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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

tarlatamab (TBC)

(Amgen Canada Inc.)

Indication: For the treatment of adult patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after at least two prior lines of therapy including platinum-based chemotherapy.

August 23, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

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Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Tarlatamab
Indication: For the treatment of adult patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after at least two prior lines of therapy including platinum-based chemotherapy.
Name of Patient Group: Joint Submission by Lung Cancer Canada, Lung Health Foundation, and Canadian Cancer Survivor Network
Author of Submission: Winky Yau - Lung Cancer Canada, Lindsay Timm - Canadian Cancer Survivor Network, & 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 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 (www.lunghealth.ca) legally known as the Ontario Lung Association, is registered with the CADTH and pCODR, and stands as a cornerstone of trust and reliability in the Canadian healthcare and public health systems. Lung Health Foundation 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. We are governed by a dedicated board of directors and supported by a team of approximately 40 employees alongside thousands of passionate volunteers. Together, we work tirelessly to improve the lung health of Canadians, driving positive change and fostering a brighter, healthier future for all.

2. Information Gathering

Data Collection:

The information discussed throughout this submission consists of the thoughts and experiences of small cell lung cancer patients and their caregivers. They were collected through virtual interviews conducted by Lung Cancer Canada directly with the patients. All interviews were conducted in July and August 2024.

Demographic Data:

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Small cell lung cancer (SCLC) represents only about 10-15% of the lung cancer patient population in Canada. Because tarlatamab is a new treatment for SCLC that received FDA approval in May 2024 and is still currently undergoing NOC review under Health Canada, it was quite difficult to source patients who have specific experience on the drug, especially Canadians. However, we were able to speak to 3 patients who have extensive stage small-cell lung cancer and have experience with the drug as per the indication of this submission, two Canadians and one American. Their demographics are summarized in the chart below, and specific treatment experience can be found in section 6.

Name	Patient/ Caregiver	Gender	Age	Type of Lung Cancer	Diagnosis Date	Location	Source
GC	Patient	M	74	Extensive Stage SCLC	October 2022	New Brunswick (CAN)	Phone Interview
MW	Patient	F	65	Extensive Stage SCLC	May 2023	Rhode Island (USA)	Video Interview
WL	Patient	M	Mid/late 60s	Extensive Stage SCLC	July 2023	Ontario (CAN)	Phone Interview

3. Disease Experience

GC had always been living life to the fullest and was a very fit and active individual – prior to his retirement a few years ago, he worked for 42 years as a firefighter and loved his job, and was an avid golfer competing in tournaments each year. He had always been tall and had a large 6 ft 6 in stature, but when his wife noticed in spring of 2022 that he started to unintentionally lose weight quickly, it seemed odd, but tests and PET scans came back normal, so she attributed it to his other medications for diabetes. He kept losing weight and by July, he was at 160 lbs and "looked like a skeleton", but had no other respiratory symptoms. His wife pushed for more thorough testing, and in late October after a third CAT scan, doctors confirmed he had small cell lung cancer with a mass in his right hilum, and metastases in his brain and lymph nodes. When he got the diagnosis, doctors said he only had about 8-12 weeks to live without treatment, which GC recalls "*changed the entire trajectory of my life, but [I] was willing to battle this"*.

MW had been no stranger to small cell lung cancer, as her brother and father had both passed away within months of being diagnosed with the same disease at quite extensive stages. Ever since, she has kept a healthy lifestyle – she ate well, exercised, relaxed on cruises with her husband, and played pickleball at least once a week. At the beginning of 2023, she started noticing some wheezing out of her nose and upper airway, and also had to use her inhaler more often while playing pickleball, but didn't think much of it and attributed it to asthma or allergy symptoms. By April, she had caught a cold that wouldn't resolve, so she visited her doctor who ordered a chest x-ray, and further testing confirmed a diagnosis of small cell lung cancer in the right lung, with metastasis to the right adrenal gland. In her interview, MW recalls she had nearly no symptoms and even continued playing pickleball the day of her diagnosis, and was very grateful her case was caught relatively early, compared to her brother and fathers' cases. After her diagnosis, she received treatment with chemotherapy and immunotherapy before moving onto tarlatamab in November 2023, which she has been on ever since.

WL had always been accustomed to spending lots of time outdoors and at nights as he worked in highway maintenance, so during the summer of 2023 when there was a rather significant wildfire season in Ontario, he noticed he had been coughing more than usual and also felt short of breath. However, he didn't think much of it since he just attributed it to his line of work, the wildfire smoke, being outdoors for long hours, and also being a former smoker. It hadn't bothered him so when he went to his family doctor for an annual physical exam, he had been feeling fine and

didn’t think to bring it up. But his GP noticed it right away and scheduled him for a chest x-ray to be sure, which unexpectedly found a mass in his lungs. More tests and scans followed, which eventually confirmed a diagnosis of SCLC at the end of July 2023. He started treatment shortly after with first-line chemotherapy, then switched back and forth between immunotherapy and more chemo before eventually starting the tarlatamab clinical trial in June 2024, which he had been on ever since.

Small cell lung cancer is an aggressive type of lung cancer, representing roughly 10-15% of all lung cancer cases with a high symptom burden, rapid disease progression, and poorer outcomes; yet in recent years, there have been few developments in new treatment options for those with SCLC. Currently, the standard treatments available beyond first line therapy remains chemotherapy, potentially immunotherapy, and experimental trials, but there are very limited options beyond that, especially for extensive stage SCLC. Although most patients have a positive response to initial therapy, duration of response is limited and progression usually occurs within months. As a result, there is an urgent unmet need for new treatments in this population in second-line and beyond.

Tarlatamab is a newly FDA-approved immunotherapy drug to treat small-cell lung cancer via a targeted mechanism of action that guides T-cells to specifically target and destroy cancer cells that have the DLL3 protein expressed on their surfaces, whereas healthy cells have DLL3 found inside rather than on the surface. Since DLL3 is present in most small-cell lung cancer patients, this therapy has significant potential to become a new standard of care therapy that presents patients with a much more targeted option than existing systemic therapies.

The phase 2 DeLLphi-301 trial showed very encouraging results while evaluating the efficacy and safety of two different doses of tarlatamab in patients with advanced-stage small-cell lung cancer who had already undergone prior treatments. As per the trial results, the median progression-free survival of the 10 mg group was 4.9 months and 3.9 months for the 100mg arm, while the median overall survival was 14.3 months for the 10mg group [1]. Estimates of overall survival for the 10 mg group at 6 months and 9 months were 73% and 68% respectively, and 71% and 66% respectively in the 100-mg group [1]. The study results are very promising for the SCLC patient population and tarlatamab represents a new and additional immunotherapeutic approach for the disease in Canada.

