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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

acalabrutinib (Calquence)

(AstraZeneca Canada Inc.)

Indication: Acalabrutinib in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL).

April 7, 2025

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

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CADTH

CADTH Reimbursement Review
Patient Input Template

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: Acalabrutinib (Calquence)

Indication: Acalabrutinib in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL).

Name of Patient Group: Lymphoma Canada

Author of Submission: Gurjot Basra, Manager of Patient Programs, Research, and Advocacy

1. About Your Patient Group

Lymphoma Canada is a national Canadian registered charity whose mission it is to empower patients and the lymphoma community through education, support, advocacy, and research. Based out of Mississauga (ON), we collaborate with patients, caregivers, healthcare professionals, and other organizations and stakeholders, to promote early detection, find new and better treatments for lymphoma patients, help patients access those treatments, learn about the causes of lymphoma, and work together to find a cure. Resources are provided in both English and French. www.lymphoma.ca

2. Information Gathering

The data presented in this submission was collected from an online anonymous patient survey, created and promoted by Lymphoma Canada (LC) available from January 31st to April 6th, 2025. The link was promoted via e-mail to patients registered in the LC national emailing list and made available via social media outlets, including Twitter, Instagram, and Facebook accounts. The survey had a combination of multiple choice, rating, and open-ended questions. Skipping logic was built into the survey so that respondents were asked questions only relevant to them. Open-ended responses were noted in this report verbatim, to provide a deeper understanding of patient perspectives. 102 responses were collected amongst those who had Mantle Cell Lymphoma (MCL). Information from this survey was used to identify the main areas of concern for patients with MCL, with 8 confirmed responses for experience with the therapy under review, Acalabrutinib in combination with bendamustine and rituximab. Of the 8 patients who received this therapy, 5 were male and 3 were female, ages ranging from 35-74. 5 of these patients were from Canada, and 3 were from the United States.

Please see tables 1-4 below for demographic and relevant information of all survey respondents. The majority of patients lived in Canada (78%), between the age of 65 and 74 (37%) or 75 and 84 (25%), female or male (50% for both), and were diagnosed 3-5 years ago (31%), 9-10 years ago or greater (26%), or 1-2 years ago (21%).

Table 1: Country of respondents from Lymphoma Canada survey

Respondents	CAN	USA	Australia	China	United kingdom	Skipped	Total
Patients with Mantle Cell Lymphoma	53	12	1	1	1	34	102

Table 2: Age range of respondents from Lymphoma Canada survey

Respondents	Age (years old)										
	18-24	25-34	35-54	45-54	55-64	65-74	75-84	84-89	Over 90	Skipped	Total
Patients with Mantle Cell Lymphoma	0	1	2	11	11	25	17	1	0	34	102

Table 3: Gender of respondents from Lymphoma Canada survey

Respondents	Gender				
	Female	Male	Prefer Not to Answer	Skipped	Total
Patients with Mantle Cell Lymphoma	33	34	1	34	102

Table 4: Number of years ago respondents were diagnosed with Mantle Cell Lymphoma

Respondents	Years						
	<1	1-2	3-5	5-8	9-10	Skipped	Total
Patients with Mantle Cell Lymphoma	9	18	26	10	22	17	102

3. Disease Experience

At Diagnosis

Through Lymphoma Canada's online survey, patients were asked to rate a list of physical symptoms on a scale of 1 (no impact) to 5 (significant impact) in regards to their quality of life upon diagnosis. The most common reported symptoms rated as a four or five were: Fatigue/lack of energy (34%), enlarged lymph nodes (27%), night sweats (22%), indigestion, abdominal pain or bloating (20%), weight loss (19%), low platelet counts (16%), and high white blood cell counts (leukocytosis) (14%).

Respondents of the survey were also asked to select from a list of psychosocial impacts they experienced when diagnosed with MCL. Of the 85 patients that responded to this survey question, 69% experienced anxiety, 68% experienced stress of diagnosis, 61% had fear of progression, 39% experienced difficulty sleeping. Other responses included challenges with the frequency of healthcare appointments (26%), fear of not being able to continue daily activities (24%), depression (22%), and problems concentrating (22%), and fear of not being able to attend school/work (21%).

