CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

polatuzumab vedotin (Polivy)

(BC Cancer Lymphoma and Myeloma Tumour Group)

Indication: Polivy (polatuzumab vedotin for injection) in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) is indicated for the treatment of adult patients with previously untreated large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma, Epstein-Barr virus-positive (EBV+) DLBCL NOS, and T-cell/histiocyte rich LBCL.

December 6, 2024

CADTH

CADTH Reimbursement Review
Patient Input Template

Name of Drug: Polatuzumab vedotin

Indication: Polivy (polatuzumab vedotin for injection) in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) is indicated for the treatment of adult patients with previously untreated large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma, Epstein-Barr virus-positive (EBV+) DLBCL NOS, and T-cell/histiocyte rich LBCL that are classified as activated B-cell-like (ABC) lymphoma subtype.

Name of Patient Group: Lymphoma Canada

Author of Submission: Gurjot Basra and Sarah Eisinga, 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 used in the original submission, created and promoted by Lymphoma Canada (LC) available from February 2 to March 13, 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 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. 89 responses were collected. Information from this survey was used to identify the main areas of concern for patients with Large B-cell lymphoma, with 4 confirmed responses for experience with Polatuzumab vedotin. Three of these patients indicated they live in Canada, and other in Italy. Please see tables 1-4 below for demographic and relevant information of all survey respondents. The majority of patients lived in Canada (94%), between the age of 55 and 74 (64%), female (58%), and were diagnosed 1- 5 years ago (61%) with Diffuse Large B-cell lymphoma subtype (89%). Table 5 provides a breakdown of subtype specific information. Overall, the information and analysis below is similar to the original submission, as this was a recent survey with information that is still applicable.

Table 1: Country of respondents from Lymphoma Canada survey

Respondents	CAN	USA	Italy	New Zealand	Skipped	Total

Patients with Large B-cell lymphoma	47	1	1	1	47	50

Table 2: Age range of respondents from Lymphoma Canada survey

Respondents	Age (years old)						
	25-34	35-54	55-64	65-74	75-89	Skipped	Total
Patients with Large B-cell lymphoma	3	6	12	20	9	47	50

Table 3: Gender of respondents from Lymphoma Canada survey

Respondents	Gender			
	Female	Male	Skipped	Total
Patients with Large B-cell lymphoma	29	21	47	50

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	9	21	20	9	10	20	69

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 (DLBCL)	82
High grade B-cell Lymphoma	3
EBV+ DLBCL	1
T-cell/histiocyte-rich LBCL	1
Transformed DLBCL	2
Total	89

3. Disease Experience

At Diagnosis

Through the 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 three or higher were: fatigue (59%), bodily aches and pains (42%), night sweats (42%), enlarged lymph nodes (41%) and a reduced appetite (33%). Several patients left comments for this question indicating severe back pain and constipation were also negative symptoms experienced at the time of diagnosis.

Respondents of the survey were also asked to select from a list of psychosocial impacts they experience when diagnosed with LBCL. Of 69 patients, 81% were impacted by stress of diagnosis, 79% experienced anxiety/worry, and 60% were afraid of progression, 51% inability to continue daily activities, and 47% had difficulty sleeping. When asked to provide additional details about the challenges faced during diagnosis, several patients commented on how the COVID-19 pandemic felt them feeling isolated, with minimal support. Below are a selection of patient responses from the survey:

- “I was diagnosed during Covid. Talked to my GP over phone where we discussed lab results, need for a biopsy, results, next steps etc. Covid made being given a cancer diagnosis very isolating.”
- “While I had uncomfortable symptoms for a while, and was having lots of tests done, I was not at all expecting a cancer diagnosis until I did my own research and pretty much had it figured out. Receiving a diagnosis, over the phone, during the height of COVID was quite alarming.”
- “I felt lonely, like nobody really cared. No nearby resources.”
- “Due to Covid I was left to face this on my own since family was not allowed in hospital”
- “Challenged faced living in a rural community that I had to travel an hour and a half one way for chemo because my home hospital would not do this specific chemo. This had financial impacts as well as trying to find someone to drive me.”
- “Putting your plans on hold (travel etc.) and not being able to participate safely in large group activities. Difficult telling family and friends about the diagnosis.”

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), majority of patients rated symptoms such as fatigue (42%), bodily aches (25%), and headaches (17%) as an impact of 3 or higher on their current quality of life. Patients also indicated they recently experienced mental health challenges such as fear of progression/relapse (66%), stress of having cancer (56%) and anxiety/worry (42%).

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. Ability to exercise (41%), ability to travel (39%), spending time with family and friends (36%) and the ability to work, school and volunteer (34%) were rated as a 3 or higher by 59 patients. Many patients left comments in this section and a selection of quotes are included below:

- "Afraid to do long walks/ hikes like I used too in case I run out of energy to return"
- "I still attend the Lymphoma Support Group of Ottawa to give hope to others Just as I was given hope by meeting people who had been cured or in remission for many years."
- "Some days I don't have the energy to do things around the house. Other days I'm great and get a lot done. Energy levels are getting better now that treatment is complete. Working on getting more physical by walking. Still short of breath when walking. Working on improving that."
- "Being immunocompromised I mask indoors still so this limits restaurants or group eating events. I'm grateful for the Evusheld shots protection against covid BA-4 and BA-5. I'm less concerned about covid now than some of the other viruses circulating now. Ir RSV etc."
- "Never felt as energetic after 3 years of treatment. Know this will probably come back."
- "I have an oncologist who I see every 3 months and she's totally on top of my current health. I'm living a full life, making music, travelling, seeing friends, going to plays, concerts, walking, shopping, nothing holding me back. Being born in Canada is like winning the lottery!"

