improved Outcomes

There is a serious unmet need for a treatment option that is specific to EGFR Exon 20 patients that not only treats their disease successfully and delays 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. These outcomes play an integral role in the goals patients have in their treatment decisions, including:

Improved management of their disease symptoms of non-small cell lung cancer
Delaying disease progression and settling patients into long-term remission for improved survivorship
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 | Type of amivantamab experience | Period on amivantamab | Duration on amivantamab | Line of treatment with amivantamab | Currently on amivantamab? |
|---|---|---|---|---|---|---|---|
| LC | June 2020 | Manufacturer's Expanded access program | Monotherapy | January 2022 – Feb 2023 | 13 months | 2nd line | No |
| IN | January 2022 | PAPILLON Clinical Trial | Monotherapy | May 2022 - Present | 25 months | 1st line | Yes |
| VE | 2017 | PAPILLON Clinical Trial | Ami+chemo combination | March 2021 - Present | 39 months | 2nd line | Yes |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| DK | July 2019 | Manufacturer's Compassionate Access | Monotherapy | June 2023 - Present | 12 months | 3rd line + | Yes |
| SP | October 2021 | PAPILLON Clinical Trial | Ami + chemo combination | December 2021 – February 2024 | 26 months | 1st line | Deceased |
| KL | November 2022 | Private insurance + manufacturer compassionate access | Monotherapy | May 2024 - present | 2 months | 2nd line | Yes |
| JZ | May 2022 | Manufacturer compassionate access | Monotherapy | June 2024 - present | 2 months | 4th line | Yes |
| JG | April 2022 | Private insurance coverage | Monotherapy | February 2024 - present | 4 months | 2nd line | Yes |
| SJ | Unknown | Unknown | Monotherapy | March 2024 - Present | 2.5 months | Unknown | Yes |

**Amivantamab is effective at treating patients' disease.**

At diagnosis, **IN** 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. 2 years later, IN still continues to be on the treatment in 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.

**VE** was first diagnosed with stage 1 lung cancer in 2017 and had a lower lung lobectomy and 12 rounds of adjuvant chemotherapy, which kept her disease-free for 4 years, until she progressed in both lungs four years later in 2021. Biomarker testing found she was EGFR Exon 20 positive, so her oncologist enrolled her into the PAPILLON trial which she has remained on for over 3 years and counting. VE's scans have remained clear with no growth, and she has a good quality of life.

When **LC** started 2nd line treatment with amivantamab, he had "hundreds" of small brain lesions, metastases in his bones, liver, and lymph, in addition to the lungs. He was on amivantamab for a year which was very successful in treating his metastases, most notably in his liver and brain. He previously had 7-8 lesions in his liver that were completely resolved with amivantamab. Even when he progressed and stopped treatment, his liver remained free of tumours for an extra 6 months, so LC says he's grateful he essentially gained nearly 1.5 years in his liver. Although he saw the most response in his liver, other tumours around his body also responded while on amivantamab.

**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.

Prior to amivantamab, **JG**'s first-line treatment kept her NED for about 19 months until a new tumour showed up in January 2024. She started amivantamab in February and has continued to be on it since, where her latest scans have remained stable with no tumours growing or shrinking.

At diagnosis, **KL** had tumours in both lungs, brain mets, in addition to a pleural effusion. Her first line treatment with carboplatin was successful in shrinking the tumours by 50% and cyber knife radiotherapy treated her brain metastases. She started treatment with amivantamab in May 2024 and so far has had 5 infusions, but at the time of her interview in June, she was due to have her first follow-up scan in a few weeks, so at the time she was unable to comment on how effective the drug has been on her disease.

**The side effects of amivantamab are manageable over time or with supplementary medications.**

Amongst the patients interviewed for this submission, the most common side effects reported included facial and scalp rashes, cuts on fingers and toes, paronychia, eye dryness, sensitivity to the sun, fatigue, skin sensitivity, and nausea, which are all in line with reported adverse events from the PAPILLON clinical data. Other, less common side effects noted by patients included low appetite, mild peripheral neuropathy, muscle aches, tinnitus, and GI issues (constipation or diarrhea).

**IN** 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.

Unfortunately, **SJ** was one of the few patients who had severe reactions to his first few treatments - he had pustules all over his face and intense rashes on his chest and upper back, which fortunately have since settled down to resemble severe acne that is manageable with antihistamines, proper creams and therapeutic soaps. He also frequently has nosebleeds, in addition to other common side effects like paronychia and sensitivity to the sun. However, SJ says he's grateful that the drug is keeping him alive and so far, effective at treating his disease.

Most patients agreed the AEs were relatively mild and did not impact their ability to go about their daily lives. They were able to manage the side effects with creams/lotions or supplementary medications, or in the case of sun sensitivity, wearing protective clothing, hats, and high protective factor sunscreen. More importantly, all 100% of patients interviewed stated that although the side effect burden was challenging to adjust to at first, especially in the case of rashes being noticeable externally, they would not consider discontinuing treatment as the hope of survival outweighs the negatives. Patients reiterated that they'd much rather deal with some manageable rashes or GI side effects that are relatively mild if it means the drug is keeping them alive.

