CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

epcoritamab (Epkinly)

(AbbVie Corporation)

Indication: For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

November 27, 2023

Patient Group Input

Name of Drug: Epcoritamab

Indication: Epcoritamab is indicated for the treatment of adult patients of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

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 October 3 to November 20, 2023. 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 was also promoted by the Lymphoma Research Foundation in the US amongst eligible helpline callers. 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. 33 responses were collected amongst those who had Large B-cell lymphoma (LBCL). Information from this survey was used to identify the main areas of concern for patients with LBCL, with 1 confirmed response for experience with Epcoritamab. This patient preferred not to disclose gender information, but lived in Australia and is 90+ years old.

Please see tables 1-4 below for demographic and relevant information of all survey respondents. The majority of patients lived in Canada (86%), between the age of 45 and 54 (22%) or 65 and 74 (22%), male (50%), and were diagnosed 5-8 years ago (27%), 1-2 years ago (23%), or less than a year ago (23%), with most diagnosed with Diffuse Large B-cell lymphoma, not otherwise specified (53%).

Table 1: Country of respondents from Lymphoma Canada survey

Respondents	CAN	USA	Australia	Skipped	Total
Patients with Large B- cell lymphoma	12	1	1	19	33

Table 2: Age range of respondents from Lymphoma Canada survey

Respondents	Age (years old)							
	35-54	45-54	55-64	65-74	75-84	Over 90	Skipped	Total
Patients with Large B-cell lymphoma	1	4	2	4	2	1	19	33

Table 3: Gender of respondents from Lymphoma Canada survey

Respondents	Gender			
	Female	Male	Skipped	Total
Patients with Large B-cell lymphoma	6	7	20	33

Table 4: Number of years ago respondents were diagnosed with Large B-cell Lymphoma

Respondents	Years						
	<1	1-2	3-5	5-8	9-10	Skipped	Total
Patients with Large B-cell lymphoma	5	5	4	6	2	11	33

Table 5: Subtype of Large B-cell lymphoma of survey respondents

Subtype of Large B-cell Lymphoma	Number of respondents
Diffuse Large B-cell Lymphoma, not otherwise specified	10
DLBCL arising from follicular lymphoma	5
DLBCL arising from primary mediastinal B-cell lymphoma	2
DLBCL arising from high-grade B-cell lymphoma	3
DLBCL transformed from indolent lymphoma	1
DLBCL: Double-hit lymphoma	1
Skipped	11
Total	33

Information from a submission on Epcoritamab (for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL), refractory or relapsed after at least 2 lines of systemic therapy, ineligible or failing CAR-T) to HAS, the France health technology assessment agency, prepared by ELLyE (ENSEMBLE LEUCÉMIE LYMPHOMES ESPOIR) was used to highlight key takeaways of this indication, particularly for the "Experience with drug" section of this submission, as experience is limited in Canada. The France submission was sent to HAS earlier in 2023, and was based on a survey regarding the use of Epcoritamab for diffuse large B-cell lymphoma conducted by ELLyE with 9 survey respondents, supported by results of the Lymphoma Coalition's 2022 survey on the experience of patients suffering from lymphoma or CLL. Only responses from patients with diffuse large B-cell lymphoma (171 patients managed in France) were used in this contribution.

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 five were: Fatigue/lack of energy (23%), body aches and pains (18%), enlarged lymph nodes (18%), bodily swelling (18%), neutropenia (18%), and shortness of breath (18%).

Respondents of the survey were also asked to select from a list of psychosocial impacts they experienced when diagnosed with LBCL. Of the 22 patients that responded to the survey question, 55% were impacted by stress of diagnosis, while 50% were fearful of progression and experienced anxiety/worry. Other challenges included fear of not being able to attend school/work (41%), problems

concentrating (41%), and fear of not being able to continue daily activities (36%). When asked to provide additional details about the challenges faced during diagnosis, several patients commented on difficult symptoms and increased anxiety/fears of dying:

- "Lost the ability to walk. One Wednesday I was golfing, the next Wednesday I could not walk. Resulted in not being able to golf which was a large part of my physical activity and socializing."
- "I wasn't able to finish my degree. I also had to quit my job because my memory problems got worse everyday."
- "Itching is very real and very hard"
- "Severe pain in lower back, once diagnosed fear of dying consumed us"
- "Isolation and anxiety paramount. went from covid isolation straight into cancer. severe anxiety and death anxiety."

Current Quality of Life

To understand the factors which currently impact patients with Large B-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), 35% of patients rated fatigue/lack of energy as a 4 or 5, and 15% of patients rated bodily aches, indigestion, abdominal pain or bloating as a 4 or 5. This matches what was observed in the France HTA submission, as intense fatigue was reported by 60% of patients surveyed.

Over 50% of patients in Lymphoma Canada's survey did not experience an enlarged spleen, fever, high white blood cell count, low platelet count, weight loss, frequent infections, anemia, chest pain, or reduced appetite in their current quality of life. This correlates with the age range of the survey respondents, with most being diagnosed 5-8 years ago.

Patients also indicated they recently experienced mental health challenges such as fear of progression/relapse (60%), stress of having cancer (55%) and depression or anxiety/worry (35%).

Daily Activities

Regarding day-to-day activities, patients with Large B-cell lymphoma rated several factors on a scale of 1 (no impact) to 5 (very significant impact) which impacted their daily life. Of the 20 respondents who completed the question, the ability to travel (45%), ability to fulfill family obligations (40%), work, school and volunteer (35%), ability to spend time with family and friends (30%) were rated as a 4 or higher. Many patients left comments in this section and a selection of quotes are included below:

- "Social activities have pretty much disappeared as part of my life. I take a lot of medicines and regular blood tests and even though a lot of costs are covered by provincial plans. Not all costs are covered. And for example last year, we still spent about $2,400 of our dollars on medical related treatments and drugs"
- "Can't work physically or mentally - incapable. Use a walker to move around. Have Homecare daily for bathing , Physio and walks. Appetite down , lost 50 lbs. Needed many transfusions during different chemos. Constantly going to emerg with these side effects of chemo - hemorrhaging, blood clots in lung, bleeding in urine, bowels, …confusion , hear voices during chemo, can't be logical can't follow
- conversations. Very depressed and anxious."
- "Just over two months out of yescarta car-t after 1st and 2nd line treatment fails. one year non stop of treatments. recovery is painful and slow. inability to do normal things in life. crippling fear of recurrence."