When asked to provide additional details about the challenges faced during diagnosis, several patients commented on difficult symptoms and increased anxiety/fears:

- "The unknown information caused worry and difficulty sleeping. stayed away from concerned friends and family members."
- "Of course after diagnosis I was worried and scared about my cancer. At diagnosis, I was concerned about the annoyance in my throat."
- "Fear of treatment side effects"
- "Fear of dying and leaving my children without a mother."
- "very hard, I had been sick for two years with severe sinus but wasn't diagnosed"
- "Searching for information online only added to the stress since it was not positive in the outcomes"
- "Had to take stress leave from work"
- "Emotional toll on family members"
- "I am 42 so the diagnosis was shocking- it was difficult to understand what my prognosis might be. Lots of worry around limited lines of treatment available"
- "Frustration at the lack of effective treatments and lack of a cure. Knowing that the disease will recur with whatever treatment I undertook."
- "The diagnosis was a shock as not a cancer one hears about. Information from Drs. and support from wife was very important"

Current Quality of Life

To understand the factors which currently impact patients with Mantle Cell Lymphoma, respondents were asked a similar style of questions from the diagnosis section of the survey. On a scale of 1 (no impact) to 5 (significant impact), 25% of patients rated fatigue/lack of energy as a 4 or 5, and 14% of patients rated low white blood cell counts (neutropenia) as a 4 or 5.

Patients also indicated they recently experienced mental health challenges such as fear of progression/relapse (75%), stress of having cancer (43%), difficulty sleeping (39%), anxiety/worry (35%), and problems concentrating (26%).

Daily Activities

Regarding day-to-day activities, patients with Mantle Cell Lymphoma rated several factors on a scale of 1 (no impact) to 5 (very significant impact) which impacted their daily life. Of the 77 respondents who completed the question, the ability to travel (36%), ability to work, school and volunteer (27%), ability to spend time with family and friends (21%), and ability to exercise (18%) were rated as a 4 or higher. Many patients left comments in this section and a selection of quotes are included below:

- “Depression is a long lasting side-effect that people don't understand. I'm afraid at any sign of a relapse or recurrence. I have a personal support worker twice a week to help me with my shower, laundry, light meal preparation and household care. Mobility issues prevent me from attending a lot of group activities. I'm afraid to have hip surgery because I live alone and likely will not be eligible for recovery in a rehab centre. I can't travel alone anymore, even locally, and rarely socialize. Isolation has increased, especially since Covid. When I was first diagnosed with Mantle Cell Lymphoma, it was so rare that my results and biopsies were sent to the US for confirmation. There's no question that cancer changed my life and changed who I am today.”
- “I worry a little about my financial situation if the mantle cell lymphoma comes back since I will be retiring in a few years.”
- “I am now in remission so afraid of a relapse”
- “always in the state of the unknown - will I achieve remission, how long will I live”
- “Struggling probably more in mental health than physical health which is stopping me returning to work”
- “I have young children- when they have colds and illnesses I have to isolate from them to prevent becoming ill. I can’t work my usual job (I’m a firefighter). At the moment i receive sick pay but that will finish soon and its likely i will not be able to return for at least another year as i am handing an auto SCT. My wife has had to do everything whilst working and getting me to appointments.”
- “Because of my weak immune system, routine daily outings (ex: grocery shopping, appointments) and social occasions are a big risk to my health. A simple cold will last for 3 months or turn into a pneumonia. I have to be very careful about what I eat so I almost never eat out at restaurants.

Everything must be well-cooked, well washed, pasteurized, etc. Socially, my family, friends and colleagues are worried about infecting me with a cold, the flu, etc. Socially, it can be very isolating, especially in the winter."

- "Lost the interest to meet friends or attend any social group."
- "Having to be always aware of a compromised immune system"
- "Immunosuppression from MCL maintenance and clinical trial of Acalabrutnib created a secondary cancer - mouth cancer, which is severely impacting my day-to-day life."
- "Our travel away from home is dictated by the schedule of my maintenance treatments every 3 months for the next 2 years. Coming off the prednisone after 10 months of high doses daily was a very big adjustment to my joints and muscles. It has taken several months to begin to feel more normal in my daily activities and to start to build back some muscle strength. Physiotherapy has helped me. I have struggled with a sensitive stomach and now need to avoid certain foods."

Summary

For many patients, to live with MCL means living with fatigue/lack of energy, abdominal issues, anxiety/stress, and a fear of progression/relapse, all of which have a significant impact on a person's quality of life.

4. Experiences With Currently Available Treatments

Patients who completed the Lymphoma Canada survey were asked if they required immediate treatment following their diagnosis or if they were on Watch and Wait for a period of time (> 1 month) before starting treatment. 65% of patients required immediate treatment while 35% were on watch and wait.

Patients were also asked how many lines of treatment they received to treat their Mantle Cell Lymphoma. The majority of patients indicated they received 1 (56%) or 3+ (22%) lines of treatment, see Table 6.

Table 6: Number of lines of therapy survey respondents received

Respondents	Have not yet received therapy	1	2	3+	Skipped	Total
Patients with Large B-cell lymphoma	4	43	13	15	27	102

In the front-line setting, 35% of patients received BR (Bendamustine, Rituximab), 30% of patients received R-CHOP chemotherapy (rituximab,cyclophosphamide, doxorubicin, vincristine and prednisone), 30% received

a stem cell transplant, and 12% received R-DHAP (rituximab, dexamethasone, cytarabine, cisplatin) or BEAM Therapy (carmustine (BiCNU) or lomustine (CCNU), etoposide, cytarabine (Ara-C, cytosine arabinoside), and melphalan). In second line or beyond, 15% of patients received treatment with BTK inhibitors (ibrutinib, acalabrutinib, zanubrutinib).