**Patients agreed that amivantamab did not significantly impede their functionality or independence, and were able to maintain a good quality of life.**

As a retired elder, **VE** lives with her husband in a high-rise apartment, and had always been very healthy, never-smoker, and had no symptoms that led to her diagnosis aside from a persistent cough. When her disease came back in 2021 after being stable for 4 years, VE and her husband both recently hired PSWs to help them out with some chores around the house, particularly for laundry and cleaning, a decision made due to their other comorbidities. VE says although she struggles with fatigue and having minimal energy to take care of household tasks, having her PSW has been an immense help. Her son also helps do their grocery shopping, so she has more time to focus on her health and caring for her husband. She is still functional and enjoys walking around her apartment building often, going to the drug store and shops across the street, and even went on a 4-day trip to Niagara Falls recently. VE hopes to go on more cruise trips with her husband next year and continues to enjoy her hobbies like colouring, watching hockey games and socializing with her neighbours in the apartment building she lives in.

**KL** says that while on amivantamab, the fatigue is actually worse than when she was on chemotherapy, as well as muscle and body aches which were worse in the start of treatment, but has gotten used to it over time. She says in her interview, "*it felt like the flu when my body and muscles ached, I was tired and had a mild headache, but they got better with Tylenol".* Whenever she was very tired, she agreed it somewhat impeded her ability to go about her day-to-day where she'd have to push herself to do things, even just getting dressed and taking a shower took energy; however, she wouldn't say it severely impacted her functionality where she felt exclusively bedridden - she had no issues eating and doing basic ADLs. On days where she feels fine, she has no issues going about her daily activities - she can run errands, grocery shop, clean the house, cook meals, and socialize with friends and coworkers in town. She likes to stay active by going on

walks outside or on her treadmill, plays pickleball, and often practices yoga. KL says she still believes she has a good quality of life, and although she doesn't foresee herself going back to work since she's near retirement, she is just taking it one day at a time, grateful that she's able to make memories with her young-adult children and travel with her husband.

4 of 7 patients interviewed - **LC, IN, JZ** and **JG** - said they have no issues at all with going about their activities of daily living; they are able to clean, cook, grocery shop, and even spend time with family and friends quite often. They did need to rely on their spouses or family members driving them to their infusion appointments every few weeks because of the supplementary Benadryl given during infusion that makes them sleepy and groggy. Nonetheless, they are all able to otherwise drive themselves to run errands on days outside of their travels for treatment.

**Amivantamab has given patients a hope for the future and return to hobbies they enjoy, such as travelling and exercising.**

**JG** says that throughout her treatment with amivantamab (and even on her previous line of therapy), she was able to continue her active lifestyle, running 4 miles every day (including on treatment days after getting home from the hospital), playing multiple sports including water aerobics, tennis, and pickleball. She remains active every day and enjoys sharing her hobbies with her kids, who also now play tennis regularly, and is grateful she has been able to maintain a great quality of life with amivantamab, even saying others may not even notice she'd have lung cancer if not mentioned.

**LC** and his wife agreed his quality of life while on amivantamab was virtually unchanged from pre-diagnosis and has no issues going about his day-to-day activities like cooking, driving, or shopping. They also had to travel long distances quite frequently for his gamma-knife radiation treatments in Spokane, WA, about a 7h drive from their home in Vancouver, and most recently, from Vancouver to Edmonton every 3 weeks for his current treatment on a clinical trial. They love being outside as much as they can and enjoyed the long road trips along the US West Coast, even ensuring they made stops along the way for birdwatching, one of LC's favourite pastimes. While at home, he continues to go on long walks nearly everyday and being in nature as much as he can.

With the stability **IN** found on amivantamab, she continues to pursue 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 has another trip to Italy planned in September, and is 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 months of amivantamab treatment, IN 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.

**JZ** has been able to stay active and keep doing the hobbies he loves throughout his diagnosis, such as golfing, going on daily walks in his neighbourhood, and even started getting into patient advocacy for better lung cancer treatments and awareness in the community. He also is grateful for the various treatments that have helped extend his life, including chemotherapy, TKIs, radiation, and now amivantamab. Having 3 kids aged 15, 13, and 10 years old, JZ is incredibly happy he's still here to watch them grow up and make memories with his family while in their prime adolescent years, and even coaches them in hockey a few days a week to keep himself busy and out of the house. He has been able to travel with his family as well, even leaving for a two-week vacation to Europe a few days after his interview with LCC. Amivantamab has so far been working well for him, and even though he started treatment not long ago, he is feeling good, has no impact on his daily life, and has yet to experience any side effects from the drug.

**Some patients were able to continue working throughout their treatment.**

Most of the patients interviewed, including **IN, VE** and **DK** had retired prior to their diagnoses. However, a few others were able to go back to work or continue working throughout their diagnoses.

When **LC** was diagnosed in mid-2020, he was still working tirelessly as a metallurgical engineer working on automotive fuel cells, and truly loved his career and workplace. A few months into his first-line treatment, he went on disability leave for 3 years until officially retiring in 2023 to prioritize his health and spending more time with family, although he often still visits his old colleagues at work and is constantly keeping up on their projects and the newest research in the field.