Summary of the Disease Experience

- For many patients, to live with LBCL means living with fatigue, anxiety and stress, 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 how many lines of treatment they received to treat their Large B-cell lymphoma. The majority of 15 patients indicated they received 1 (47%) or 3 or more (47%) lines of treatment, see Table 6.

Table 6: Number of lines of therapy survey respondents received

Respondents	Have not yet received therapy	1	3+	Skipped	Total
Patients with Large B-cell lymphoma	1	7	7	14	15

In the front-line setting, 9 patients received R-CHOP, and 4 received DA-EPOCH-R. In second line, 6 patients received R-GDP, 2 received R-ICE, 3 received radiation, and 4 were on a clinical trial. In the third line of treatment, 6 patients received CAR T-cell therapy, 3 received Pola-BR, and 6 were on a clinical trial.

These patients were asked: "How satisfied were you with the number of treatment options available to you for your lymphoma?" 67% of patients indicated they were very satisfied or satisfied with their frontline

treatment options. While 29% of survey respondents gave the same rating in second-line treatment, and 43% with their third-line treatment options. This indicates patients are less pleased with their treatment options in second- and third-line settings and more treatment options need to be made available.

When asked which side effects were the most difficult to tolerate many patients indicated nausea, fatigue, joint pain, bodily aches and pain, low appetite, headache, muscle weakness, diarrhea, and bleeding. One patient remarked:

- "I was in a two week coma right after my second chemo treatment. my doctor changed my pre chemo regiman then to include 3 days of IV's prior to chemo day."

15 patients provided information about their ability to access their DLBCL treatment. 11 patients found it not difficult at all or not very difficult to access treatment, while 2 patients had some difficulty and 2 had a lot of difficulty. If patients were not able to access treatment, the main reasons were because the treatment was not available at their local cancer centre (14%), or because they lived in a community without a cancer centre (7%) or in a province where treatment was not available (7%). Here are some comments from patients in terms of difficulties regarding access to treatment in Canada:

- "I live in a small town so travel during winter can be problematic."
- "I had to travel from Victoria to Vancouver via ferry for EPOCH R treatment that was not available in Victoria. Challenges include being away from kids and family, costs"
- "car-t. as previously noted ohip funding dictates the order of things not necessarily suitable for the patient."

The most common financial implications reported for treatment for LBCL were drug costs (43%), supplementary drug costs for side effects (43%), absence from work (36%), and travelling costs (22%).

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 and almost half of respondents indicated the need for more options for 2nd and 3rd line treatment for LBCL.

5. Improved Outcomes

LBCL patients which completed the Lymphoma Canada survey were asked how important it was for a new drug to control/treat their Large B-cell lymphoma. LBCL patients indicated factors such as longer disease remission (71%), longer survival (71%), improved quality of life to perform daily activities (71%), control disease symptoms (64%), and normalize blood counts (64%), were very important to them. 7 out of these 14 patients (50%) indicated they would be willing to tolerate side effects to access new treatment options if side effects were not very severe and short term. 10 patients 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. 8 patients indicated choice is important to them (scored a 7 or higher out of 10) in "deciding which drug to take based on how it is administered i.e. via infusion (longer procedure, administered for a few hours/days) vs subcutaneous (injection, administered over the course of a few minutes) or in-hospital vs outside-hospital". When participants were asked if there is currently a need for more therapy options for patients with Large B-cell lymphomas, 8 patients (57%) answered "yes".

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

- “I just hope that there are more Doctors like Dr Robert Stevens who are always open to new treatment options and willing to treat patients asap. My experience was that some doctors only wanted to stay with existing, standard treatment approaches and not be as open to trying to meet each patients individual needs.”
- “Get away from old harsh chemos. Move to immunotherapies that are gentler and CAR T also gentler than RCHOP and gdp so was VIPOR P. The first 2 lines of threatment were horrendous I would have rather died than repeat. Radiation was ok. Car T not terrible. Immunotherapy VIPOR P was very smooth. Told I had months to live 2 x in 22 months. Just before the trial for VIPOR and now as we struggle to get glofitimab for compassionate use. Wish there was a maintenance drug after. Hate to be uncovered. Each time we stop a treatment the cancer grows bigger.”
- “Flexible treatment options based on what should be best for you to achieve remission and cure, not what OHIP dictates based on cost.”

Summary of Improved Outcomes

- LBCL 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, 1 patient indicated they were treated with Epcoritamab. This patient resides in Australia, is currently undergoing treatment and accessed the drug through a compassionate access program. The main side effects reported include infections and joint or muscle pain. Psychological impacts included depression and problems concentrating. No other responses were provided by this patient.

According to data from the France HTA submission, Epcoritamab had far fewer side effects than other 3rd line treatments. Patients interviewed reported fatigue, headaches and diarrhea. Only one patient out of 8 (who responded to their questionnaire) had to stop treatment due to adverse effects. Compared with therapies such as autograft or CAR-T, patients felt that Epcoritamab administration was very straightforward, and 3/4 of the patients surveyed felt it was less restrictive in comparison to other treatments. Subcutaneous administration contributes to this improvement. For the remaining ¼, the main constraint was frequent hospital visits.

Cytokine release syndrome is one possible side effect of this therapy. However, none of the patients interviewed had experienced this undesirable effect, which is virtually systematic with CAR-T. Patients seem to be much less apprehensive about this side effect than CAR-T patients.

Comments from the survey include:

- “I would like to thank the researchers who developed this treatment”
- “Today I have practically no more pain”
- “was on treatment with Epcoritamab for 30 months, currently in complete remission”

Summary of Drug under Review

- The patients who had undergone therapy with Epcoritamab experienced fewer side effects, primarily fatigue, headaches and diarrhea.
- Epcoritamab offers the appealing advantage of subcutaneous administration, resulting in less time to be spent in hospitals per visit (patients felt treatment was very straightforward and not very restrictive)

7. Companion Diagnostic Test

N/A

8. Anything Else?

Lymphoma Canada is an advocate for lymphoma patients and their caregivers to have access to novel lymphoma therapies. An increased number of available treatment options gives patients more choice to decide the therapy that is right for their personal goals, with their medical care team. Currently there is an unmet need in terms of 3rd line treatment options for patients with LBCL. The standard of care for 3rd line treatment for LBCL is CAR-T, however most eligible candidates are unable to receive treatment as a result of many reasons including logistical factors, disease progressing too rapidly, not having a care partner, treatment not accessible within province, and not willing to or unable to travel etc. Epcoritamab provides a viable option for these patients while aligning with patient preferences in terms of increased quality of life with fewer associated side effects. Additionally, this treatment is much quicker to implement than CAR-T, and could even make it possible to offer treatment to patients whose disease progresses too rapidly to consider CAR-T. Subcutaneous administration and the fact that Epcoritamab is a time-limited option specifically brings simplicity and real benefits for patients and caregivers alike as fewer time will need to be spent in hospitals and patients can be off treatment should they receive a complete response. Lastly, as mentioned in the France HTA submission, Epcoritamab is a drug that provides a rapid metabolic response meaning that even a lack of response can be identified quickly, and the patient's care can be adapted accordingly.