These patients were asked: “How satisfied were you with the number of treatment options available to you for your lymphoma?”. 79% of patients indicated they were very satisfied or satisfied with their frontline treatment options. While 30% of survey respondents gave the same rating in second-line treatment, and 13% with their third-line treatment options.

When asked which side effects were the most difficult to tolerate many patients indicated fatigue, nausea, insomnia, loss of appetite/weight loss, hair loss, constipation, joint pain, bodily aches and pain, neuropathy, mouth sores, muscle weakness, and diarrhea. Some patient remarks to this question:

- “I ended up in ICU immediately after autologous stem cell transplant and was almost a vegetable for 2 months, before I learned to walk again.”
- “1. Nausea after each treatment. 2. Inability to swallow after Stem Cell Transplant. I still cannot tolerate spicy food. 3. Loss of hair and being bald.”
- “Taste of food and liquids. My saliva glands were damaged from the high dose chemo during autologous stem cell transplant so it was difficult to eat food and still to this day I have some difficulty with a dry mouth although it is much better than the first 6 months after my stem cell transplant.”
- “Rash on forehead, left and right upper and lower limbs and back of body.”
- “BR – I was constipated”
- “BEAM was hard: diarrhea, nausea, fatigue, sore mouth and throat, fever, etc”
- “Pain in lower leg; persistent cough; fatigue”
- “Fatigue was extremely difficult to overcome”
- “I experienced lots of nausea, then I crashed hours after the stem cell transplant and was in crisis in ICU for several days. It took months to get my gut functioning again.”
- “Fatigue, exercise intolerance, immunosuppression”
- “Fever every month with BR”
- “15 days of radiation left me in bed for a month unable to eat.”

Of the 64 patients who provided information about their ability to access their MCL treatment, 15% of patients had some difficulty or a lot of difficulty. If patients were not able to access treatment, the main reasons were because the treatment was not available/they could not access the treatment at their local

cancer center (11%), or because they lived in a community without a cancer center (3%). The most common financial implications reported for treatment for MCL were absence from work (37%), travelling costs (33%), drug costs (20%), and supplementary drug costs for side effects (15%).

Here are some comments from patients in terms of difficulties regarding access to treatment in Canada as well as financial implications:

- "Travel to treatment centre was exhaustive."
- "BR was administered out at provincial centre (2h drive from home). Rituximab maintenance was administered at local centre."
- "Initially I travelled to a centre twice monthly for 6 cycles to a centre 200 km from my home due to space availability. However, the maintenance program was delivered at my local cancer centre."
- " The Acalabrutinib trial was not available locally"
- "The most difficult aspect was paying for parking at the hospital for treatment. I have had many, many appointments that cost over $20 for parking, and cannot claim it on my taxes."
- "Distance was the main difficulty"
- "I lost my job and due to absence was unable to participate in competitions for other positions in my workplace."

Summary of the Current Available Therapies

- Side effects of treatment and their impacts on the patient's quality of life remain a significant issue for survey respondents.

5. Improved Outcomes

MCL patients which completed the Lymphoma Canada survey were asked how important it was for a new drug to control/treat their Mantle Cell Lymphoma. MCL patients indicated factors such as longer disease remission (89%), longer survival (88%), improved quality of life to perform daily activities (79%), control disease symptoms (76%), and normalize blood counts (76%), were very important to them.

60 out of the 68 patients who responded (88%) indicated they would be willing to tolerate side effects to access new treatment options if side effects were not very severe and short term. 48 patients (71%) indicated choice is important to them (scored a 7 or higher out of 10) in deciding to take a drug based on known side effects and expected outcomes of treatment.

When participants were asked if there is currently a need for more therapy options for patients with Mantle Cell lymphoma, 57 patients (84%) answered "yes".

Comments in regards to patient expectations for new therapies to manage lymphoma included:

- “It's always good to have new therapies to consider.”
- “It would be great to have a cure and be free from treatment and appointments!”
- “I would like Health Canada to partner with their European and American counterparts to approve treatments more quickly so we’re not so far behind.”
- “Need to be able to access a range of different therapies which target MCL in different ways. Length of remission and quality of life is important. Burden of treatment is important and finding treatments which require limited contacts with hospital is important.”
- “Please find a first line treatment that is effective and provides a long-lasting remission. Please continue to support research that gives doctors and their patients options when a relapse occurs.”
- “I just hope that when I relapse there is or are treatment(s) that can help me cheat death for several more years.”
- “treatment should have fewer side effects and allow for acceptable quality of life.”
- “I am expecting more of targeted therapies rather than chemotherapy drugs which have lot of side effects.”