**SP** was self-employed and owned a landscaping business, and was able to continue working throughout her treatment. When she first started treatment in the PAPILLON trial in December 2021, she had to put her landscaping business on

hold for two months because her hospital visits were frequent, but was able to return to work throughout her treatment whenever she felt well. She made the difficult decision to close her business in June 2022 and hired additional help to complete remaining contracts prior to the closure.

Similarly, **JG** also worked as a landscaper and had no problems at all continuing her work throughout her treatments. Because one of the side effects experienced with amivantamab included sensitivity to the sun, she always wore full protective clothing and hats whenever she was outside. JG says she enjoyed her work, and even worked a couple of times per month at Lululemon, which she enjoyed to keep her out of the house.

**All patients agreed they would strongly prefer their experience on amivantamab over previous therapies.**

We asked each patient during their interviews how they would rank their experience with amivantamab in comparison to other therapies they've experienced on a scale of 1-10 (i.e., 1 being "*Amivantamab was much worse than other therapies/I would prefer other therapies to amivantamab"*, 5 being *"about the same*", and 10 being "*Amivantamab was much better than other therapies/I would prefer amivantamab to other therapies")*.

**The average ranking between all patients was 8.6, and three patients, JG, IN, and LC, ranked amivantamab a full 10 out of 10.**

**JG:** *"I don't feel sick at all and I've had relatively mild side effects to all the treatments I've been on, including amivantamab. But with my previous treatment, the constant feeling of nausea was unsettling - the rashes and skin flare-ups I get on amivantamab are 100% preferable to that. I'd much rather deal with the rashes than feeling unwell all the time."*

**IN:** *"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 to stay on it."*

**LC:** *"I'd rank my experience on amivantamab at 10. I would indeed prefer amivantamab (the least effects) over chemo (ineffective) and TKIs (more side effects, especially gastrointestinal side effects - weight loss, dehydration, nausea, fatigue, diarrhea). Many Exon 20 patients including me develop brain metastases, and if left untreated, I would've had 6-9 months to live post-diagnosis. But here I am now 4 years later, because of the right treatment. My quality of life is great and there were no significant impacts to my day-to-day life. I just hope other patients will get a chance to receive the drug and live longer, meaningful lives like mine."*

**KL** ranked her experience at 5, saying there were pros and cons to both. On chemotherapy, she knew the carboplatin was effective in treating her disease, so it was worth it to put up with the side effects, but has not yet had a follow-up scan to know how well amivantamab is actually working. With amivantamab, fatigue is the main side effect experienced that she says is more severe than while on chemotherapy, but she has good and bad days. The two-week cycles on amivantamab is shorter than when she had chemotherapy infusions every three weeks, so that's also why she feels it's harder to recover since it's a "constant cycle" of feeling good and bad, but with chemo, *"I'd have 3-4 bad days in the first week post-treatment, but the two weeks thereafter before my next treatment were perfectly normal".*

For **DK**, he also 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 20 insertions are identified using Next Generation Sequencing (NGS). NGS is routinely conducted in all patients with advanced NSCLC with a non-squamous and squamous histology, without a smoking history.

## 8. Anything Else?

There is a serious unmet need for novel targeted therapies that will prolong progression-free survival and improve health-related quality of life for patients with EGFR Exon 20 non-small cell lung cancer, but amivantamab has the opportunity to change this. Lung Cancer Canada, Canadian Cancer Survivor Network and Lung Health Foundation strongly urge the Canada Drug Agency to recognize this gap and barrier in adequate treatment options that are specific to these patients who deserve treatments that will work and increase the accessibility of these treatments for patients across Canada. We are hopeful that this may become the new standard of care in this disease and patients in this setting are not faced with a "dead end" when treatment with other TKIs or chemotherapy are no longer effective.

## 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 – Lung Cancer Canada

**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 Inc. – 2023 (LCC) | | | X | |
| Janssen Inc. – 2024 (LCC) | | | | 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:** Shem Singh

**Position:** Executive Director

**Patient Group:** Lung Cancer Canada

**Date**: July 8, 2024

### Table 2: Financial Disclosures – Canadian Cancer Survivors Network

**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 Inc. – 2023 (CCSN) | | | | X |
| Janssen Inc. – 2024 (CCSN) | | | | 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:** Lindsay Timm

**Position:** Community Engagement Manager

**Patient Group:** Canadian Cancer Survivors Network

**Date**: July 8, 2024

## Table 3: Financial Disclosures – Lung Health Foundation

**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 Inc – 2022-2024 (LHF) | | | | 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:** Jessica Buckley