Appendix: Patient Group Conflict of Interest Declaration

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

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

No

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

ELLyE (ENSEMBLE LEUCÉMIE LYMPHOMES ESPOIR) provided access to their HTA submission to HAS, the France health technology assessment agency, that we used to support our submission as experience with Epcoritamab is limited in Canada.

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: November 27, 2023

Patient Input

Name of Drug: epcoritamab (Epkinly)

Indication: For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

Name of Patient Group: The Leukemia & Lymphoma Society of Canada (LLSC)

Author of Submission: Colleen McMillan, Advocacy Lead

1. About Your Patient Group

The Leukemia & Lymphoma Society of Canada - bloodcancers.ca

LLSC is a national charitable status organization dedicated to finding a cure for blood cancers and its ability to improve the quality of life of people affected by blood cancers and their families by funding life-enhancing research and providing educational resources, services, and support. The Leukemia and Lymphoma Society of Canada is the largest charitable organization in Canada dedicated to blood cancer, our focus includes:

- Funding research from bench to bedside.
- Rethinking how a person navigates their blood cancer experience
- Providing targeted blood cancer information
- Offering tools for psychological and emotional support
- Empowering Canadians to take charge of their blood cancer experience through practical support and advocacy

2. Information Gathering

LLSC had the opportunity to collect qualitative input. LLSC conducted four 1 on 1 interviews. Two interviewees were DLBCL patients, and two interviewees were caregivers of DLBCL patients. One of these caregivers is a care partner to someone who is currently using epcoritamab. These interviews took place in November 2023. 3 interviewees reside in Canada and 1 interviewee resides in the United States.

3. Disease Experience

Diagnosis of DLBCL is not always straightforward.

Some had said that they had physically felt a lump in their neck or had a fever but were advised by doctors that they might just have a virus.

One interviewee expressed that her husband had severe back and leg pain: “The doctor thought it was his sciatic nerve and didn’t really do anything about it. We finally got an appointment with orthopedic who did an MRI and found a mass the size of a grapefruit”

Patients’ symptoms varied but all effects were described as moderate to extreme in nature. Interviewees described individual symptoms…

- Felt sick and nauseous

- Dry heaving
- Extreme night sweats (would have to change sheets in the middle of the night because they were soaking wet) – “could wring them out”
- Fever
- Extreme fatigue

One interviewee elaborated on her ongoing experience as a caregiver for her husband throughout his illness:

“He had pain in his back and the pain would go down his leg. He said the pain was throbbing, aching, stabbing pain. It started in his back on his spine. In his legs he said it feels like somebody puts a belt around his leg and just tightens it. It's actually gotten to where he couldn't walk. He’s lucky to walk from the couch to the bathroom. It's taken his mobility away and he's only 53 years old.”

“I'm putting his shoes and socks on and having to give him a bath and help him get dressed and it's just rough. I would not wish this on my worst enemy.”

4. Experiences With Currently Available Treatments

There were many different areas of concern and consideration brought forth by the patients and caregivers regarding their experiences with currently available treatments. Priorities for each are of course, different but all described pain points throughout the treatment experience.

One **patient described her efforts to make herself as comfortable as possible during treatment appointments in hospital…** “When I went to the hospital, I loaded up my backpack with a quilt, a tablet, I packed a lunch. What I had to take with me was crazy just so that I made sure I had everything that made me comfortable, because the chairs are cold, the hospital's cold. When I had to get an IV every time I went, it was uncomfortable. They had to poke me more than once, usually.”

Patients and caregivers described their difficulties regarding the management of treatment side effects. Fatigue and weakness were very common.

“The thing he complained about most was that he just didn't have any energy. He couldn't move. He was so exhausted walking from the bedroom into our living room, that used to wind him. He found even standing up from sitting on the couch used to take effort and he was very, very tired all the time and breathless.”

“He was very very nauseous. Very weak. Couldn't stand up for long periods of time. He spent most of the day sleeping. Very little appetite. Just truly unwell. “He ended up with a fever after pretty much every treatment that he did and then that resulted in a trip to the emergency room and blood work and all that stuff to check it out and make sure it wasn't an infection and that played a real part in the mental turmoil on him as well. He went into his treatment feeling scared, knowing that he was probably going to end up back in the emergency room that night, knowing that the treatment was going to likely cause a fever.”

“Fatigue. I couldn’t even walk the halls of the hospital but I had to try to keep up my strength and I didn’t want to have the shots in my stomach they would give you to help prevent blood clots”

Caregivers described the effects of their loved ones’ treatment on their daily lives. It was described as a great burden both physically and mentally, but one that they were willing to take on in order to help see their loved ones through their treatment experience.

“Trying to work full time and still be his caregiver and manage all of the symptoms and all of the appointments and the chemo and all the drugs that come after the chemo. With the treatment he was doing, he had to have inpatient clinic treatment. It was usually day one and then again on day eight. So the treatment process took about three weeks. And then once you got home, there were so many medications to

juggle. And then trying to juggle medications for his side effects and then trying to live my life as well as and trying to be my own person. Juggling everything and the side effects was just a lot. It was hard on me physically and mentally and I wouldn't wish it on anybody".

One caregiver described the change she saw in her loved one throughout the course of treatment and what she hoped he would gain from going through treatment. She wanted her loved one back as she had known him before the turmoil of treatment.