With this new treatment, patients can live longer, manage their symptoms, be independent, have a good quality of life, and even go back to work. Patients already have a huge burden coping with their lung cancer diagnosis; the battle to survive this disease should be made easier by ensuring the availability of treatments that work beyond what is already the standard in Canada. For patients with extensive stage SCLC where the treatment goal is to relieve symptoms, manage disease progression, and prolong life, tarlatamab has the potential to achieve this as an additional option in the second-line setting and beyond.

Reference:

[1] Ahn MJ, Cho BC, Felip E, Korantzis I, Ohashi K, Majem M, Juan-Vidal O, Handzhiev S, Izumi H, Lee JS, Dziadziuszko R. Tarlatamab for patients with previously treated small-cell lung cancer. New England Journal of Medicine. 2023 Nov 30;389(22):2063-75.

4. Experiences With Currently Available Treatments

In Canada, the standard of care for patients with extensive-stage small cell lung cancer remains chemotherapy, though immunotherapy has recently taken a more prominent role in the treatment paradigm for these patients. Radiation is also a standard treatment option to treat specific metastases.

Chemotherapy:

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For patients with extensive stage disease, chemotherapy is typically presented as the first-line of treatment and has been a long-standing and well-documented standard of care for SCLC patients. It is successful in treating disease, however, its duration of response is quite limited as patients often progress within several months, in addition to its harsh side effects, impact on the individual's functionality, and increases dependence on caregivers in their daily activities. These have been well documented in previous submissions.

After **GC** was diagnosed in October 2022, he immediately started chemotherapy, with durvalumab added in after the 4th treatment. In total, he had 2 sessions of chemotherapy + durvalumab - 12 treatments in the first session and 18 in the 2nd round, until he stopped both treatments in January 2024 due to neutropenia. GC recalls with chemotherapy, he didn't have nausea thanks to the medications given to him prior to treatment, but felt significant exhaustion for a few days after treatment, though he still went to work everyday when he felt well. Additionally as a diabetic, his blood sugar was very difficult to manage prior to tarlatamab, where it was consistently high on chemotherapy for roughly 1.5 weeks after each treatment and required consistent insulin. He recalls at one point, he had to check his blood sugar 6 times per day, which was difficult to work and plan around in his daily activities.

MW also started first-line chemotherapy soon after diagnosis in May 2023 - she completed 4 rounds of carboplatin and etoposide combined with atezolizumab together, noting she had a good response to treatment and the side effects were relatively manageable. She felt nausea, fatigue, light-headed, and also had to pack and move to a new home in the midst of treatment. For the first 2 days after each chemo treatment, she couldn't take on many physically demanding tasks, and even navigating stairs, bending down, and moving heavy boxes took a toll where her husband had to take care of most of the moving process on those days. However, she recalls after the first few days, she felt better and continued to go to the beach, swim, and pack up the house. She also lost her hair during the process which also decreased her morale, but was able to keep pushing along with the treatment.

WL started first-line treatment with chemotherapy in early August 2023 shortly after diagnosis, where his regimen included 3 weeks of treatment and 1 week off over a total of 3 months. Prior to even starting the treatment, his disease had spread further into his liver since his initial diagnostic scans, and only highlighted the urgency of starting treatment. Similar to GC and MW, he felt okay the first two days immediately after treatment, but started feeling the side effects on day 3 - low energy, feeling nauseous and sick, and couldn't do any physically demanding tasks. He recalls the first three months of chemo was hard on him, but was quite successful in shrinking his tumours - the liver tumour shrunk considerably where doctors could hardly measure it, and the primary lung tumour was now half the initial size. He then started immunotherapy treatment but after it was unsuccessful, he started 2 more sessions of chemotherapy over the course of several months before starting tarlatamab in June 2024.

Immunotherapy:

GC also had durvalumab in combination with chemotherapy starting after the 4th dose of chemo. GC recalls he tolerated durvalumab relatively well with no nausea or sickness, and felt slightly better than on chemotherapy. He also mentioned durvalumab exacerbated the pain and breakouts of his psoriasis and arthritis, which made it hard and painful for him to use his hands to the point where his wife had to take care of most chores around the house. Additionally, while his blood sugars on chemotherapy were consistently high, durvalumab had the opposite effect and his sugar levels were severely low. He stopped durvalumab in January 2024 because of neutropenia, and all of these issues were, as GC stated, "nearly miraculously resolved" when he started tarlatamab in May.

Similar to GC, **WL** also had treatment with durvalumab after the first 3 months of chemotherapy were successful, but unfortunately after 2-3 sessions on durvalumab, his disease had spread further so he was taken off.

Two weeks after she completed her first-line treatment with atezolizumab in combination with chemotherapy, **MW** started atezolizumab monotherapy at the beginning of September 2023, but only 4 weeks into treatment, her scans

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showed further growth again, so she stopped and was able to enroll into the clinical trial to receive tarlatamab. Because she only received atezolizumab for a short amount of time, in addition to its first treatment being in combination with chemo, MW says it was difficult to recall specific side effects from this treatment.

Radiation:

Before **MW** started treatment with tarlatamab via clinical trial in November 2023, she had to have preliminary lab work done including a brain MRI, which showed she had two small spots the size of a sprinkle on her brain. She received gamma knife radiation to treat them, and had to wait two weeks before she could begin the trial. Later on in early July 2024, she had to be removed from the tarlatamab trial because of slight growth in her hilum area, and doctors determined she needed to have 10 sessions of radiation to her chest. She didn't have many side effects from the radiation other than a mild sunburn-like effect on her skin, which was managed easily with creams.

5. Improved Outcomes

Recent advancements in SCLC research have been limited, and outcomes for patients have remained poor in comparison to the rapid developments that have been made in recent years for NSCLC. The treatment options for SCLC patients beyond first-line chemotherapy and immunotherapy have been nearly next to nil. There is an urgent need for a new treatment like tarlatamab in this disease area that:

- Is effective in controlling extensive disease and managing symptoms
- Has manageable side effects
- Allows them to have a meaningful quality of life
- Allows them to improve/maintain independence and functionality to minimize caregiver burden
- Delays disease progression
- Gives patients the freedom of an additional treatment option when they progress on standard of care or have exhausted other options

6. Experience With Drug Under Review

Name	Diagnosis Date	Drug access method	Period on Tarlatamab	Duration on Tarlatamab	Tarlatamab line of treatment	Still on tarlatamab? (Aug 2024)
GC	October 2022	Health Canada - Special Access Program	May 2024 - Present	3 months +	3rd line +	Yes
MW	May 2023	Clinical Trial	November 2023 - present	9 months +	3rd line +	Yes
WL	July 2023	Clinical Trial	June 2024 - present	2 months +	3rd line +	Yes

Tarlatamab is effective at treating disease and delaying progression.