**Position:** President & CEO

**Patient Group:** Lung Health Foundation

**Date**: July 8, 2024

CADTH

# Clinician Group Input

**CADTH Project Number:** PC0376-000

**Generic Drug Name (Brand Name):** amivantamab (Rybrevant)

**Indication:** Rybrevant in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) exon 20 insertion mutations.

**Name of Clinician Group:** Lung Cancer Canada - Medical Advisory Committee

**Author of Submission:** Dr. Susanna Cheng (lead), Dr. Shaqil Kassam, Dr. Callista Phillips, Dr. Dorothy Lo, Dr. Brandon Sheffield, Dr. Stephanie Snow, Dr. Vishal Navani, Dr. Mark Vincent, Dr. Ron Burkes, Dr. Michela Febbraro, Dr. Silvana Spadafora, Dr. Parneet Cheema, Dr. David Dawe, Dr. Quincy Chu, Dr. Natasha Leighl, Dr. Rosalyn Juergens, Dr. Mahmoud Abdelsalam, Dr. Paul Wheatley-Price, Dr. Geoffrey Liu, Dr. Kevin Jao, Dr. Randeep Sangha, Dr. Nathalie Daaboul, Dr. Alison Wallace, Dr. Jeffrey Rothenstein, Dr. Cheryl Ho, Dr. Sunil Yadav, Dr. Catherine Labbé, Dr. Kirstin Perdrizet, Dr. Nicole Bouchard, Dr. Biniam Kidane, Dr. Normand Blais

## 1. About Your Clinician Group

Lung Cancer Canada (LCC) 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 provide 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 countries.

www.lungcancercanada.ca

## 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 entirely independent of the manufacturer (Janssen).

## 3. Current Treatments and Treatment Goals

#### *1.1.1.1 Canadian NSCLC patients with an EGFR Exon 20 insertion are rare.*

Lung cancer is the most common cancer diagnosis in Canada, with an estimated 1 in 15 Canadians receiving a diagnosis in their lifetime [1]. In 2022, lung cancer is again projected to be the leading cause of cancer deaths, accounting for 24.3% of cancer deaths [1]. The projected number of new lung cancer cases in 2022 will be 30, 000 (1); of these, approximately 88% will be diagnosed with non-small cell lung cancer (NSCLC)[2,3].

While the prognosis and outcomes of lung cancer have improved in recent decades, largely as a result of novel, innovative therapies and increased awareness of the risk factors, this disease remains the deadliest cancer in Canada [1,2]

Today, targetable molecular alterations are identified in approximately 60% of lung adenocarcinoma patients in Western populations and 80% among Asian populations, most commonly occurring in the *epidermal growth factor receptor* (*EGFR*) [3].

In Canada, approximately 15% of patients with NSCLC present with mutations in the epidermal growth factor receptor (EGFR) gene [6]. EGFR mutations include the common Exon 19 deletions and the L858R mutations, which make up 85-90% of the mutations we see. The remaining 10-15% of EGFR mutations consists of the rare, uncommon mutations, which can be further subdivided into: "sensitizing" or

"non-sensitizing".

*EGFR* mutations can be categorized based on the type of mutation and the exon in which they occur. Exon 19 deletions (ex19del) and exon 21 L858R point mutations account for up to 90% of all *EGFR* mutations and are often referred to as common sensitizing *EGFR* mutations (c*EGFR*m) [4]. The third most frequently occurring mutations are exon 20 insertion mutations (ex20ins) and represent approximately 1–12% of all *EGFR* mutations, and 0.1–4% of all NSCLC mutations [5]. According to some estimates, patients with EGFR Exon 20 insertions make up between approximately only 200-10000 new patients diagnosed each year in Canada [1].

The treatment of patients with *EGFR* mutations has been revolutionized by tyrosine kinase inhibitor (TKI) targeted therapy. The recommended first-line therapy for advanced-stage patients with c*EGFR*m in Canada is the third-generation kinase inhibitor, osimertinib [7].

Unfortunately, ex20ins are associated with limited response to TKIs [8]. Compared with other *EGFR* mutations, patients with ex20ins have especially poor prognosis, with markedly reduced sensitivity to approved *EGFR* kinase inhibitors [8]. One reason why EGFR TKIs do not work in patients with an EGFR Exon 20 insertion is because the small size of the binding pocket for the ATP kinase interferes with the binding of the TKI. Studies with other TKIs such as mobocertinib failed to meet its primary end point of PFS based on the outcome of the phase 3 EXCLAIM-2 trial (NCT04129502) and hence has been withdrawn from market [9].

In addition, there is data to show that checkpoint inhibitors either alone or in combination with chemotherapy have reduced efficacy in patients harboring EGFR exon 20 insertion mutations [10]. In addition, patients with EGFR mutations were excluded from the KEYNOTE189 trial as checkpoint inhibitors have not shown efficacy in the EGFR driver mutation population [12 ]. The current first line therapy for advanced stage patients with EGFR exon 20 insertion mutations is only platinum doublet chemotherapy.

The prognosis for patients with locally advanced or metastatic NSCLC EGFR Exon 20 insertion mutations remain poor, mostly because they have few treatment options and lack of effective targeted therapies.

Several real-world studies, including one from Alberta [5], have demonstrated that patients with EGFR Exon 20 insertions have much poorer outcomes in terms of median PFS and medial overall survival than patients with common EGFR mutations[ 11].

In the first line setting, platinum-based chemotherapy is associated with a response rate of 23-29% and median progression free survival of 3.4-6.9 months. Patients with common sensitizing EGFR mutated NSCLC have a median overall survival of up to 38.6 months [13], recent analyses of real world data obtained from patients with advanced NSCLC with EGFR exon 20 insertions showed a reduced median overall survival ranging from 16.2 - 24.3 months , with a 5 year overall survival of 8% with chemotherapy alone [14,15].