Honestly, I was just looking for glimpses of him and the way he was before treatment. He's a very comedic person. He always carries the little kids around and he likes to make jokes and I lost that sense of him. Seeing him be able to get up and sit down at the table with us to have a meal and carry on a conversation and kid around like he usually would, being able to take a shower without feeling completely winded, those were the little things that I was looking for. His meals were very touch and go, picking at things here and there, but never actually able to sit and have appetite to eat

The mental and psychological impacts of treatment weigh heavily on patients as well as caregivers and make a difference in overall health and healing. The mental health impact of the patient's illness begins in pre-diagnosis and continues throughout the treatment experience. When DLBCL is persistent and patients go into their second and third lines of treatment still feeling so unwell physically and experiencing unrelenting treatment side effects, the burden of these side effects is evident and impede their ability to remain mentally well.

"He was very, very down on himself because he was having all these side effects and he was feeling so terrible. He was thinking, okay, I'm feeling all this way, this is not going to work. I'm worried that I'm doing this for nothing for the most part. It was a very dark time. And then finding out that the chemo had stopped working and things were still regenerating faster than they had expected that was really the final thing that deteriorated his mental health. He really wasn't doing well and he had to be started on antidepressants. Overall it was just a very, very terrible time for his mental health."

"He was feeling so low from being away from home and his life, and then not feeling well enough to even do anything. Feeling so isolated, I guess, is the word. But also feeling isolated in the way that no one understood what he was going through."

"The loss of my hair and nails had a significant psychological impact. I started to lose my hair then it stopped, when it started again, I took it as a sign that I was done for – this was it – I was dying."

The financial burden of treatment was described as immense and overwhelming. The ability of both patients and caregivers to continue working was interrupted and the cost of the different aspects of treatment contributed to further financial loss.

"He ended up going on long term disability. He wasn't in a position to work. He was just too unwell. So going on disability was the only option."

"We were able to get help with grocery and gas cards from the cancer centre but once he moved to another cancer centre, they didn't do that"

"I wasn't as stressed out about the illness and the treatments, because I knew everything was going okay with that. My biggest stress was the financial stressor, for sure."

"I own my own business and I was off of work completely for 6 months and then part time for another 6 months. The financial aspect was difficult and so was keeping my business going."

Having to travel away from home to access treatment contributes to financial loss and so much more. Patients and caregivers shared their difficult experiences of having to travel away from home for treatment.

"For first line treatment my dad had to leave his home community and go to our local cancer centre 2 hours away from home but for a second line of treatment, the chemo couldn't be done in the community cancer centre so he actually had to come live a 7 hour drive

away in St. John's with me and my partner. He was away from his home and living in a place that he wasn't familiar with while doing treatment. So, on top of being unwell, you're not in your comfortable surroundings. Being able to have an injection and being able to go home on the same day would have been incredible. Then he had to go for CAR-T treatment and had to go from Newfoundland to Ottawa and leave the province for months which was just another huge hit. I had to go with him as well and leave my partner and my job behind because he had to have a caregiver come to Ontario with him. If he was in a position where he had the option of getting an injection and going home to his own house, live his own life, I think his mental health would have been much better than it was. And he would have had a very different outlook."

"I spent 67 days in hospital. 45 days initially, then each infusion was 5 days long. I was 2 hours away from home and I didn't see my kids for most of that time. My daughter is afraid of hospitals and my son had a busy hockey schedule. My husband would go back and forth. Being away from home and work was beyond hard."

"I knew it before, but I really know the challenges of transportation now and the cost and things like that. For people who need to go for more than just one appointment, you know what they go through? It can bankrupt people."

Patients and caregivers talked about the lack of treatment options. The theme of these conversations was that additional treatment options = additional hope for patients and loved ones.

"What if the CAR-T didn't work? What would our options be? Would it be like, okay, there's nothing else go home kind of thing? It's scary knowing that there's not a ton of other options out there right now that have great results."

"New treatments coming available could mean everything! Even after remission the little cancer devil lives on your shoulder and you're worried about relapsing. Knowing there is an additional treatment available gives me emotional fortitude and comfort."

"He didn't even make it through one chemo session. He was hurting so bad and the doctor he was seeing said there was nothing else he could do for him. They sent us to another cancer centre and that's where we've been since. They told him it's stage four and they said if this treatment doesn't do anything, then there's nothing else to do. I was scared. I cried. He cried."

"I was really scared to start with because the doctor wanted him to do the CAR-T treatment and I looked at the downside of it because the percentage that you could be healed was 40 out of 100 and death was one of the side effects which sounded really really bad and I was scared of that."

"The day we found out the treatment wasn't working, when the hematologist told us that stem cell transplant was no longer an option and we talked about CAR-T and going out of province, which he didn't want to do, the hematologist was scared that she was going to have to find something to try to be a third line treatment and she didn't know of anything that she thought was going to work. She thought that CAR-T was going to be the only option and if we didn't do it, that was pretty much it."

5. **Improved Outcomes**

Interviewees expressed that patients and caregivers all just want a small sense of normalcy in a time of fear, confusion, and uncertainty. The ability to stay close to home, to their support systems and familiarity and to be able to meaningfully participate in their lives as they did before illness and treatment.

"A medication that came with less side effects and could be offered closer to home definitely would have been much easier on him overall. His mental health wouldn't have deteriorated, I think, as much as it did because if there weren't as many side effects, he could have continued doing things that he liked to do

during his chemo. He lost a sense of himself because he wasn't able to do the things he liked to do. He wasn't able to keep up with his hobbies and whatnot. He wouldn't have felt so isolated during the journey."

Patients want to be a part of the process and to have a choice of treatment options. They want to feel involved and be able to maintain a small amount of control in a time of chaos.

"His hematologist was like, here's what I think is your best bet, here's what I recommend doing. There was no discussion. It was like, here you go, here's your prepped regimen on a sheet of paper. Here you go."

Patients have a deep unmet need for additional treatment options.

"I think the decision to continue with treatment or not would really have depended on the success of the other treatment options that would be next. If he were told, well 39% of people went into remission after this treatment then yes but otherwise I think he would have said enough is enough and stepped away."

"Having options is just a huge deal for anyone. Knowing that there are other options that are being offered if we need them is truly amazing to me."

6. **Experience With Drug** Under Review

Epcoritamab is a new treatment in Canada. One caregiver from the United States spoke to us about her experience with epcoritamab. Her husband is currently receiving epcoritamab treatment. This caregiver described their treatment experience with epcoritamab thus far…

This patient is early in their epcoritamab experience. He has been on epcoritamab for a month and has had four doses.