Summary of Improved Outcomes

- MCL patients identified factors important for novel treatments, which included longer life span, longer remission, better quality of life and fewer side effects.
- A majority of patients believe it is very important to have choice in their treatment decision and a variety of treatment options to choose from.

6. Experience With Drug Under Review

From survey responses, 8 patients indicated they were treated with Acalabrutinib in combination with bendamustine and rituximab with no prior treatment. These patients reside in Canada (5), and the United States (3). 1 patient was 35-44 years old, 2 patient was 45-54 years old, 3 patients were 55-64 years old, and 2 patients were 65-74 years old. 3 patient accessed this therapy as part of a clinical trial, 2 via private insurance, 2 patients received this treatment through a compassionate access program (manufacturer company) and 1 through Medicare or public care. In terms of the stage of their cancer journey, 3 patients relapsed after treatment with acalabrutinib in combination with bendamustine and rituximab, 2 patients are

about to undergo treatment/just began treatment, 2 patients have been in remission for 1-2 years following this therapy, and 1 patient is in new remission (less than 6 months).

The main side effects reported included fatigue (4 patients), diarrhea (3 patients), low white blood cell count (neutropenia) (2 patients), and 2 patients did not experience any side effects. 1 patient had an allergic reaction to bendamustine. Psychological impacts included anxiety/worry (4 patients), and fear of progression/relapse (3 patients), loss of sexual desire (1 patient), depression (1 patient) and isolation (1 patient).

In terms of overall experience with this therapy, 5 patients rated it as very good, 1 patient rated it as good, while 1 patients rated it as satisfactory, and 1 rated it as poor. However, all 8 said they would recommend it to other patients with MCL.

Comment shared by one of the respondents from the survey:

- “I am handling the treatment fairly well, but I'm not sure if the insomnia is because of the chemotherapy or from acalabrutinib”
- “I started taking this pill 2 weeks ago so I don't have a lot of experience, but I certainly haven't experienced some of the major side effects that could potentially be associated with this drug. Ie mouth sores nausea. I generally feel fine.”
- “I had a serious allergic reaction to bendamustine so my chemo protocol was changed.”

Summary of Drug under Review

- The patients who had undergone therapy with experienced fewer side effects, primarily diarrhea and fatigue.
- All 8 patients who received this therapy would recommend the therapy to other MCL patients.

7. Companion Diagnostic Test

N/A

8. Anything Else?

Lymphoma Canada advocates for lymphoma patients to have access to innovative treatment options, such as Acalabrutinib in combination with bendamustine and rituximab for previously untreated mantle cell lymphoma (MCL) patients. The availability of novel therapies provides patients with more personalized treatment choices, allowing them to work closely with their healthcare team to determine the best plan based on their individual needs and goals.

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.

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
AbbVie				X
AstraZeneca				X
Gilead				X
Novartis			X	
Roche		X		
Incyte			X	
BMS				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: Gurjot Basra
Position: Manager of Patient Programs, Research, and Advocacy -
Patient Group: Lymphoma Canada
Date: April 7, 2025

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: **PC0413-000**
Generic Drug Name (Brand Name): **acalabrutinib (Calquence)**
Indication: **Acalabrutinib in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are ineligible for stem cell transplant (SCT).**
Name of Clinician Group: **LLSC Pharmacist Network**
Author of Submission: **Colleen McMillan**

1. About Your Clinician Group

LLSC Pharmacist Network - This is a group of pharmacists with an interest in blood cancer

2. Information Gathering

LLSC gathered input via comprehensive interviews with pharmacists from Canadian clinics who have experience managing and supporting the treatment of oncology patients

3. Current Treatments and Treatment Goals

For adult patients with MCL who are ineligible for stem cell transplant, the standard of care in the first-line setting includes combination therapies such as bendamustine and rituximab (BR) or bortezomib, rituximab, cyclophosphamide, doxorubicin and Prednisone (VR-CAP). The choice of regimen often depends on patient-specific factors such as age, comorbidities, and other contraindications to SCT. These therapies are commonly used in clinical practice to provide effective treatment for patients who are not suitable for transplant.

The ideal treatment for MCL should focus on prolonging survival, improving quality of life, minimizing toxicity, and reducing the burden on both patients and caregivers. The combination of acalabrutinib, bendamustine, and rituximab offers a promising option to meet these critical goals, providing an opportunity for more effective disease control in this vulnerable patient population.

Although bendamustine-rituximab provides some benefit, acalabrutinib, a second-generation BTK inhibitor, has emerged as a promising addition to the treatment paradigm. When combined with bendamustine and rituximab, acalabrutinib has demonstrated enhanced efficacy in this patient population, improving PFS and offering a more durable response compared to chemotherapy alone. The addition of acalabrutinib is especially important for transplant-ineligible patients who have poor prognosis or who may experience rapid disease progression with traditional chemotherapy.