There is a significant unmet need for novel targeted therapies that will prolong PFS and improve health-related quality of life (HRQoL) for patients with EGFR Exon 20 insertions.

The ideal treatment for patients with an EGFR exon 20 insertion is one that directly inhibits the driver mutation. The treatment should be well tolerated, with a predictable and low toxicity profile. The response should be durable and correlate with an improvement in quality of life.

## 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.*

There is a significant unmet need for novel targeted therapies that will prolong PFS and improve health-related quality of life (HrQoL) for patients with EGFR Exon 20 insertions.

The only currently available treatment for NSCLC patients with EGFR Exon 20 insertions is chemotherapy platinum doublet followed by Docetaxel single agent chemotherapy. These agents are not novel and have low efficacy, low duration of efficacy and can cause significant toxicity with poor tolerability resulting in reduced quality of life [7]. Patients with EGFR Exon 20 insertions do not respond to currently available EGFR TKIs nor to checkpoint inhibitors [8, 12]. As a result, they are often excluded from clinical trials in the NSCLC realm that focus on the sensitizing EGFR mutations or those with known potential responses to checkpoint inhibitors.

There have been no approved novel therapies for patients with EGFR Exon 20 insertions in Canada. There is a serious need to address the lack of novel treatment options for this group.

## 5. Place in Therapy

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

*1.1.1.2 The current submission is for amivantamab in combination with platinum-based doublet in the first line setting for NSCLC patients with EGFR Exon 20 insertions. This agrees with the indication and trial results of the PAPILLON study [16].*

PAPILLON study is a phase 3 international, randomized trial, 1:1 ratio for patients with advanced NSCLC with EGFR Exon 20 insertions who had not received previous systemic therapy. Patients were randomized to receive intravenous amivantamab plus chemotherapy or chemotherapy alone. A total of 308 patients were randomized with 153 in the amivantamab chemo arm and 155 in the chemo arm. Progression free survival was significantly longer in the amivantamab - chemotherapy group than in the chemotherapy group (median 11.4 months and 6.7

months, respectively, hazard ratio of 0.40 and CI of 0.3-0.53, P value < 0.001). At 18 months, progression free survival was reported in 31% of the patients in the amivantamab-chemo group and only in 3 % of the chemo group [16]. Overall response rate was 73% in the Amivantamab-chemo arm compared with 47% in the chemo arm alone.

Median Progression free survival in the second line setting (PFS2) was longer for the amivantamab - chemo arm compared to other second line therapy (i.e. docetaxel, amivantamab etc..) alone (HR 0.493, CI

0.32-0.76, p=0.001) supporting the use of first line amivantamab chemo. Notably, of those patients receiving other second line therapy alone, 76% received subsequent amivantamab single agent as second line therapy.

Interim overall survival analysis showed a favorable trend for the combination amivantamab-chemo arm. Of special note ,66% of patients crossed over to amivantamab in the second line setting who were on the chemotherapy arm alone.

Amivantamab is a unique bispecific monoclonal antibody that binds to the extracellular domain of both EGFR and MET receptors, blocking the binding of both EGF and MET ligands to their receptors. This blockade leads to inhibition of downstream activation and signaling processes resulting in cell death.

As we have learned from the literature and clinical practice, targeted therapies against driver mutations should ideally be offered in a first line setting for maximal efficacy. The results of the PAPILLON study supports the first line use of Amivantamab with platinum doublet chemotherapy for met NSCLC Exon 20 insertion positive 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?*

The NSCLC patients most likely to respond to amivantamab-platinum double chemotherapy combination are those with EGFR exon 20 insertion mutations. Patients need to have adequate performance status and organ function that would be required for systemic chemotherapy to be considered for this combination.

The PFS benefit was observed across all subgroups according to race, sex, age, history of smoking, ECOG performance status ( 0-1) and even those with a history of brain metastases.

Patients with EGFR Exon 20 insertions 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.

### 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?*

Amivantamab + platinum-based doublet chemotherapy directly helps to address the unmet treatment need in this uncommon patient population. This targeted drug in combination with platinum-based doublet chemotherapy has shown to significantly improve response rates, progression free survival and overall survival compared to real world controls.

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, In general patients in clinical practice are often seen and evaluated every 6-9 weeks with a variety of radiological imaging modalities, usually to evaluate baseline disease sites response status as well as assess any clinically relevant symptoms determined to be side effect and that may affect HRQoL.

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.

The magnitude of response will vary across patients but should not vary across physicians.

HRQoL outcomes are often more subjective and are harder to evaluate . HRQoL comprises mental, physical and social well-being, all of which are affected by the tumor burden and/or adverse events.

Education of the drug side effect profile, for both physicians and patients , would be beneficial for both to help maintain patients on therapy to achieve best results. The combination of amivantamab and chemotherapy demonstrated a safety profile consistent with the safety profiles of the individual agents, with low rates of treatment-related discontinuation (7%). The rates of overall adverse events ( AEs) were compatible between both treatment arms. The side effects of the combination Amivantamab and chemo are generally manageable and amivantamab's tolerability profile is similar to currently available targeted therapies in NSCLC. This combination fulfills an unmet need in this rare population with poor prognosis.