We asked this **caregiver to explain what factors were considered by the patient and his family when deciding whether or not to go ahead with epcoritamab treatment.**

"The doctor said that there was this new antibody that had been approved and we looked at the information on it. We read that the side effects weren't bad other than some dizziness, nausea, it was nothing that bad other than CRS, so it was just something we had to try. We knew we had to try something because we have a new grandbaby coming in January and he knew if he wanted to see the baby he had to do something because the doctor said it could only be a few months if he didn't do anything, it would kill him. We decided to try it."

This caregiver explained what a typical epcoritamab treatment appointment looks like for the patient…

"He's doing 12 weekly treatments and they'll do a pet scan after the 8th one to see exactly what it's done, and then after 12 treatments it'll go to every two weeks for so many sessions and then it'll go to once a month. It's going to be at least a year we'll be doing this."

"In a treatment appointment we do labs, then we see the nurse practitioner or the doctor, either one. They let us know what his activity level is where his cancer is and then we go to the infusion lab where they give him Zofran, Benadryl and steroids. Then we wait an hour and then they give him his epcoritamab shot and then we wait two hours before we can go home. Treatment takes about 5-6 hours from beginning to end."

The caregiver described the treatment side effects the patient has experienced since starting epcoritamab treatment…

“He's been okay. [Out of all the treatments he has had] this has had the least amount of side effects. After day three of steroids he'll spike a temperature, but he’ll take Tylenol and it'll go down.” After the fourth dose, the patient experienced nausea and general weakness.

This caregiver described the promising progress that her husband has made since starting epcoritamab treatment…

“His LDH started at over 800 and it's now 535. It's dropped so epcoritamab is doing something. After the second treatment it started to go down.” She also reported that her husband’s pain has decreased since starting epcoritamab.

The caregiver spoke about the financial burden they have experienced due to treatment…

They relayed that they live 75 miles away from where they go to have the treatment done and that their daughter is helping to cover their bills at the moment because they can’t keep up. They have had to pay for some aspects of previous treatment, so they have gotten behind financially. They have had to accept help from their previous cancer centre with grocery and gas cards but at their current cancer centre there is no such help available.

7. **Companion Diagnostic Test** - N/A

8. **Anything Else?**

Patients need access to additional treatment options that are shown to be effective in treating their disease while offering limited side effects. Epcoritamab has shown great success in trials in third line patients who have had an exhaustive treatment experience up to this point in the treatment of their disease. This treatment option could offer hope and relief to many third line patients. As a subcutaneous injection, this treatment is not as invasive as other treatments to patients’ quality of life. Although it is currently only being done in the cancer centre, it could potentially be offered closer to patients’ homes, disturbing their home life in a less invasive way than other treatments and allowing for continued support for patients from their loved ones.

We would strongly advise CADTH to recommend epcoritamab treatment for reimbursement and allow Canadians to have access to this needed third line medication for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

Appendix: Patient Group Conflict of Interest Declaration

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

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

No

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

No

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

Table 1: Financial Disclosures

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

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AbbVie Inc.				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: Colleen McMillan
Position: Advocacy Lead
Patient Group: Leukemia & Lymphoma Society of Canada (LLSC)
Date: **November 27, 2023**

Clinician Group Input

CADTH Project Number: PC0334-000

Generic Drug Name (Brand Name): Epcoritamab

Indication: For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

Name of Clinician Group: Lymphoma Canada

Author of Submission: John Kuruvilla, Chai Phua, Shannon Murphy

1. About Your Clinician Group

Lymphoma Canada, a national non-for-profit organization for Canadian lymphoma and CLL patients, coordinated the group clinician response. 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: John Kuruvilla, Chai Phua, Shannon Murphy

2. Information Gathering

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

Relapsed or refractory Diffuse Large B-Cell Lymphoma (RR-DLBCL) in Canada is managed with different goals based on prior therapies utilized and the feasibility of the patient undergoing potentially aggressive curative approaches. Treatment decisions are initially made at the time for first disease progression (typically after R-CHOP chemotherapy or similar) that divide patients into two subgroups: patients are eligible for aggressive curative intent procedures and patients that are ineligible for these more intensive therapies.

In patients that are eligible for more aggressive therapy, the goal is potentially curative with the use of salvage chemotherapy and autologous stem cell transplantation (ASCT). Health Canada has now approved CD19 directed chimeric antigen receptor T-cell therapy (CART) in the second-line curative setting and we are currently awaiting reimbursement at the provincial level. Currently, CART is funded as a third-line curative therapy for patients that do not respond to second-line chemotherapy or progress following ASCT. A subgroup of patients that are not eligible for ASCT-based approaches would be appropriate for second-line chemotherapy and could be considered for CART as a third-line therapy. Patients that have disease progression post CART or for those patients that cannot receive CART for medical and/or social reasons (lack of access, geographic restrictions etc.) do not have another curative intent therapy readily available.

In contrast, the group of patients that are not eligible for curative ASCT-based or CART approaches are not curative with standard approaches. Much like the patients that ultimately progress post ASCT/CART or are unable to receive these treatments due to progressive disease or for other reasons, these patients are managed with palliative approaches. This may include the anti-CD79b antibody drug conjugate (ADC) polatuzumab vedotin which is given with bendamustine and rituximab (Pola-BR; available in most provinces with the exception of Quebec) or the anti-CD19 antibody tafasitamab in combination with lenalidomide (now approved

solely in Quebec[29]) which are novel therapies that have been available recently. Historically, a small percentage of patients might have pursued allogeneic stem cell transplant (allo-SCT) but the vast majority of patients in this setting were managed with a variety of palliative chemotherapy regimens (single agents including gemcitabine, IV combination approaches, oral combinations including alkylators and prednisone, single agent corticosteroids), radiation therapy in patients with bulky or symptomatic sites or clinical trials in select centres. Multiple novel agents (ibrutinib, lenalidomide, tafasitamab, selinexor) have had compassionate access programs but generally do not have Health Canada approvals or provincial funding for RR-DLBCL.