When **GC** got the diagnosis of small cell lung cancer, doctors initially told him he had approximately 8-12 weeks to live without treatment. He had a mass in his right hilum and metastatic spread to his brain, spine, and lymph nodes. He

started tarlatamab in May 2024, approximately 1.5 years after diagnosis, and has remained on it ever since. GC says his scans shortly after his first few treatments on the drug showed slight shrinkage in some tumours but stabilization in others. However, GC has already noticed a significant change in his symptoms, where the drug has completely relieved his pain almost everywhere, especially in his sternum, and feels “better and better each day”. Unfortunately, his most recent scans on Aug 9 showed his disease had spread once again into his pelvic bone and lymph nodes, and his oncologist is leaning towards taking him off the drug and into a different clinical trial. However, GC says he is grateful that tarlatamab has bought him extra time and was still able to live a great quality of life for the 3 months while on it.

Since starting tarlatamab in late November 2023, **MW** has had 17 treatments of it and has been tolerating it very well and all of her scans have since shown significant shrinkage everywhere except the right adrenal gland. She had the adrenal gland removed in mid-April 2024, and subsequent scans were good, until July 2nd, when there was slight growth in her hilum area. As mentioned in Section 4, she had to end the trial and received 10 sessions of radiation to the chest, which she completed in mid-August. However, her oncologist was able to have MW continue to receive the drug off-trial and will resume tarlatamab treatment shortly thereafter.

Two of three patients experienced Cytokine Release Syndrome (CRS) during their first infusion.

During **GC**’s first treatment of tarlatamab, he received the initial 1 mg tester dose roughly around noon, but by 10pm his symptoms escalated quickly. He became restless, had “incredible pain” in his thigh where he felt exactly where the drug was attacking the metastases in his body. Around 2am, his blood pressure had dropped, the pain had now spread across his back, legs, and chest, was confused, and his temperature had skyrocketed and he became very hot. GC’s wife (who is a retired nurse practitioner) was permitted to stay with him overnight and she recalled seeing how “out of it” he was. She recalls, *“he didn’t seem like himself and was saying things to me that seemed so out of place and out of sorts*”. He also developed arrhythmias during the first night in hospital but received medication for it, and also had a catheter since he developed numbness in his left leg and couldn't walk. By the time his wife came back to the hospital the next day, he was much more alert and slowly felt better and more like himself. Ultimately, it took GC about 1.5 days after the first dose to recover, but seeing how dramatic and scary the reaction was during the first dose, she was very nervous and reluctant about him continuing the treatment, but ultimately GC chose to move forward and received the 2nd dose while still in-patient, and they recalled that this time, the reaction “didn’t even come close to what happened the first time”.

WL had milder CRS symptoms than GC, but also had to receive the treatment as an inpatient for the first few doses. On the first dose, he felt fine all day, ate dinner and then went to sleep with no issues. When the nurses woke him up around 2am, he felt a bad headache and “didn’t feel right”, but his vitals were good so he went back to sleep. Around 6am, he had spiked a high fever, felt even worse, had an elevated heart rate, and had a stomach ache, which were treated via IV medication, and WL felt much better within 30 mins. He was discharged 2 days later and everything was fine until about 30 hours after receiving his 2nd dose, he spiked a fever again and he was readmitted and monitored for another 3 days. His 3rd dose was also received as an inpatient and monitored for 48 hours, but had no reaction and has since received the drug as an outpatient. WL recalls he had relatively moderate symptoms compared to other patients, but it was just scary for him and his wife with the unknown, especially around the first dose.

Side effects were significant during the first treatment (as expected) but dramatically improved over time.

As a result of the difficult CRS symptoms that **GC** experienced during the first dose, he remained in the hospital for 10 days while receiving subsequent tarlatamab doses, but overtime the reactions became much milder. At the time of his interview in July, GC says most of the effects from that first dose when he experienced CRS has almost completely resolved, and now has very minimal side effects. He noted fatigue, loss of appetite, and metallic taste in his mouth as the main adverse effects nowadays, but they don’t impede his day-to-day life. GC also lost 20 lbs while in the hospital and still has trouble maintaining and gaining back the weight since the metallic taste also correlates with the loss of appetite and struggles with eating, but he has learned work-arounds to help himself eat like using plastic utensils, enjoying certain cold foods and citrus flavours, and avoiding red meat. In addition, GC had struggled with psoriasis and arthritis mutilans for decades, and while on durvalumab, his psoriasis got worse and had trouble gripping things with his

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left hand. However, his arthritic symptoms have unexpectedly resolved with tarlatamab and can now easily grip with his left hand after years of not being able to. GC now receives the drug as an outpatient without requiring a wheelchair, and says that all the side effects he experiences are certainly manageable with simple lifestyle adjustments with almost no impact on his day-to-day life.

Similarly, **WL** also has not had any adverse reaction since his second dose of tarlatamab, and his side effects now are very minimal. He notes he only felt slightly nauseous a few times and struggles with dehydration, but he has a nurse help hook him up to IV at home and feels fine afterwards. He recalls compared to chemotherapy when he constantly felt nausea and low energy, he feels almost normal in between doses with next to no side effects.

Luckily, **MW** did not experience cytokine release syndrome and was able to go home a couple hours after receiving her first dose. Even during her first infusion, she only had mild flu-like symptoms for 1-2 days. She developed a headache, mild fever, and chills about 4 hours after being sent home and symptoms only lasted for about a day. MW says she felt basically normal after that, and even had a large Thanksgiving dinner with family a few days later. Ever since, she returned for infusions every 2 weeks and the only side effects she has nowadays are feeling slightly more tired, and altered taste, which was difficult to manage what to eat but has learned to work around, such as avoiding processed foods. She says that both of these mild effects have next to no impact on her daily life or functionality.

Quality of life was significantly improved on tarlatamab compared to previous therapies. Patients agreed their current lifestyle is quite similar to pre-diagnosis.