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

Factors for consideration when deciding to discontinue amivantamab -chemotherapy combination are similar to any other cancer therapy: namely disease progression and lack of clinical benefit.

In addition, adverse events may require patients to discontinue amivantamab temporarily or more permanently in some cases. In the PAPILLON study, treatment-related discontinuations of amivantamab were low (7%). Similar rates of discontinuation of all study agents due to Adverse events were seen in both arms.

### 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]?*

Ideally, amivantamab-chemotherapy combination should be administered at a Cancer Centre or hospital setting, by personnel experienced in administering these agents.

Amivantamab is an intravenous drug administered weekly for the first 4 weeks then every 3 weeks starting week 7 of cycle 3 with chemotherapy. Amivantamab chemotherapy combination would continue until disease progression or unwanted toxicity. Based on the toxicity, either amivantamab or chemotherapy may be discontinued or held while continuing the other drug.

Adverse reactions, particularly infusion reactions, can occur especially during the first week of cycle 1 , mainly due to Amivantamab infusion, PAPILLON study reports the incidence of infusion-related reactions in 42% of the amivantamab -chemotherapy group and 1% in chemotherapy group. This is a lower reported infusion for the PAPILLON study compared to the CHRYSALIS cohort D study due to the administration of Amivantamab in a "split manner". The first dose of amivantamab is divided into day 1 (350mg) and day 2 (700mg or 1050 mg based on weight). The majority of infusion-related reactions were limited to the first infusion and were grade 1 (10.5%) grade 2 (50.3%) in severity based on other amivantamab clinical trials [17].

Infusion-related reactions as per protocol can be prevented with the use of pre-treatment corticosteroids, antihistamines and acetaminophen. Future infusion -related reactions can be managed prospectively by slow administration (delivering the dose over 6 hours) or continuing use of corticosteroids prophylactically for cycle 2 or later.

As most infusion reactions are experienced during the first week of treatment and not experienced subsequently, it is very manageable. As reported, infusion reaction reactions very rarely lead to drug discontinuation. Management of amivantamab infusion reactions are well published [18]. Many cancer centers have had access to compassionate Amivantamab and have already developed infusion protocols, nursing/pharmacist and patient education modules. Other physicians may have gained experience with amivantamab using infusion clinics.

## 6. Additional Information

EGFR exon 20 insertion positive patients have historically been the most disheartening to manage, t hey have not been able to benefit from any of the recent major advances in the management of lung cancer.

They do not respond to any of the commonly used EGFR TKIs we have for those with the sensitizing EGFR mutations, they do not respond to checkpoint inhibitors which have benefited those without EGFR mutations. The only treatment they are offered is the standard chemotherapy regimens that have existed for the last 2 decades. This truly is a group of patients with the greatest unmet needs. Many of these patients are never smokers. Some are young. They find it difficult to comprehend why there is nothing other than chemotherapy for them.

Oncologists are very excited about the results of the PAPILLON study and the potential benefits for this groups of patients. The statistically significant and clinically meaningful improvement in PFS with a hazard ratio of 0.395 is impressive. The data from the PAPILLON study supports the use of Amivantamab-platinum double chemotherapy combination as the standard of care in the first line setting for patients with NSCLC harboring EGFR exon 20 insertion mutations.

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### 1.1.2

## 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.

### *1.1.2.1 Declaration for Clinician 1*

**Name:** Susanna Cheng

**Position:** Medical Oncologist, Sunnybrook Hospital; Associate Professor, University of Toronto

**Date:** July 8, 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 |
| Merck | X | | | |
| BMS | X | | | |
| AstraZeneca | X | | | |
| Janssen | X | | | |
| Roche | X | | | |
| Amgen | X | | | |

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

| New or Updated Declaration for Clinician 2 | |
|---|---|
| **Name** | Michela Febbraro |

| | |
|---|---|
| **Position** | Medical Oncologist, Algoma District Cancer Program |
| **Date** | July 8, 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* | ☐ | ☒ | ☐ | ☐ |

| **New or Updated Declaration for Clinician 3** | |
|---|---|
| **Name** | *Biniam Kidane* |
| **Position** | *Associate Professor, Dept of Surgery, University of Manitoba* |
| **Date** | July 8, 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* | ☒ | ☐ | ☐ | ☐ |

| | | | | |
|---|---|---|---|---|
| | | | | |

***1.1.2.2***

| **New or Updated Declaration for Clinician 4** | |
|---|---|
| **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** | July 8, 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* | ☒ | ☐ | ☐ | ☐ |
| | | | | |

**Declaration for Clinician 5**

**Name: NATHALIE DAABOUL**

**Position: Hematologist-Oncologist, Université de Sherbrooke**

**Date:** July 8, 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.**

**Table 1: Conflict of Interest Declaration for Clinician 6**

| Company | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| Amgen | x | | | |
| AstraZeneca | x | | | |
| BMS | x | | | |
| Eisai | x | | | |
| Jazz | x | | | |
| Merck | x | | | |
| Novartis | x | | | |
| Pfizer | x | | | |
| Sanofi | x | | | |
| Takeda | x | | | |
| Taiho | x | | | |