Patients with RR-DLBCL are incurable if they have experienced disease progression following ASCT/CART or are ineligible for these procedures. Treatment is given in this setting to improve disease-related symptoms and health related quality of life (HRQOL), reduce the likelihood of disease progression and the development of symptoms that would warrant hospitalization and to reduce the likelihood of developing immediate life-threatening toxicities. The available palliative therapies do not change the natural history of the disease and typically have progression-free survival (PFS) and overall survival (OS) in the range of a few months. While polatuzumab has become an important option in the past couple of years, it is important to recognize that this agent is being used in the pre-CART setting and now has demonstrated efficacy as part of primary therapy for DLBCL (and likely to move earlier in the disease course based on these data).

4. Treatment Gaps (unmet needs)

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

The key unmet need in RR-DLBCL remains effective therapy that can put the disease into remission for prolonged periods resulting in favourable overall survival and quality of life. While CART has provided an important new treatment for many patients, both CART and ASCT are difficult and challenging therapies given the need for patients to travel to expert centres within their province (and potentially to another province) to receive treatment. This significantly limits potential access for patients that live in rural areas or have cultural/language/diversity issues that can prevent them from traveling to major metropolitan academic centre to receive specialized care. Additionally, the current availability of CAR-T therapy for R/R DLBCL is significantly constrained as limitations primarily stem from manufacturing challenges, which restrict widespread access to this advanced treatment. Regional disparities exacerbate this issue, as only a select number of sites are equipped to offer CAR-T therapy. Compounding these difficulties, there is a notable scarcity in healthcare staffing, further impeding the delivery of this potentially life-saving therapy. Overall, the population that may be eligible for CART/ASCT that cannot receive it for these reasons has a significant unmet medical need.

As outlined above, patients that experience disease progression despite receiving ASCT/CART need effective therapies to manage their lymphoma. For patients that cannot receive ASCT/CART due to fitness/comorbidity, effective therapies have simply not been available beyond the more recent availability of pola-BR (and tafasitamab-lenalidomide in Quebec). New options are needed in this setting.

5. Place in Therapy

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

As outlined above, patients that are ineligible/unable to receive ASCT/CART or have disease progression following ASCT/CART are in need of new options for treatment. Epcoritamab represents a significant new therapy in RR-DLBCL. This T-cell engaging (TCE) antibody targets CD3 on patient T cells along with CD20 on lymphoma cells and leads to tumour cell death via immunologic mechanisms. Longer-term data demonstrates that a proportion of patients have achieved complete remission (CR) and remain free of disease recurrence beyond 12 months. This stability of CR is potentially similar to CART and if confirmed may be the first sign that TCE represent another curative treatment paradigm in RR-DLBCL.

This is the second of multiple T-cell engaging antibodies that are being developed in lymphoma and there are others being evaluated in multiple tumour types. As a TCE, epcoritamab is an “off-the-shelf” therapy that has the potential to be given in any hospital/cancer centre with clinicians trained in the management of this type of antibody. Based on current data, epcoritamab would be given as a monotherapy in patients that have experienced disease progression post-CART or are ineligible for CART following at least two lines of prior therapy. Given the favourable efficacy and toxicity associated with epcoritamab, it is expected that this drug (or similar

agents) would become the default choice for the majority of patients in this setting. There will be a group of patients that are typically older and frailer that would be managed with simpler and clearly palliative approaches.

Unlike traditional CAR-T therapies, which require complex and time-consuming individualized manufacturing processes, T-cell engaging therapies are often 'off-the-shelf' products. This key attribute significantly reduces manufacturing time and associated costs, potentially making these therapies more readily available to a broader patient population. Moreover, the 'off-the-shelf' nature of T-cell engaging therapies could alleviate regional access issues by enabling distribution to a wider range of treatment centers, not limited to specialized facilities. This broader distribution capability could, in turn, help reduce healthcare disparities and provide a more equitable treatment landscape. In addition, the subcutaneous formulation of epcoritamab will reduce chemotherapy chair time which often translates to health care cost savings. Plus the potential for full outpatient delivery of therapy further improves associated treatment burden (studies ongoing).

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?

Epcoritamab would be used in the third-line or beyond setting. Based on the currently available data, there are no obvious subgroups of patients that are more likely to derive benefit from epcoritamab. The phase II data have subset analyses associated with them but they are underpowered to address benefit in specific populations and these retrospective analyses would only be hypothesis-generating.

RR-DLBCL has a fairly homogeneous outcome in the third-line and beyond setting when non-curative therapies are employed with survival typically measured in weeks to months. Rarely, patients may present asymptomatically and thus could be observed briefly in the absence of curative therapy. Patients with localized disease could be considered for radiation therapy if appropriate based on the site of disease and prior history of radiation. There are no additional tests (and no companion diagnostic) for epcoritamab. CD20 testing is routinely available but not routinely performed in patients with RR-DLBCL that are multiply treated and in the palliative setting. Misdiagnosis is uncommon as imaging and biopsy is frequently performed in this setting looking for treatment failure (which tends to occur fairly early in patients undergoing second or third-line treatment).

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

Response endpoints along with time-to-event endpoints (PFS and OS) are typically used in clinical practice and aligned with clinical trials. Patients with aggressive lymphomas typically undergo CT and/or FDG PET scan (if available) to assess response and are followed while on treatment and following completion of treatment. Clinically meaningful response would be partial response (PR) or complete response (CR) which is typically determined using CT/PET-CT. This is consistently applied using standardized criteria by physicians that treat lymphoma across the country. Based on the available data from the epcoritamab registrational study, this treatment demonstrates a high level of efficacy with favourable overall and CR rates, progression-free and overall survival particularly when compared with data from other trials and real-world evidence in this setting.

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

As with most therapies given in patients with RR-DLBCL, disease progression will be the most common reason to discontinue epcoritamab therapy. A proportion of patients will achieve remission and continue on treatment. Adverse events in patients receiving treatment were generally low grade and would not require treatment discontinuation. However, in some patients that may develop high grade (ie. grade 3 or greater) cytokine release syndrome (CRS), neurotoxicity or severe infectious toxicity (grade III or greater, requiring hospitalization or life threatening), clinicians may elect to discontinue treatment due to the potential for recurrent high-grade events. Epcoritamab treatment includes treatment until progression as has been seen with some novel therapies approved in lymphoma. This approach has not been a standard in DLBCL and we expect that in the minority of patients that continue in longer term remission on treatment without significant toxicity that patients and clinicians may discuss discontinuation of treatment in CR due to multiple concerns which may include patient convenience.

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]?