By the time he started first-line treatment with chemotherapy, **GC**'s wife recalls he was weak and exhausted, and couldn't even shower himself, so she had to step in to care. She had to help bathe him, cook meals, clean the house, grocery shop, and he was slow at using the stairs. After the first few tarlatamab treatments, the side effects had gradually become quite minimal, the numbness in his left leg is now subsiding, his back and leg pain is gone. Within 2 weeks, he was able to walk without the use of a walker, and even started to get back to work. Because of the brain mets, he was also not allowed to drive for 8 months, so his wife had to drive him to all his hospital appointments while also running errands for the home. But as of August 2024, he's now able to drive himself again, his pain has resolved, can go to the store for errands with no issues, enjoys meeting with friends, and has even returned to playing golf and is competing in a golf tournament this summer. Although GC's wife was incredibly nervous about him going into the second dose, they said they were so happy they did. GC reiterates his quality of life now is great, he has his independence and mobility back, feels mentally stronger and more energetic, and ultimately, his hope/outlook has completely turned around 360 degrees since starting the treatment.

For **MW**, she says that her quality of life while on tarlatamab is nearly comparable to pre-diagnosis, although she's not nearly as active as before but has no issues in her day-to-day life. She cleans the house, shops for groceries, drives into town to run errands, and does lots of physical activity when she can. As both her and her husband are quite physically active, she has gone back to swimming, walks as much as she can, rides her electric bike, and is soon hoping to get back to playing pickleball as well. MW says she faces the fact that she still has cancer and feels more tired now, but being able to have her independence, functionality, and great quality of life are all values she "wouldn't trade for anything", thanks to the success she found with tarlatamab.

Similarly, **WL** also says after the scariness of the initial doses, he has had no reaction ever since and minimal side effects, and continues to have a good quality of life in between treatments. He has no problems caring for himself, doing housework, cooking, grocery shopping, and meeting with friends in the 1.5 weeks between treatments. He has no issues driving and did attend one of his hospital appointments alone once, but his wife likes to accompany him to each appointment for emotional support.

Patients agreed their overall experience with tarlatamab was significantly better than previous therapies.

Patients were asked during their interviews how they would rank their experience with tarlatamab overall in comparison to other therapies they've experienced on a scale of 1-10; 1 being "*Tarlatamab was absolutely worse than other*

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therapies/I would strongly prefer other therapies to tarlatamab", 5 being *"about the same*", and 10 being " *Tarlatamab was absolutely better than other therapies/I would strongly prefer tarlatamab to other therapies"*.

The average ranking was a 9.5, where both GC and MW ranked their experience at a 10, and WL ranked an 8.5, showcasing the strong preference for tarlatamab over other therapies like chemotherapy and immunotherapy.

For **MW,** she said there was "no comparison" to her previous treatment of chemotherapy, and **GC** says *"there is no buying what I've gotten out of the drug - it has been so successful"*. On tarlatamab, both are able to live relatively normal lives, and have almost no side effects. MW recalled that the success of chemotherapy and immunotherapy disease stayed relatively unknown to her, but she was able to see and even feel the results of tarlatamab relatively quickly, which had an incremental boost to her morale as she continued treatment.

All three patients are currently living great quality of lives, and are able to look beyond their diagnosis and into the future. **WL** is just focusing on maintaining his health and keeping his life afloat. With GC and MW being in retirement, they are still able to have incredible quality of lives that allow them to get back to activities they feel joy with - **GC** is working part-time again and **MW** is enjoying life and staying active with her husband. Tarlatamab has given these patients their livelihoods back whilst treating their disease and giving them the time and freedom to spend with their loved ones, which seemed impossible at diagnosis with such an aggressive disease. Innovative drugs like tarlatamab are an urgent need for SCLC patients when they've exhausted other options, and tarlatamab has shown to achieve this.

One patient even continues to work throughout treatment.

A few weeks after starting tarlatamab, **GC**'s outlook and side effects had improved so drastically that he even returned to work. He had been a firefighter for 42 years and still loved his job even after retiring years ago, and since finding success with tarlatamab in May 2024, he continues to work part-time a few days per week for a health and safety company to maintain their air packs. He says that tarlatamab had completely turned his outlook on life around after being diagnosed with small-cell lung cancer almost 2 years ago, but is very happy he's able to give back to the community and be a good citizen even after officially retiring. His wife noted he was eager to get back to work to keep his mind and body active with a positive outlook.

GC said during his interview, *"I love what I do, being an active member of society. I should have been at work today but only took the day off to speak with [LCC]. Compared to only 2 months ago before I started the drug, today just feels like a normal Friday where I have my coffee in the morning and get ready for work. I'm so incredibly grateful for how tarlatamab has completely turned my quality of life around"*.

WL hasn't gone back to work since his diagnosis in July 2023, which he is eager to do for financial reasons. He worked as a highway maintenance worker and spent a lot of time outdoors at night, and especially during the summer, it was tough for his body to be outdoors for extended periods during the peak wildfire season last year, when he considered going back but his cancer had progressed. However when speaking with LCC, WL is eager to get back as soon as he can thanks to the good quality of life he's been able to maintain while on tarlatamab.

7. Companion Diagnostic Test

Tarlatamab for SCLC does not require any biomarker testing.

8. Anything Else?

No

Appendix: Patient Group Conflict of Interest Declaration

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

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

No

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

No

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

Table 1: Financial Disclosures

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

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen 2022 - LCC			X	
Amgen 2023 - LCC			X	
Amgen 2024 - LCC			X	
Amgen 2023 - CCSN			x	
Amgen 2024 - CCSN			x	
Amgen 2023 - LHF			x	
Amgen 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: Shem Singh
Position: Executive Director
Patient Group: Lung Cancer Canada
Date: August 22, 2024

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CADTH

CADTH Reimbursement Review
Clinician Group Input Template
CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0351-000
Generic Drug Name (Brand Name): tarlatamab
Indication: For the treatment of adult patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after at least two prior lines of therapy including platinum-based chemotherapy.
Name of Clinician Group: OH (CCO) Lung Cancer Drug Advisory Committee
Author of Submission: Dr. Donna Maziak, Dr. Andrew Robinson, Dr. Peter Ellis, Dr. Stephanie Brule, Dr. Mihaela Mates

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.

3. Current Treatments and Treatment Goals

An ideal treatment would prolong life and minimize toxicity. Extensive stage small cell lung cancer patients have a very dismal prognosis.

The current main treatment is palliative care/best supportive care.

Treatment in third line is not, or marginally effective, particularly when platinum refractory.

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.