This targeted approach can result in greater disease control. It offers the potential for deeper and longer-lasting responses and may delay symptom recurrence.

In the treatment of MCL, particularly in transplant-ineligible patients, several treatment goals should be prioritized. First and foremost is the goal to ***prolong overall survival (OS)*** by extending life expectancy. An ideal treatment for MCL would aim to achieve durable responses that significantly improve overall survival with fewer relapses. Another key goal is to ***delay disease progression***. MCL is an aggressive disease, and progression is common after initial treatment, therefore, an ideal therapy should strive to maintain patients in remission for as long as possible. In addition, it is important to ***improve progression-free survival (PFS)***, minimizing the need for further aggressive interventions and maintaining disease control. ***Enhancing quality of life*** is equally essential. This includes alleviating symptoms related to the disease and improving health-related quality of life by reducing the need for frequent hospitalizations and supportive care, helping patients manage both the physical and emotional burdens of MCL. ***Minimizing treatment toxicity and adverse effects*** is also crucial. An ideal treatment should reduce adverse effects and improve tolerability and overall health. Furthermore, an ideal therapy should aim to ***increase independence***, helping patients preserve or restore their ability to carry out daily activities, maintain work, and stay socially engaged. Finally, treatments should ***reduce the burden on caregivers***. By improving patient outcomes and minimizing the need for frequent healthcare visits or hospitalizations, treatments can lessen the emotional and logistical strain on caregivers.

The combination of acalabrutinib with bendamustine and rituximab represents a significant advancement in the treatment of transplant-ineligible MCL. This combination targets the underlying disease mechanism, improving PFS and offering patients a more durable response compared to the current standard of care. Moreover, it can delay disease progression and reduce symptoms.

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.

Current treatments for transplant-ineligible MCL, particularly BR, may not adequately address the need for long-term, durable disease control, particularly for patients with rapid progression.

Acalabrutinib may offer more effective disease control and improve patient outcomes in this challenging and high-risk patient population.

There is a clear and pressing need for treatment options that can provide deeper, more durable responses in transplant-ineligible MCL patients. Current standards of care do not always provide optimal outcomes, particularly in terms of PFS. For many patients, even after achieving an initial response, disease progression can occur within a relatively short timeframe, or patients can fail to respond. As a result, these patients are left with few therapeutic options, and the likelihood of relapse or progression remains high.

Acalabrutinib is a promising solution to fill the gap left by current treatments. Unlike traditional chemotherapy regimens, which indiscriminately target both malignant and healthy cells, acalabrutinib offers a more targeted approach, potentially leading to improved efficacy and better outcomes in terms of PFS and resulting in deeper, more durable responses compared to the standard chemotherapy treatments.

5. Place in Therapy

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

Acalabrutinib, when combined with bendamustine-rituximab, could offer an improved treatment option for first-line transplant-ineligible MCL patients, particularly those who might experience rapid disease progression or suboptimal responses to chemotherapy alone. It complements the existing regimen and may lead to better clinical outcomes in this patient population.

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?

Acalabrutinib is best suited for transplant-ineligible patients, particularly older individuals or those with significant comorbidities who cannot tolerate more aggressive treatments. It is least suitable for patients with bleeding disorders, uncontrolled infections, or those on medications that may interact with acalabrutinib. Careful screening and monitoring are essential to ensure the benefits outweigh the risks.

Patients who are transplant-ineligible are most suited for treatment with acalabrutinib. This includes individuals who are unable to undergo stem cell transplantation due to advanced age, comorbidities, or other factors such as frailty or poor performance status. These patients may derive significant benefit from a targeted therapeutic approach, such as acalabrutinib.

Patients with rapid disease progression may benefit from the sustained efficacy and improved tolerability of acalabrutinib, which can provide a more durable response and enhance quality of life.

On the other hand, patients who have severe bleeding disorders or are at an increased risk of bleeding may be less suitable for treatment with acalabrutinib, as BTK inhibitors can interfere with platelet function, increasing the risk of bleeding complications. Additionally, uncontrolled infections are a contraindication for acalabrutinib, as the drug may impair immune function.

Polypharmacy is a key consideration when prescribing acalabrutinib, as drug interactions can impact treatment safety and efficacy. Patients on blood thinners or other medications that interact with acalabrutinib are at a higher risk for bleeding complications. A thorough review of the patient's current medications is essential to identify and manage potential interactions, ensuring safe and effective use of acalabrutinib.

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?

Outcomes used to determine treatment response include PFS and disease control.

These are crucial for evaluating the effectiveness of therapy and ensuring patients are not experiencing significant adverse events. Regular assessments are necessary to monitor patient's response and guide decision-making. Treatment response is typically assessed every 2-3 months, though the frequency may be adjusted, and more frequent monitoring may be warranted if signs of disease progression or significant side effects are observed.