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

| **New or Updated Declaration for Clinician 6** | |
|---|---|
| **Name** | *Dr. Geoffrey Liu* |
| **Position** | *Medical Oncologist* |
| **Date** | July 8, 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 | | | |
| | | | | |

| **New or Updated Declaration for Clinician 7** | |
|---|---|
| **Name** | *Ronald Burkes* |
| **Position** | *Medical Oncologist Mount Sinai Hospital* |
| **Date** | July 8, 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* | ☐ | ☐ | ☐ | ☐ |

**Declaration for Clinician 8**

Name: Silvana Spadafora
Position: Medical Oncologist, Algoma District Cancer Program
Date: July 8, 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**

| Company | 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 | | X | | |
| Merck | | X | | |
| Novartis | | X | | |

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

**Conflict of Interest Declaration for Clinician 9**

Name: Dr. Kevin Jao
Position: Medical Oncologist, Hôpital Sacré-Cœur, Montreal
Date: July 8, 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 | ☒ | ☐ | ☐ | ☐ |

**Declaration for Clinician 10**

Name: Dr Catherine Labbé
Position: Head of Respiratory Medicine Service, Université de Laval
Date: July 8, 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 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 |
| 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 11

Name: Dr Nicole Bouchard
Position: Respirologist, Sherbrooke University Hospital
Date: July 8, 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 11**

| 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 12

Name: Dr Randeep Sangha

Position: Medical Oncologist, Cross Cancer Institute
Date: July 8, 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 12**

| 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 13

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: July 8, 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 13**

| 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.

Declaration for Clinician 14

**Name:** Stephanie Snow

**Position:** Professor Dalhousie University, Medical Oncologist QEII Health Sciences Centre, Halifax, NS

**Date:** July 8, 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 15**

| 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 | | | 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 16

Name: Dr. Shaqil Kassam
Position: Medical Oncologist, Southlake Regional Hospital
Date: July 8, 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 16**

| | 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 17

Name: Dr. Rosalyn Juergens
Position: Chair, LCC Medical Advisory Committee; Medical Oncologist, Juravinski Cancer Center
Date: July 8, 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 17**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$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 | | | |

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

## Declaration for Clinician 18

Name: Dr. Mark Vincent
Position: Medical Oncologist, London Regional Cancer Centre
Date: July 8, 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 18**

| 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 19

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: July 8, 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 |
| BMS | Advisory role, Honoraria and travel grants | ☐ | ☒ | ☐ | ☐ |

## Declaration for Clinician 20

Name: Dr. David Dawe
Position: Medical Oncologist, CancerCare Manitoba
Date: July 8, 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 20**

| 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 21

**Name:** Dorothy Lo

**Position:** Medical oncologist

**Date:** July 8, 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 21**

| 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 | | | |
| Sanofi | x | | | |
| Novartis | x | | | |
| astellas | | x | | |
| Eisai | x | | | |
| Astra Zeneca | x | | | |

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

| New or Updated Declaration for Clinician 22 | |
|---|---|
| **Name** | *Quincy Chu* |
| **Position** | *Medical Oncologist, Cross Cancer Institute* |
| **Date** | July 8, 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** |
| *Abbvie* | ☒ | ☐ | ☐ | ☐ |
| *Amgen* | X | | | |
| *Astra Zeneca* | ☒ | ☒ | ☐ | ☐ |
| *AnHeart* | ☒ | ☐ | ☐ | ☐ |
| *BMS* | ☒ | ☐ | ☐ | ☐ |
| *Boehringer Ingelehim* | ☒ | ☐ | ☐ | ☐ |
| *Eli Lilly* | ☒ | ☐ | ☐ | ☐ |
| *Jazz* | ☒ | ☐ | ☐ | ☐ |
| *Johnson and Johnson* | ☐ | ☒ | ☐ | ☐ |
| *Merck* | ☒ | ☐ | ☐ | ☐ |
| *Pfizer* | X | | | |
| *Novartis* | ☒ | ☐ | ☐ | ☐ |
| *Roche* | ☒ | ☒ | ☐ | ☐ |
| *Sanofi* | ☒ | ☐ | ☐ | ☐ |
| *Takeda* | ☒ | ☐ | ☐ | ☐ |

Declaration for Clinician 23

**Name:** Brandon Sheffield

**Position:** Pathologist

**Date:** July 8, 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** |
| Amgen | | | X | |
| AstraZeneca | | | X | |
| Bayer | | | X | |
| Biocartis | | | X | |
| Boehringer-Ingelheim | | | X | |
| Cell Marque | | | X | |
| Elevation Oncology | | | X | |
| Eli Lily | | | X | |
| EMD Serono | | | X | |
| Incyte | | | X | |
| Janssen | | | X | |
| Merck | | | X | |
| Novartis | | | X | |
| Pfizer | | | X | |
| Roche | | | X | |
| Thermo Fisher | | | X | |
| Turning Point Therapeutics | | | X | |

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

Declaration for Clinician 24

**Name:** Callista Phillips

**Position:** Medical Oncologist and Clinical Lead, Oncology Clinic, Joseph Brant Hospital

**Date:** July 8, 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 24**

| 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 | X | | | |
| Bayer | X | | | |
| Roche | X | | | |