Treatment that can prolong life or quality of life are not being met. A treatment option for fit patients for whom conventional therapy has failed is needed. The average life expectancy after progression is 2 to 3 months.

5. Place in Therapy

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

It would be after platinum doublet and durvalumab treatment for most patients, and often either one retreatment or a second marginal agent such as topotecan. The drug would be a last line of treatment most likely (unless a very good response and late progression). It would not be used in combination with other treatments at this stage. It would not be used as a first line treatment. It would only be used in select patients with a higher physiologic reserve than a typical small cell lung cancer patient, as patients would be required to have adequate physiologic reserve.

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?

Treatment would be best suited for fit patients with a performance status of 0-1, with progressive small cell lung cancer, with the capacity for self management and adequate physiologic reserve.

It would be stage IV patients with small cell lung cancer.

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?

Treatment benefit would typically be assessed using both clinical parameters (reduction in symptoms), and radiologic parameters, with imaging every 6-12 weeks for the first year.

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

Significant toxicity that does not resolve, unequivocal disease progression.

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]?

Currently this should be administered in cancer centres, with the first cycle administered as an inpatient, with rapid access to supportive medications such as dexamethasone and tocilizumab. A 24-hour observation hospitalization was trialed in this study, but centres may feel comfortable with a 48-hour observation period.

Ideally, this drug is giving in a centre with staff with specialized training, knowledge and comfort with cytokine release syndrome and immune-cell associated neurotoxicity management i.e. familiar with T cell engaging therapies.

6. Additional Information

This is a highly difficult to treat patient population, with a fairly high upfront non-monetary cost for this therapy, in terms of risks of CRS etc. The 40% response rate seen in the early phase clinical trial, and the duration of response, show that this is an effective drug, and the duration of benefit is always updated.

This therapy currently requires inpatient administration at least initially. This will create some resource issues for many hospitals that are under major pressure on inpatient beds. It will also likely not be able to be administered in some smaller hospitals, particularly in the community setting.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation.

Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH (CCO) provided a secretariat function to the group.

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

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Donna Maziak
Position: Lead, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 16-08-2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add 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: 10-08-2024

☒ 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. Peter Ellis
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 12-08-2024

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

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Amgen – Advisory board meeting	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. Stephanie Brule
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 16-08-2024

☒ 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
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 5

Name: Dr. Mihaela Mates
Position: Member, OH (CCO) Lung Cancer Drug Advisory Committee
Date: 16-08-2024

☒ 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.

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0351-000
Generic Drug Name (Brand Name): Tarlatamab
Indication: Advanced Small-cell lung cancer previously treated with two or more lines of systemic therapy.
Name of Clinician Group: Lung Cancer Canada – Medical Advisory Committee
Author of Submission: Dr. Shaqil Kassam (lead), Dr. Vishal Navani, Dr. Normand Blais, Dr. David Dawe, Dr. Dave Stewart, Dr. Shantanu Banerji, Dr. Nicole Bouchard, Dr Callista Phillips, Dr. Mahmoud Abdelsalam, Dr. Stephanie Snow, Dr. Parneet Cheema, Dr. Rosalyn Juergens, Dr. Alison Wallace, Dr. Biniam Kidane, Dr. Kevin Jao, Dr. Mark Vincent, Dr. Geoffrey Liu, Dr. Silvana Spadafora, Dr. Lacey Pitre, Dr. Quincy Chu, Dr. Barb Melosky, Dr. Ron Burkes, Dr. Michela Febbraro, Dr. Nathalie Daaboul, Dr. Catherine Labbé, Dr. Cheryl Ho, Dr. Paul Wheatley-Price, Dr. Randeep Sangha, Dr. Sunil Yadav

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 have been providing clinician input for submissions of new lung cancer drugs to the HTA process for many years. The LCC MAC consists of clinicians and key opinion leaders in the field of lung cancer across the country.

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 (Amgen).

3. Current Treatments and Treatment Goals

Small cell lung cancer (SCLC), accounting for 10-20% of lung cancer cases annually in Canada and 10-15% globally (Rudin et al, 2015), is an aggressive subtype of lung cancer with neuroendocrine differentiation, and characterized high growth rate, rapid doubling time, and early establishment of

widespread metastatic lesions (Gustafsson et al, 2008). About one-third of patients present with limited stage disease (LD-SCLC) that can be treated with concurrent platinum/etoposide chemotherapy and thoracic radiation followed by consolidation durvalumab therapy (Spigel, JCO 2024). The remaining two-thirds have extensive disease (ED-SCLC), for which the treatment is mostly systemic therapy.

Currently, most patients with extensive stage disease are treated with a combination platinum/etoposide and Anti-PDL1 therapy for 4 cycles followed by Anti-PDL1 maintenance therapy until disease progression or intolerance (Pas-Ares et al. Lancet Oncology 2019, Horn et al, NEJM 2018). Despite initial high sensitivity to first-line chemotherapy with response rates in the range of 60-70%, most patients with ED-SCLC develop drug resistance and typically die within 9-13 months from diagnosis; even with the addition of anti-PDL1 therapy, only 18% of patients are still alive at 36 months from diagnosis (Rudin et al, 2015;Paz-Ares et al, ESMO Open 2022).

Treatment options for SCLC patients with disease recurrence after initial combined chemoradiotherapy followed by consolidation durvalumab for LD-SCLC or patients with ED-SCLC with progression after chemotherapy ± anti-PDL1are limited and depend on the time from the last cycle of platinum-based chemotherapy to disease progression or recurrence, ECOG performance status, and patient wishes based on toxicity and efficacy. For patients with ECOG 0-2 and disease progression or recurrence at least 3-6 months from the last dose of platinum-based chemotherapy (platinum-sensitive disease), treatment options include:

1. Retreatment with platinum/etoposide: A phase III study comparing retreatment with carboplatin/etoposide versus topotecan demonstrated an improvement in median progression-free survival (mPFS, 4.7 m versus 2.7 m, p=0.0041, HR=0.57), higher response rate (ORR, 49% versus 25%, p=0.0024), and lower incidences of grade 3 or higher toxicity (14% versus 22%) in the carboplatin/etoposide-treated patients, with similar incidence of hematological toxicity except higher incidences of grade 3-5 neutropenia and febrile neutropenia in the topotecan-arm (14% versus 25% and 6% versus 11%, respectively) and median overall survival (mOS) of 7.5 months. (Baize et al. Lancet Oncol 2020). Patients with LD-SCLC who had not received consolidation durvalumab after Chemoradiotherapy could be candidates for retrial of Platinum Etoposide + Anti-PDL1 as these patients would have been candidates to be randomized into the Caspian Trial.