Epcoritamab as an antibody-based treatment that is an “off-the-shelf” therapy. It can be given in any hospital or cancer centre that has the ability to admit and monitor patients that are receiving anti-cancer therapy. Early toxicity events including CRS are possible

and may require inpatient monitoring and management. Clinicians will require education and experience in the management of CRS and neurotoxicity. Similar to the rollout of CART to academic cell therapy centres, individual centres that start using epcoritamab will benefit from training for clinicians in areas (emergency rooms, intensive care units, chemotherapy units, inpatient hematology/oncology units) that may care for patients that receive these drugs. Standard management guidelines are available from academic centres that are currently being made available to any centre requesting them. Many clinical trial centres have had experience TCE with multiple agents. Currently, multiple centres in the community are poised to conduct additional trials of TCE that will provide hands-on training for staff to manage these toxicities. Subcutaneous administration is an advantage with this agent given the challenges many institutions face in chemotherapy units.

6. Additional Information

TCE represent the next generation of transformative therapies in the lymphoma field. There is no doubt that these agents represent a highly effective "off the shelf" treatment for patients that can be given in many hospitals or cancer centres and does not need to be limited to academic centres with ASCT/CART programs. Canada was the first country to have regulatory approval for Epcoritamab and we have no funding available for this while the drug is now potentially available in other countries. Epcoritamab is another important alternative and we hope to have this agent available for Canadians in the near term.

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.

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

No\

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

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: John Kuruvilla

Position: Chair, Scientific Advisory Board, Lymphoma Canada Date: 27-11-2023

☒ 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**
Abbvie		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 2

Name: Chai W. Phua

Position: Adult Hematologist, LHSC, London Date: 27-11-2023

☒ 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
Abbvie	X			
Sanofi	X			
CSL	X			
Beigene	X			
AstraZeneca		X		
EusaPharma	X			
FORUS Therapeutics	X			
Bayer	X			
Octapharma	X			
Janssen	X			

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

Declaration for Clinician 3

Name: Shannon Murphy

Position: Member, Lymphoma Working Group, Canadian Cancer Trials Group Date: 27/11/2023

☒ 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 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
Abbvie	X			
Add company name				
Add or remove rows as required				

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

Clinician Group Input

CADTH Project Number: PC0334

Generic Drug Name (Brand Name): Epcoritamab (Epkinly)

Indication: For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

Name of Clinician Group: Ontario Health (CCO) Hematology Cancer Drug Advisory Committee

Author of Submission: Dr. Tom Kouroukis

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 in a DAC meeting.

3. Current Treatments and Treatment Goals

Current treatment options in third line or beyond include Polatuzumab-BR, Rituximab-chemotherapy, chemotherapy, and radiation. Tafasitamab and lenalidomide are options that are privately covered.

Treatment goals are to prolong life, delay disease progression, and alleviate 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.

There are no treatments available for long term remissions if the patient is not CAR-T eligible.

5. Place in Therapy

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

This drug can be used in third line or beyond, if the patient was previously treated with CAR T-cell therapy, or ineligible for CAR T-cell therapy, as per the trial.

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?

As per the trial criteria.

Patients who have had prior alloSCT, should be eligible for epcoritamab.

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, symptom improvement.

Treatment response should be assessed as per usual practice.

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

Disease progression, 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]?

Inpatient and outpatient settings.

Centers with expertise in managing CRS and neurotoxicities.

6. Additional Information

We may need to ensure there is adequate tocilizumab supply for CRS management.

We would like CADTH to review and comment upon fixed duration versus continuous therapy with BiTEs in rrDLBCL.

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.

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.

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.

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. Tom Kouroukis

Position: OH-CCO Hematologic Cancer Drug Advisory Committee lead

Date: 16-11-2023

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

Table 1: Conflict of Interest Declaration for Clinician 1

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

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

Declaration for Clinician 2

Name: Dr. Selay Lam

Position: OH-CCO Hematologic Cancer Drug Advisory Committee member

Date: 16-11-2023

☒ 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
Abbvie		X		
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 3

Name: Dr. Lee Mozessohn

Position: OH-CCO Hematologic Cancer Drug Advisory Committee member

Date: 16-11-2023

☒ 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: Dr. Jordan Herst

Position: OH-CCO Hematologic Cancer Drug Advisory Committee member

Date: 16-11-2023

☒ 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: Dr. Guillaume Richard-Carpentier

Position: OH-CCO Hematologic Cancer Drug Advisory Committee member

Date: 16-11-2023

☒ 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				

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

Declaration for Clinician 6

Name: Rami El-Sharkawy

Position: OH-CCO Hematologic Cancer Drug Advisory Committee member

Date: 16-11-2023

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

Table 5: Conflict of Interest Declaration for Clinician 6

	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				

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

Declaration for Clinician 7

Name: Dr. Pierre Villeneuve

Position: OH-CCO Hematologic Cancer Drug Advisory Committee member

Date: 21-11-2023

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

Table 5: Conflict of Interest Declaration for Clinician 7

	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				

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

Clinician Group Input

CADTH Project Number**:** PC0334-000

Generic Drug Name (Brand Name): epcoritamab (Epkinly)

Indication: For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

Name of **Clinician Group:** LLSC Nurses Network

Author of Submission: Marlie Smith RN, BScH, BNSc, MN – Please direct any inquiries regarding this submission to Colleen McMillan, Advocacy Lead, The Leukemia & Lymphoma Society of Canada (LLSC) [redacted]

1. About Your Clinician Group

LLSC Nurses Network - This is a group of nurses with an interest in blood cancer

2. Information Gathering

LLSC gathered input via interviews and a roundtable discussion with six nurses with various cancer and DLBCL **patient experience from various centres across Canada**

3. Current Treatments and Treatment Goals

First line – RCHOP combination chemotherapy – rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate

Second line -- GDP chemotherapy (gemcitabine, dexamethasone, cisplatin), sometimes ICE chemotherapy is used as well (*ifosfamide, carboplatin, and etoposide)*
If they reach remission in second line – Stem cell/bone marrow transplant

If remission wasn't achieved -- CAR-T treatment

Third line – If CAR-T treatment was not successful or the patient was ineligible for CAR-T treatment the patient would be referred to best supportive/palliative care. In some cases, there are different lines of IV treatment or oral treatment that we can try but we don't tend to think that those options are going to offer the patient a long-term benefit.