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

Discontinuation of treatment with acalabrutinib should be considered if significant adverse effects arise, such as severe bleeding, increased infection risk, or poor tolerability that cannot be effectively managed. Additionally, if there is lack of efficacy or disease progression despite continued therapy, discontinuation may be necessary. The decision should be based on a thorough evaluation of the patient's overall health, comorbid conditions, and response to therapy. Close monitoring is essential in determining whether the risks of continuing treatment outweigh the potential benefits.

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]?

Treatment with acalabrutinib in combination with BR is appropriate in outpatient or specialized settings, where patients can receive regular monitoring and supportive care. These settings provide the necessary resources for assessing treatment response and managing potential side effects.

6. Additional Information

Acalabrutinib, when combined with bendamustine and rituximab (BR), is expected to improve PFS in first-line, transplant-ineligible patients. However, the use of this therapy requires careful consideration of several factors.

Key safety concerns include bleeding risks, potential infections, and cardiovascular side effects, which may be more pronounced in older patients with comorbidities. While the oral dosing regimen of acalabrutinib simplifies administration, patient education is crucial to ensure proper adherence, appropriate dose adjustments, and vigilant monitoring for potential side effects. Pharmacists play a pivotal role in educating patients about managing oral therapy, recognizing and addressing adverse effects, and preventing harmful drug interactions.

There is a higher risk of **infections** due to the immunosuppressive nature of acalabrutinib, bendamustine, and rituximab. Patients must be closely monitored for signs of infection throughout treatment. Proactive measures, such as the use of antibiotics, may be necessary to prevent or treat infections. Early detection and intervention are critical to reducing the potential for serious complications.

Patients may require dose reductions or discontinuation due to **side effects**, especially bleeding or infections. These adjustments are essential to minimize adverse effects while maintaining the therapeutic benefits of acalabrutinib. Continuous assessment of the patient's clinical status is required to determine the appropriate course of action in managing side effects.

Acalabrutinib is administered orally, which offers convenience over intravenous therapies. However, adherence to oral medications can be challenging, especially in older patients who may have difficulty managing daily regimens. Furthermore, **polypharmacy**, common in this patient population, poses a risk for drug interactions, particularly with medications like anticoagulants. It is vital to provide **patient education** by offering clear instructions regarding dosing schedule and recognizing potential drug interactions.

As the treatment landscape evolves, there is growing interest in shifting away from traditional chemotherapy approaches. However, further clinical data are needed to assess whether this shift could become routine practice.

Considering treatment sequencing, it is important to recognize that combining therapies with different mechanisms of action may exhaust multiple lines of treatment at once. In the transplant-ineligible population, especially among older patients with comorbidities, the likelihood of tolerating two lines of therapy may be lower. This consideration underscores the need for careful patient selection, as there is a notable attrition rate following frontline treatment.

As we await further data, it will be important to closely monitor long-term outcomes.

7. Conflict of Interest Declarations

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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: Liam Berrigan
Position: Pharmacist, Moncton Hospital Oncology Clinic
Date: 07-04-2025

☒ **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**
Beigene	x			
Janssen	x			

Pfizer	x			
Knight Therapeutics	x			
GlaxoSmithKline	x			
Sanofi	x			

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

Declaration for Clinician 2

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 2: 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**
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: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
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: PC0413-000
Generic Drug Name (Brand Name): Acalabrutinib (Calquence)
Indication: Acalabrutinib in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL).
Name of Clinician Group: Lymphoma Canada Scientific Advisory Board
Author of Submission: Dr. John Kuruvilla, Dr. Diego Villa, Dr. Pamela Skrabek, Dr. Shannon Murphy

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

Lymphoma Canada, is a national non-for-profit organization for Canadian lymphoma and CLL patients, that assisted in the administrative coordination of the group clinician response. Lymphoma Canada was not involved in the development of the content of the submission. For more information about Lymphoma Canada, please visit www.lymphoma.ca.

The following clinicians, leading experts in lymphoma across Canada, have provided feedback on this therapeutic for the submitted indication:

Dr. John Kuruvilla (lead), Dr. Diego Villa, Dr. Pamela Skrabek, and Dr. Shannon Murphy

2. Information Gathering

Please describe how you gathered the information included in the submission.

Clinicians provided responses to the questions in the submission based on research results, clinical experience, and understanding of patient needs and challenges

3. Current Treatments and Treatment Goals

Mantle cell lymphoma (MCL) is an incurable subtype of non-Hodgkin's lymphoma although there is some disease heterogeneity with both more indolent or more aggressive presentations possible. Historically, the median survival for patients with MCL was approximately three years but this has improved substantially through treatments defined by randomized controlled trials including immunochemotherapy with rituximab-based regimens, the use of autologous stem cell transplantation (ASCT) in eligible patients, and rituximab maintenance as part of primary therapy. The majority of MCLs behave more like the aggressive B cell lymphoma and requires aggressive treatment. Observation may be considered in asymptomatic patients if they have no other indication for therapy such as cytopenias related to lymphoma.