2. IV topotecan or CAV Chemotherapy: Topotecan demonstrated comparable ORR (24.3% versus 18.3%, p=0.285), mPFS (13.3 weeks versus 12.3 weeks, p=0.552), and mOS (25 weeks versus 24.7 weeks, p=0.795) to cyclophosphamide/adriamycin/vincristine (CAV) in SCLC patients with disease progression at least 60 days from the last dose of chemotherapy (von Pawel et al. JCO 1999). The randomized phase II study comparing IV and oral topotecan in SCLC patients who had disease progression at least 6 months from the last dose of chemotherapy in the first-line setting reported an ORR of 15%, mPFS of 13.1 weeks, and mOS of 25.1 weeks, with 16.4% requiring dose reduction due to common grade 3 or 4 toxicities such as neutropenia, thrombocytopenia, and anemia (von Pawel et al. JCO 2001). Similar ORR (21.9%), mPFS (14.6 weeks), and mOS (35 weeks) were reported in the IV topotecan-arm of a phase III study comparing IV to oral topotecan in SCLC patients with recurrence or progression after first-line chemotherapy (Eckhardt et al. JCO 2009). A meta-analysis of

both IV and oral topotecan in the platinum-sensitive setting reported an ORR of 17% and a 1-year OS rate of 27% (Horita et al. Sci Rep 2015)

3. IV Lurbinectedin: Lurbinectedin is an alkylating agent that has Health Canada approval but is not funded publicly in Canada for patients with metastatic small cell lung cancer (SCLC) who have experienced disease progression on or after platinum-based chemotherapy. It is administered at a dose of 3.2 mg/m^2 intravenously (IV) every three weeks. In an open-label study SCLC who had no brain metastases and had progressed on or after platinum-based chemotherapy, 8 percent of whom had also received prior immunotherapy, the overall response rate (ORR) to lurbinectedin was 33 percent according to an independent review committee. The median duration of response was 5.1 months, with 25 percent of responding patients experiencing a duration of response exceeding six months. Among patients with resistant relapse (chemotherapy-free interval <90 days), the ORR was 22 percent, with a progression-free survival (PFS) of 2.6 months and an overall survival (OS) of 5 months. For patients with sensitive relapse, the ORR was 45 percent, with a PFS of 4.5 months and an OS of 11.9 months. Serious adverse reactions occurred in 10 percent of patients, with neutropenia and febrile neutropenia being the most common. (Trigo et al, Lancet Oncology 2022). It is of particular interest that Lurbinectedin did not receive a positive Cadeth review and has not received public reimbursement, this is of particular consequence as Lurbinectedin is well tolerated, efficacious and maximizes quality of life as it requires a fraction of the visits to cancer centres compared to the more widely used topotecan. In addition, due to lack of reimbursement, Lurbinectedin does not have commercial supply in Canada, is not available for private pay use.

For patients with ECOG 0-2 and progression or recurrence of disease while on treatment or less than 3 months from the last dose of platinum-based chemotherapy (platinum-resistant or refractory), treatment options are very limited even for those who wish for further treatment:

1. IV topotecan: A meta-analysis reported an ORR of 5% and a 1-year OS rate of 9% in platinum-refractory SCLC patients treated with IV and oral topotecan (Horita et al. Sci Rep. 2015).
2. CAV with an ORR of 5% (Tiseo et al. JTO 2007).
3. Lurbinectedin: See above.

After patients have progressed on second-line therapy, data on subsequent treatment options is limited, and decisions are typically made through a collaborative process between the clinician and patient. Treatment may be offered to patients with adequate performance status and acceptable hematologic parameters. Evidence supporting single-agent chemotherapies is primarily derived from older Phase II trials with sample sizes typically ranging from 50 to 100 patients.

Single-agent chemotherapy options include:

- Paclitaxel, with response rates of 30% (Smit et al., British Journal of Cancer, 1998)

-Temozolomide, with a response rate of 16% (Pitanza MC et al., Clinical Cancer Research, 1998)

- Gemcitabine, with a response rate of 12% (Hoang T et al., Lung Cancer, 2003)

While these treatments can provide palliation of rapidly progressing symptoms, they may have significant toxicities, and their impact on survival is uncertain. Given this, there is a significant need for better-tolerated therapies that provide patients not only palliation but also survival benefits after having progressed on two previous lines of therapy.

The Phase II Delphi-301 trial investigated tarlatamab in patients with relapsed/refractory small cell lung cancer (SCLC) who had progressed after two or more lines of therapy. The trial enrolled 222 patients across multiple sites, with 188 patients receiving either a 10 mg or 100 mg dose in both parts 1 and 2 of Delphi-301. The 10 mg dose was chosen for further evaluation. In the 10 mg group, the objective response rate was 40%, and the median progression-free survival (PFS) was 4.9 months. The overall survival rates at 6 and 9 months were 73% and 68%, respectively. Common adverse events included cytokine-release syndrome (51%), decreased appetite (29%), and ICANS (8%). Grade 3 or higher adverse events occurred in 59% of patients. Despite the toxicities, the manageable safety profile and notable antitumor activity suggest that tarlatamab offers a promising option for heavily pretreated SCLC patients.

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

The goals of treatment in the recurrent or relapse setting for SCLC who have progressed after 2 previous lines of therapy are:

1. Improvement in mOS
2. Prolonged mPFS and prolonged duration of response
3. High response rate and high and rapid reduction of tumour burden
4. Reasonable toxicity with low incidence of dose modification and immature termination of treatment due to toxicity
5. Improvement of health-related quality-of-life and disease-related symptoms.

Current treatment options are limited in their evidence base, and it is uncertain whether the data are applicable in the contemporary setting, where patients are often treated with both chemotherapy and immunotherapy in earlier lines. While small Phase II trials, as mentioned in Section 3, have provided some data on response rates, they have not demonstrated unequivocal survival benefits. Furthermore, patients who have undergone two lines of chemotherapy often have compromised hematologic reserves, making them less suitable for additional systemic chemotherapies. Therefore, there is a pressing need for novel, chemotherapy-free regimens.

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

Tarlatamab could potentially fit into the current treatment paradigm for small-cell lung cancer (SCLC) by addressing a significant unmet need in patients with extensively pretreated disease who have had at least 2 prior systemic therapies.