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

| **New or Updated Declaration for Clinician 25** | |
|---|---|
| **Name** | *Vishal Navani* |
| **Position** | *Medical Oncologist, University of Calgary* |
| **Date** | July 8, 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 26

Name: Dr. Parneet Cheema
Position: Medical Director of Cancer Care, William Osler Health System
Date: July 8, 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 26**

| 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 |
| Bristol Myers Squibb | Advisory board/Honoraria | ☒ | ☐ | ☐ | ☐ |
| Merck | Advisory board/Honoraria | ☒ | ☐ | ☐ | ☐ |
| Astrazeneca | Advisory board/Honoraria | ☒ | ☐ | ☐ | ☐ |
| Roche | Advisory board/Honoraria | ☒ | ☐ | ☐ | ☐ |
| Novartis | Advisory board/Honoraria | ☒ | ☐ | ☐ | ☐ |
| | | ☐ | ☐ | ☐ | ☐ |

## Declaration for Clinician 27

**Name:** Dr. Paul Wheatley-Price
**Position:** Medical Oncologist, The Ottawa Hospital. Associate Professor, Department of Medicine, University of Ottawa
**Date** July 8, 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 27**

| 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.

### Declaration for Clinician 28

Name: Dr Jeffrey Rothenstein
Position: Medical Oncologist, Lakeridge Health
Date: July 8, 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 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** |
| Roche | x | | | |

### Declaration for Clinician 29

Name: Dr. Cheryl Ho
Position: Medical Oncologist, BC Cancer
Date: July 8, 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 29**

| 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 |
| Bayer | Advisory role | ☒ | ☐ | ☐ | ☐ |
| Roche | Advisory role, travel, research grants | ☐ | ☐ | ☐ | ☒ |

### Declaration for Clinician 30

Name: Dr. Natasha Leighl
Position: Medical Oncologist, Princess Margaret Cancer Center
Date: July 8, 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 30**

| 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 31

Name: Dr. Kirsten Perdrizet
Position: Medical Oncologist, Princess Margaret Cancer Center
Date: July 8, 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 31**

| Company | | Check Appropriate Dollar Range |
|---|---|---|

| | Nature or description of activities or interests | $0 to 5,000 | $5,001 to 10,000 | $10,001 to 50,000 | In Excess of $50,000 |
|---|---|---|---|---|---|
| | | ☐ | ☐ | ☐ | ☐ |
| | | ☐ | ☐ | ☐ | ☐ |

## Declaration for Clinician 32

**Name:** Normand Blais
**Position:** Medical Oncologist, CHUM Cancer Center, Montreal
**Date:** July 8, 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 32**

| 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.

CADTH Project Number: PC0376

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

Indication: in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) exon 20 insertion mutations.

Name of Clinician Group: OH (CCO) Lung Cancer Drug Advisory Committee

Author of Submission: Dr. Donna Maziak

## 1. About Your Clinician Group

OH(CCO)'s Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program

## 2. Information Gathering

Information was gathered by email and finalized in a videocall.

## 3. Current Treatments and Treatment Goals

The current treatment available includes platinum-based chemotherapy possibly with immunotherapy.

This is an important group with an unmet need and no funded targeted therapies despite Health Canada approval. The combination of platinum-based chemotherapy plus amivantamab represents the most effective upfront therapy.

The goals of treatment include PFS, quality of life, and potential for OS gain.

## 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.

These patients have worse survival than patients with common EGFR mutations and need improved therapy options. Access to targeted therapies for this group can significantly improve outcomes.

There are poor outcomes with current available treatments.

Limitations include an additional IV drug with loading doses, incremental toxicity.

## 5. Place in Therapy

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

This will be used in the first line setting in combination with pemetrexed/platinum-based agent.

This treatment can replace pembrolizumab or ipilimumab/nivolumab.

### 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?

All patients with *EGFR* Exon20 insertion mutations are suitable for first line therapy.

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?

Response, PFS, symptom improvement, with scans completed every 9 to 12 weeks.

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

Disease progression, unacceptable toxicities.

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 settings would include outpatient cancer centers, or satellite facilities. Specialists with experience in using systemic therapy in cancer care.

## 6. Additional Information

Amivantamab may have some resource implications. There are high rates of infusion reactions for the first cycle, therefore long infusion times. However, there was data presented at ASCO for a subcutaneous formulation that will help with these two issues. There will be added toxicity from combining chemotherapy with an EGFR targeted agent that might impact on tolerability, however this still represents a more effective treatment option.

## 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:** Donna Maziak

**Position:** Lead, OH (CCO) Lung Cancer Drug Advisory Committee

**Date:** 18-06-2024

☒ **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 | | | | |
| 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. Andrew Robinson

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

☒ 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** |
| Add company name | | | | |
| 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. Stephanie Brule

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

☒ 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**

| | **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. Peter Ellis

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

☒ 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** |
| 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 5

Name: Dr. Natash Leighl

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 18-06-2024

☒ 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**

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

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

## Declaration for Clinician 6

Name: Dr. Sara Kuruvilla

Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee

Date: 14-06-2024

☒ 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 6**

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

* 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 Cancer Drug Advisory Committee

Date: 14-06-2024

☒ 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 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 |
| Add company name | | | | |
| Add company name | | | | |
| Add or remove rows as required | | | | |

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