For younger patients often less than age 70 or with favourable comorbidity profiles, aggressive chemotherapy regimens including anthracycline-based chemotherapy combined with cytarabine-based treatment are generally used for induction treatment and followed by consolidative ASCT. Maintenance therapy with rituximab is offered after induction/ASCT. For patients who are not eligible for a stem cell transplant but who require first line therapy, therapy with Bendamustine and Rituximab (BR) is the current standard of care based on data from the STIL-1 trial that demonstrated improved PFS over R-CHOP chemotherapy in addition to a more favorable toxicity profile. These patients do not receive ASCT. However, rituximab maintenance is also offered to these patients. The median PFS for patients undergoing ASCT as part of primary therapy for MCL approaches 8-10 years while patients receiving R-chemo that are ineligible for transplant will have median PFS in the range of 3-5 years.

BTK inhibitors (ibrutinib and more recently, the second-generation agents acalabrutinib and Zanubrutinib) are oral agents considered standard of care across the world as monotherapy in patients with relapsed/refractory MCL and have been subsequently evaluated in combination approaches. Trials have not been performed comparing individual BTK inhibitors and clinicians tend to make decisions around the usage of specific agents based on drug access as well as differences in individual toxicity profile. For example, head-to-head comparisons in chronic lymphocytic leukemia show acalabrutinib has a more favorable toxicity profile than ibrutinib. Recently, clinical trials have evaluated the inclusion of BTK inhibitors into the primary treatment of patients with MCL including randomized controlled trials in non-ASCT and ASCT populations. These trials have demonstrated improvements in PFS, the defined primary endpoint of these clinical trials.

The ECHO study randomized the addition of acalabrutinib (given until progression or significant toxicity) to the established standard of BR followed by maintenance rituximab. With a median follow-up of 45 months, the addition of acalabrutinib significantly improved PFS (median 66.4 vs 49.5 months) without excessive toxicity. It is important to note that all 3 trials that have incorporated BTK inhibition into the primary treatment setting (one with ibrutinib in younger ASCT-eligible patients and one with ibrutinib in combination with BR in older non-ASCT eligible patients) demonstrated increased toxicity including infection. However, the safety profile of acalabrutinib-BR (A-BR) in ECHO appears more favourable than the ibrutinib-BR combination.

PFS remains an important endpoint in MCL. Maintained remission with acceptable quality of life is an important goal of care for patients and clinicians. PFS has been the endpoint that has defined major shifts in care in MCL with the use of bendamustine as the preferred chemotherapy regimen, the addition of rituximab to chemotherapy and the use of ASCT in eligible patients. Overall survival has been seen in trials evaluating maintenance rituximab and it is important to recognize crossover was employed in ECHO which makes it unlikely that an OS advantage would be demonstrated particularly since the sample size was not designed to evaluate OS as the primary endpoint.

4. Treatment Gaps (unmet needs)

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

The most important goal of therapy for MCL is to produce durable clinical responses and remission that may prolong life. Relief of disease-related symptoms to improve health related quality of life is an important objective; this requires treatments with low toxicity. Treatments that are finite and not continued indefinitely may be preferable to patients although extended duration therapy with maintenance rituximab is commonly

employed and stopped at two years. Improved outcomes for non-ASCT eligible patients remain an important priority as the majority of MCL patients are older and would not be eligible for more intensive approaches.

In the absence of curative therapy for MCL, the goal of primary treatment is similar to other incurable lymphomas where the longest remissions that can be achieved with favourable toxicity and patient reported QOL are typically pursued. The addition of acalabrutinib to BR improves PFS without excessive toxicity which remains an important goal of therapy for patients with MCL

5. Place in Therapy

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

At present, A-BR would be used in most patients who would typically receive BR which is the standard in Canada for older patients with MCL ineligible for ASCT. The patient population in Canada for A-BR would mirror the clinical trial population as a first choice regimen for older patients.

These patients would typically receive a BTK inhibitor as the preferred second-line approach in MCL. It would not be expected that these patients would use another similar BTK inhibitor as their next therapy. Alternative approaches could include CD19 directed CAR-T cell therapy in selected patients, targeted agents (for example, a noncovalent BTK inhibitor such as pirtobrutinib, a BCL2 inhibitor such as venetoclax), or chemotherapy.

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

In patients with MCL, there will be two patient populations – an older/frailer population that would not be eligible for more aggressive therapy and a patient population that will typically be younger, without comorbidity and with good performance status that would be eligible for ASCT. Younger patients eligible for ASCT would not be considered for this type of therapy. Very frail patients would also not be candidates for a combination chemotherapy approach.