Tarlatamab represents a novel approach to cancer treatment by utilizing its bispecific T-cell engager mechanism. This drug uniquely targets delta-like ligand 3 (DLL3) on cancer cells and CD3 on T cells, effectively drawing T cells close to the cancer cells and enabling them to destroy the cancer cells directly. Unlike chemotherapy, which relies on broad-spectrum cytotoxic effects on rapidly dividing cells, tarlatamab's action is highly specific. (Ahn et al, NEJM 2023). Given this novel mechanism of action, an argument could be made that tarlatamab may offer a viable treatment option for patients who have only had one prior treatment and are not candidates for further chemotherapy due to hematologic issues or previous chemotherapy-related toxicities.

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?

Based on the study results from Delphi-301, the most suitable candidates for tarlatamab are patients with extensively pretreated small-cell lung cancer who have exhausted two or more lines of therapy, who retain an adequate performance status. Specifically, tarlatamab is well-suited for:

1. **Patients with Extensive-Stage Small-Cell Lung Cancer with an ECOG of 0-1**: The study primarily involved patients with advanced small-cell lung cancer who had previously been treated with at least two lines of therapy. Tarlatamab has demonstrated promising antitumor activity in this heavily pretreated population.
2. **Patients Who Cannot Tolerate Further Cytotoxic Therapy**: Given the limited treatment options and poor prognosis in heavily pretreated cases, patients who have experienced significant and non-resolving side effects from prior cytotoxic therapies (Organ dysfunction, hematologic toxicities) but still have disease progression after only 1 previous line of therapy, and retain a good performance status may benefit from tarlatamab as an alternative treatment option.
3. **Patients regardless of DLL3 Expression**: While tarlatamab is a DLL3-targeted therapy, it is noteworthy that its efficacy was observed irrespective of DLL3 expression levels, as shown by the Delphi-301 trial. This means that even patients with low or undetectable DLL3 expression can still benefit from tarlatamab. As such patient inclusion should not be predicated on DLL3 expression
4. **Patients Who Can Manage Potential Adverse Effects**: Patients should be prepared for potential side effects such as cytokine-release syndrome and neurotoxic events (ICANS), though these are generally manageable with supportive care and occur less frequently with the tarlatamab10 mg dose. Patients however with poor performance status, or poor physiologic reserve should consider tarlatamab with caution, as CRS and ICAN side effects can be difficult to recover from.
5. **Patients with good social support**: Although tarlatamab is a very efficacious treatment option, the toxicities are different and require on going vigilance for toxicities even after patients have left the systemic therapy suit.

6. **Requirement for inpatient admission for step up dosing**: See section 5.5

Overall, tarlatamab represents a viable option for patients with advanced small-cell lung cancer who have progressed beyond conventional treatments and cannot tolerate additional cytotoxic 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?

Monitoring patients with extensively treated small cell lung cancer (SCLC) requires a comprehensive approach that focuses on both symptom palliation and disease progression. These patients often present with significant symptoms, making it crucial to assess and manage symptom palliation at least once per month. While radiographic response is an important aspect of monitoring, it should not be the sole method used. Regular clinical evaluations are essential to ensure that the patient's quality of life is maintained. Imaging studies should be conducted approximately every 8 weeks or as clinically indicated, allowing for timely adjustments to the treatment plan based on both clinical and radiographic findings. This balanced approach ensures that patients receive optimal care tailored to their evolving needs.

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

In the context of the Delphi-301 trial, it is important to recognize that tarlatamab's mechanism of action differs from traditional therapies, and radiographic progression without clinical progression should not be the sole factor for discontinuing treatment. Bispecific antibodies, such as tarlatamab, may require time to demonstrate their full therapeutic potential, as evidenced by similar experiences with tebentafusp. This is due to unique mechanisms of action that lead to novel tumour response kinetics, including prolonged periods of disease stability often without evidence of objective imaging response. Therefore, clinical benefit should be assessed holistically, considering both radiographic and clinical responses over time before making treatment discontinuation decisions.

5.5 What settings are appropriate for treatment with Tarlatamab? Is a specialist required to diagnose, treat, and monitor patients who might receive tarlatamab?

Tarlatamab should be administered in specialized centers equipped to handle its unique infusion protocol and potential toxicities. Based on the Delphi-301 trial, patients should initially receive step-up dosing in an inpatient setting where they are closely monitored for cytokine-release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). The risk of CRS significantly diminishes after the step-up dosing period, but the risk of ICANS remains low yet consistent across subsequent infusions. Generally, adverse events tend to be grade 2 or less. Patients should be admitted for 24 hours post-infusion, provided no significant toxicities are observed; otherwise, they should remain hospitalized until symptoms resolve to Grade 0. Centers, whether academic or community-based, must collaborate with ICU, neurology, emergency

medicine, and infectious disease specialists to ensure comprehensive care and rapid intervention if required. Additionally, these centers must have access to appropriate rescue medications. Once transitioned to outpatient infusion, centers must monitor patients for 0-4 hours post-infusion and ensure ongoing vigilance by caregivers at home.

Tarlatamab represents the first regulatory body approved BiTE agent in thoracic malignancies and second in all solid tumours (after Health Canada approved and provincially available tebentafusp). There is increasing understanding and comfort amongst medical oncologists in managing the unique toxicities associated with BiTEs post their emergence. These therapies represent the vanguard of novel immunotherapeutic approaches for patients with poor prognosis malignancies.

6. Additional Information

Tarlatamab represents a novel treatment option for patients with extensively treated small cell lung cancer (SCLC), demonstrating promising efficacy and a manageable safety profile in the Phase II Delphi-301 trial. This trial, which included a substantial cohort of 222 patients, revealed objective response rates and landmark progression-free survival (PFS) and overall survival (OS) figures that are unprecedented in this patient population. Specifically, the 10 mg dose of tarlatamab achieved a 40% response rate, with a median PFS of 4.9 months and 6- and 9-month OS rates of 73% and 68%, respectively. Although toxicities such as cytokine-release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were observed, they were predominantly manageable, with most events being grade 2 or less. The trial underscores tarlatamab's potential as a valid treatment alternative for patients who have progressed on two or more prior lines of therapy or are otherwise not candidates for further conventional treatments.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   No

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

   No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Shaqil Kassam
Position: Medical Oncologist, Southlake Regional Hospital
Date: August 23, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
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 2

Name: Quincy Chu
Position: Medical Oncologist, Cross Cancer Institute, Edmonton, AB
Date: August 23, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 2