The most important goals of treatment for DLBCL are to prolong life, delay disease progression, improve symptoms such as fatigue, breathlessness, and pain, to reduce the severity of symptoms, improve quality of life, increase ability to maintain independence and the patient's ability to participate meaningfully in life, increase patients' and caregivers' ability to maintain employment, and reduce the burden on caregivers

4. Treatment Gaps (unmet needs)

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

- There is a need for effective and tolerable treatments in third line treatment of DLBCL.
- At this point in their treatment, patients are very frail due to the toxicities of past treatments and both mental and physical treatment fatigue. They may have varying GI symptoms such as nausea, poor appetite, vomiting, diarrhea, constipation. They have usually lost muscle mass and weight and are generally unwell. Their gait may be unsteady. Some require a walker or a wheelchair.
- Common symptoms of their DLBCL are often fatigue pain and shortness of breath. Clinically, we observe that these have significant impact on quality of life.
- Formulations are needed to improve convenience – Length of time spent in hospital for treatment is a burden on patients and their families. Treatment options that offer less time in hospital could make a significant difference in patient and caregiver quality of life. Treatment is all consuming for both patients and caregivers so any treatment that has the potential to offer less time in hospital is immensely beneficial.
- When patients get to the stage before they start third line treatment, mentally they are in a negative space. By third line treatment these patients and their caregivers are devastated that they are still fighting their disease and that nothing thus far has worked for them. They are worried and feel like they have let their families down. The disappointment they feel from previous treatment failing them is hard to bear and the hopes of previous treatments working for them have been dashed. They have gone through a roller coaster of emotions and experience guilt and shame. They feel that somehow, they have done something wrong because they have failed treatment. They're already in an advanced state of their disease and they are grieving and trying to cope with their circumstances. These patients have a more flat affect than in earlier stages of treatment and they suffer from information exhaustion. They're often angry that other treatments haven't worked and they find it difficult to engage or feel hopeful about treatments. Those that have access to psychosocial counselling require more resources and health care professional time.
- Treatment closer to home – Some patients must travel not just across their province but across the country to receive treatment, uprooting their lives and the lives of their caregivers. The financial and psychological impact of such drastic upheavals have a significant impact on patients' overall health and mental wellness and the isolation these patients feel while going through treatment and being away from their home communities and support systems are unbearable. Treatment options that have the potential to be offered within a patient's home community could have a significant benefit to both patient and caregiver overall health and wellness and could also lessen the financial burden of treatment on patients and caregivers. Travel comes with a lot of caregiver burnout.

5. Place in Therapy

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

In regard to the indication up for review, this treatment would take place in third line after two or more lines of systemic therapy for patients who have previously received or are unable to receive CAR-T cell therapy.

In comparison to treatments such as LENA+TAFA which is an infusion and has a heavy appointment commitment, this treatment, as a subcutaneous injection, could mean significantly less resource time and could potentially be offered in a community cancer centre. The patient would receive this treatment as an outpatient. This treatment could possibly become a more feasible and more well-favored option than currently available treatments.

This is a new treatment with very limited Canadian experience. None of the respondents in this submission have direct experience with the treatment under review.

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?

Examples of a clinically meaningful response for these patients could be improved survival, improvement in their blood work and less presence of cancer cells in their bone marrow, improvement of symptoms. A reduction in symptoms including pain, breathlessness and fatigue would help contribute to a better sense of overall wellbeing. Improved functionality would also be important indicators of response.

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

Disease progression or treatment toxicity would be factors in deciding whether to discontinue treatment.

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]?

Although this is currently being offered in a cancer centre, it could potentially be supported in a community setting. Patients would need to start the first few injections in a cancer centre but for those that remain stable with no concerns for adverse reactions, community settings are possible. This would require the right education and the right support. The treatment modality is subcutaneous injection and nurses are trained in how to give these injections and already giving them in community hospital settings.

More training may be required based on the capabilities of the staff in each centre. Examples of training required could be recognizing and dealing with any adverse events that could be potentially associated with treatment, recognising and treating localized skin reactions, education on the treatment option itself, and chemotherapy/immunotherapy certification may be required based on the mandate and location of the hospital.

6. Additional Information

Immunotherapies are usually better tolerated in comparison to chemotherapy. Treatment toxicities are important to consider in third line as this is a patient population that has a high level of treatment experience.

The possibility and potential of patients and caregivers being able to remain close to home and receive this subcutaneous treatment option could make a significant difference in patient outlook and outcomes. epcoritamab (Epkinly) could potentially also offer a less resource intensive treatment option for healthcare providers and would be welcome in an era where health human resources are constrained.

We would advise CADTH to recommend epcoritamab (Epkinly) treatment for reimbursement and to assist in increasing access to this needed medication for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS), DLBCL transformed from indolent lymphoma, high grade B-cell lymphoma (HGBCL), primary mediastinal B-cell lymphoma (PMBCL) or follicular lymphoma Grade 3B (FLG3b) after two or more lines of systemic therapy and who have previously received or are unable to receive CAR-T cell therapy.

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.

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

No

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

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: Theresa Whiteside RN, BN, CON(C)

Position: Clinical Resource Nurse, Systemic Therapy Unit /Urgent Care Clinic – CancerCare Manitoba

Date: 27-11-2023

☒ **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: Jordana Jones RN, BN

Position: Clinical Resource Nurse - Western Manitoba Cancer Centre – Prairie Mountain Health

Date: 27-11-2023

☒ 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: Dior Caruso MN-NP Adult, CHPCN(C)

Position: Nurse Practitioner, Complex Malignant Hematology - Princess Margaret Cancer Centre

Date: 27-11-2023

☒ 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**
AbbVie Inc	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: Jennifer Holmes RN

Position: Nurse - St. Michael's Hospital

Date: 27-11-2023

☒ 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: Amanda Strandberg BScnH, RN

Position: Lymphoma RN - The Ottawa Hospital General Campus

Date: 27-11-2023

☒ 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.

Declaration for Clinician 6

Name: Marlie Smith RN, BScH, BNSc, MN

Position: Clinical Nurse Specialist - Adolescent and Young Adult (AYA) Program - Princess Margaret Cancer Centre, University Health Network

Adjunct Lecturer - Lawrence S. Bloomberg Faculty of Nursing, University of Toronto

Date: 27-11-2023

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

Table 6: Conflict of Interest Declaration for Clinician 6

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

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