There are no specific concerns from a diagnostic standpoint and no useful predictive biomarker available in routine clinical practice.

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?

Are outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

What would be considered a clinically meaningful response to treatment? Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Examples: improved survival; reduction in the frequency/severity of symptoms (provide specifics regarding changes in frequency, severity, etc.); attainment of major motor milestones; ability to perform activities of daily living; improvement of symptoms; and stabilization (no deterioration) of symptoms.

Standard clinical parameters would be used to document clinical response including CT scans and in some situations, PET scans. Bloodwork and assessments of organ function and routine blood counts are also used. Typically imaging is performed at baseline, at the midpoint of chemotherapy and at the end of

chemotherapy to document remission. Testing in clinical practice would be similar to that performed in the conduct of clinical trials.

Clinicians may image through maintenance rituximab or at the end of this treatment. Serial imaging has not been typically performed in patients receiving BTK inhibitors in RR-MCL but could be considered at infrequent intervals (ie. q6 monthly) and may be performed in this setting.

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

Progression of disease (typically based on imaging or laboratory findings) would indicate treatment failure. Toxicity is the other reason to discontinue treatment with acalabrutinib. In this setting, considerations would include significant or recurrent infection, bleeding, atrial fibrillation or hypertension that is difficult to medically control.

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]?

As an oral therapy that is well tolerated and being given with a well-established immunochemotherapy regimen, acalabrutinib with BR can be administered in any setting where cancer patients may be seen allowing for these patients to be treated and followed in their local community. This therapy can be safely delivered on an outpatient basis across Canada without the need for patients to travel to academic tertiary institutions.

6. Additional Information

Recent trials have also demonstrated the benefit of BTK inhibitors (ibrutinib) in patients eligible for ASCT. Increasingly, the incorporation of a BTK inhibitor as part of primary therapy for all patients eligible for combination is accepted as a global standard of care.

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. John Kuruvilla
Position: Chair, Lymphoma Canada SAB; Hematologist Princess Margaret Cancer Centre
Date: 2-Apr-2025

☒ **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

Clinician Information	
Name	John Kuruvilla
Position	Hematologist, Princess Margaret Cancer Centre
Date	5-Nov-2021
☒	**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				
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	☒	☐	☐	☐
Astra Zeneca	☐	☒	☐	☐
Beigene	☒	☐	☐	☐
Eli Lilly	☒	☐	☐	☐

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

Declaration for Clinician 2

Name: Dr. Diego Villa
Position: Medical Oncologist; BC Cancer – Vancouver Cancer Centre
Date: 4-Apr-2025

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

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Janssen	x			
AstraZeneca		x		
BeiGene		x		
Eli Lilly	x			

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

Declaration for Clinician 3

Name: Dr Pamela Skrabek
Position: Hematologist, Associate Professor
Date: 5-Apr-2025

☒ 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**
Hoffmann-La Roche Ltd.	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: Shannon Murphy
Position: Member, Lymphoma Working Group, Canadian Cancer Trials Group
Date: 5/April/2025

☒ 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
Abbvie	X			
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: **PC0413-000**
Generic Drug Name (Brand Name): acalabrutinib (Calquence)
Indication: Acalabrutinib in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL).

Manufacturer Requested Reimbursement Criteria[1]:
Acalabrutinib in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) *who are ineligible for stem cell transplant (SCT).*

Name of Clinician Group: Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee ("OH(CCO) Hem DAC")
Author of Submission: Dr. Tom Kouroukis and Dr. Jordan Herst

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 via emails/teleconference/Teams meeting.

3. Current Treatments and Treatment Goals

Currently treatment as outlined in the flow chart (Figure 1) from reference link below – most commonly, these patients who are not ASCT eligible would be treated with bendamustine-rituximab with or without cytarabine.

Reference: https://canadianhematologytoday.com/article/view/3-2-gong_et_al/pdf_en

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.

Not all patients respond well to current therapies, disease is not curable, and eventually all patients will relapse.

5. Place in Therapy

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

Acalabrutinib will be an addition to current treatment with BR.

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

Best suitable would be those patients who are not candidates for aggressive therapies. If patients are at higher CV bleeding risks, they may be less suitable for BTKi 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?

Standard lymphoma response measures.

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

Disease progression or significant 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]?

Outpatient administration for this regimen.

6. Additional Information

<Enter Response Here>

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) PDRP provided secretariat support 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 <u>each clinician</u> 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. Tom Kouroukis
Position: Lead, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 06-March-2025

☒ **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. Jordan Herst
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 07-March-2025

☒ 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
AstraZeneca	x			
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 3

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
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 4

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 4: Conflict of Interest Declaration for Clinician 4

	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 5

Name: <Enter full name>
Position: <Enter currently held position>
Date: <DD-MM-YYYY>

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

Table 5: Conflict of Interest Declaration for Clinician 5

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

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