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

Amgen	X			
AnHeart	X			
Astellas	X			
Astra Zeneca		X		
Boehringer Ingelheim	X			
BMS	X			
Daichii Sankyo	X			
Eli Lilly	X			
GSK	X			
Janssen	X			
Meck	X			
Novartis	X			
Ocellaris	X			
Pfizer	X			
Roche		X		
Takeda	X			

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

Declaration for Clinician 3

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: August 23, 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 3

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

New or Updated Declaration for Clinician 4	
Name	Michela Febbraro
Position	Medical Oncologist, Algoma District Cancer Program
Date	August 23, 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 5	
Name	*Biniam Kidane*
Position	*Associate Professor, Dept of Surgery, University of Manitoba*
Date	August 23, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
AstraZeneca	☐	☐	☒	☐
Merck	☒	☐	☐	☐
Roche	☐	☒	☐	☐
Bristol Myers Squibb	☒	☐	☐	☐
Medtronic	☒	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	*Dr. Alison Wallace*
Position	*Assistant Professor Department of Surgery, Division of Thoracic Surgery and Department of Pathology, Dalhousie University. Thoracic Surgeon QEII HSC, Halifax. NS.*
Date	August 23, 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 7

Name: NATHALIE DAABOUL
Position: Hematologist-Oncologist, Université de Sherbrooke
Date: August 23, 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 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
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 8	
Name	*Ronald Burkes*
Position	*Medical Oncologist Mount Sinai Hospital*
Date	August 23, 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 9

Name: Silvana Spadafora
Position: Medical Oncologist, Algoma District Cancer Program
Date: August 23, 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 9

	Check appropriate dollar range*			
Company	**$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 10

Name: Dr. Kevin Jao
Position: Medical Oncologist, Hôpital Sacré-Cœur, Montreal
Date: August 23, 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 11

Name: Dr Catherine Labbé
Position: Head of Respiratory Medicine Service, Université de Laval
Date: August 23, 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 11

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 12

Name: Dr. Rosalyn Juergens
Position: Chair, LCC Medical Advisory Committee; Medical Oncologist, Juravinski Cancer Center
Date: August 23, 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 12

	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			

Declaration for Clinician 13

Name: Dr. Paul Wheatley-Price
Position: Medical Oncologist, The Ottawa Hospital. Associate Professor, Department of Medicine, University of Ottawa
Date August 23, 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 13

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

Pfizer	X			
Bayer	X			
Novartis	X			

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

New or Updated Declaration for Clinician 14	
Name	*Vishal Navani*
Position	*Medical Oncologist, University of Calgary*
Date	August 23, 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 15

Name: Normand Blais
Position: Medical Oncologist, CHUM Cancer Center, Montreal
Date: August 23, 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

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie	Advisory Board and Honoraria	☒	☐	☐	☐
Amgen	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Advisory Board and Honoraria	☒	☐	☐	☐
Beigene	Advisory Board and Honoraria	☒	☐	☐	☐
Bristol-Myers Squibb	Advisory Board and Honoraria	☒	☐	☐	☐
EMD Serono	Advisory Board and Honoraria	☒	☐	☐	☐
Merck	Advisory Board and Honoraria	☒	☐	☐	☐
Novartis	Advisory Board and Honoraria	☒	☐	☐	☐
Pfizer	Advisory Board and Honoraria	☒	☐	☐	☐
Roche	Advisory Board and Honoraria	☒	☐	☐	☐
Sanofi	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Research Funding to institution	☐	☐	☐	☒

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

Declaration for Clinician 16

Name: Dr Randeep Sangha
Position: Medical Oncologist, Cross Cancer Institute
Date: August 23, 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 16

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 17

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: August 23, 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 17

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 18

Name: Dr. Barb Melosky
Position: Medical Oncologist, BC Cancer
Date: August 23, 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
Novartis	Advisory Board	☒	☐	☐	☐
Roche	Advisory Board	☒	☐	☐	☐
Merck	Advisory Board	☒	☐	☐	☐

New or Updated Declaration for Clinician 19	
Name	*David J. Stewart*
Position	Professor of Medicine, University of Ottawa and The Ottawa Hospital
Date	August 23, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Merck Canada 2021, 2023	☒	☐	☐	☐
AstraZeneca Canada 2021, 2023	☒	☐	☐	☐
Abbvie Canada 2021, 2022, 2023	☒	☐	☐	☐
Canadian Agency for Drugs and Technologies in Health 2021	x			
Amgen Canada 2022	x			

New or Updated Declaration for Clinician 20	
Name	*Dr. Geoffrey Liu*
Position	*Medical Oncologist*
Date	August 23, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☐	☒	☐	☐
Novartis	☒	☐	☐	☐
Anheart	☒	☐	☐	☐

Takeda	X			
AstraZeneca		X		
Jazz	X			
Roche	X			
Johnson & Johnson	X			
EMD Seron	X			
Merck	X			

Declaration for Clinician 21

Name: Dr. David Dawe
Position: Medical Oncologist, CancerCare Manitoba
Date: August 23, 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 21

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 22

Name: Dr Nicole Bouchard
Position: Respirologist, Sherbrooke University Hospital
Date: August 23, 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 22

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
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 23

Name: Callista Phillips
Position: Medical Oncologist and Clinical Lead, Oncology Clinic, Joseph Brant Hospital
Date: August 23, 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
AstraZeneca	X			
Bayer	X			
Roche	X			

Declaration for Clinician 24

Name: Stephanie Snow
Position: Professor Dalhousie University, Medical Oncologist QEII Health Sciences Centre, Halifax, NS
Date: August 23, 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	
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 25

Name: Dr. Parneet Cheema
Position: Medical Director of Cancer Care, William Osler Health System
Date: August 23, 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 25

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 26

Name: Dr. Mark Vincent
Position: Medical Oncologist, London Regional Cancer Centre
Date: August 23, 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
			☐	☐	☐

Declaration for Clinician 27

Name: Dr. Cheryl Ho
Position: Medical Oncologist, BC Cancer
Date: August 23, 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 27

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 28

Name: Lacey Pitre
Position: Medical Oncologist, Systemic Therapy Lead - Northeast Region, CCO/Ontario Health
Date: August 23, 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 28

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

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

Declaration for Clinician 29

New or Updated Declaration for Clinician 33	
Name	*Shantanu Banerji*
Position	*Medical Oncologist, Manitoba CancerCare*
Date	August 23, 2024
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Astrazeneca	☐	☒	☐	☐
Roche	☐	☒	☐	☐
Add or remove rows as required	☐	☐	☐	☐