Summary of the Disease Experience

- The most common physical symptoms LBCL patients found challenging at the time of diagnosis and on their current quality of life included fatigue, bodily aches and pains, night sweats, and headaches. Top-rated psychosocial factors included stress of diagnosis, anxiety/worry, and fear of progression. Many patients also left comments that the COVID-19 pandemic made them feel isolated during diagnosis.
- There was a wide range of experiences in which LBCL symptoms impacted the daily lives of survey respondents. The ability to exercise and travel were factors which impacted most patients.

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 56 patients indicated they received 2nd or 3+ line of therapy (53%) while 41% of patients only received 1st line. See Table 6. As the indication for this CADTH submission is for previously untreated LBCL, the patient experience information in this section will focus on those with one line of therapy.

Table 6: Number of lines of therapy survey respondents received

Respondents	Have not received therapy	1	2	3	Skipped	Total
Patients with Large B-cell lymphoma	3	23	9	21	33	56

In the front-line setting, almost half of patients (48%) received the chemoimmunotherapy (CIT) R-CHOP, almost all other patients had some form or chemotherapy or CIT such as R-CHP or EPOCH-R. These patients were asked: “How satisfied were you with the number of treatment options available to you for your lymphoma?” 28% of patients indicated they were satisfied with frontline treatment options and 57% indicated they were very satisfied. 15% of survey respondents expressed dissatisfaction with treatment options available.

67% of 52 survey declared they did not have any difficulty accessing treatment for their lymphoma. Although many comments were left from patients explaining challenges and delays in accessing treatment:

- “I went to the U.S. for treatment because there were no other options other than RCHOP”
- “Standard treatment was available in my province. Could no longer work, spouse had to quit work. So moved in order to be closer to treatment.”
- “I live 50 kilometres from the hospital”
- “Location was not very difficult to access but there was a waiting list, so treatment was delayed 1 month.”

The most common financial implications reported for treatment for LBCL was absence from work (46%), drug costs (32%), travelling costs (28%), and supplementary drug costs for side effects (22%). Survey respondents left several comments when asked about the difficulties of accessing treatment in Canada:

- “It was impossible for me to get anything but RCHOP in Canada as a first line of treatment. My immune system was depleted and I did not think I would survive six rounds of RCHOP. After the first round I left Canada to look for other treatment options. It cost me everything financially but I had a better quality of life during treatment and I’m alive today.”
- “At the time CAR-T was new in the USA and not available in Canada. Now it's even available in my new home town.”
- “Could not be happier with the speed, efficiency, and results of my treatment. (All done at Sunnybrook, Toronto)”

- "I was very fortunate not to have any difficulty accessing treatment. I know it is not the case for many people in Canada.

Summary of Currently Available Treatments

- The majority of survey respondents received second or third line of treatment for their LBCL, with R-CHOP as the most common treatment regimen for frontline patients. 15% of survey respondents indicated they were dissatisfied with treatment options available to them, with several comments from patients indicating they travelled abroad to access other treatment options.
- When asked about accessing lymphoma therapy in Canada, many patients indicated they required to travel long distances, which was which challenging financially and required time off work.

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. 11 patients indicated factors such as longer disease remission (100%), control disease symptoms (91%), longer survival (100%), normalize blood counts (91%), and improved quality of life to perform daily activities (91%), were very important to them (10 out of 10). 8 of these patients indicated they would be willing to tolerate side effects to access new treatment and 7 patients indicated choice is important to them (8 or higher, of 10) in deciding to take a drug based on known side effects and expected outcomes of treatment.

A few patients left comments about managing expectations of novel lymphoma treatments:

- "I would take the recommendation of my doctor"
- "I hope that they will have long lasting effects of remission."
- "I have had wonderful care in the treatment of my lymphoma, I have great trust in my doctors"

9 out of 11 patients indicated they feel there is a need for more therapy options for patients with LBCL.

Summary of Currently Available Treatments

- Factors important to LBCL patients when considering novel therapies include longer disease remission, controlled disease symptoms, longer survival, normalized blood counts and improved quality of life to include daily activities.
- Majority of patients that completed this section of the survey feel there is a need for more therapeutic options for treatment of LBCL.

6. Experience With Drug Under Review

From survey responses, 4 patients indicated they were treated with Polatuzumab vedotin in combination with the chemotherapy R-CHP. Based on the information completed by LBCL patients in this section, the following information was gathered about the current drug under review:

- 3 patients would recommend Pola-R-CHP to other LBCL patients.
- 1 patient accessed this therapy through a clinical trial, 2 other patients accessed through Medicare or public care.
- 2 patients indicated their overall experience was very good with Pola-R-CHP and rated their experience as good.
- Side effects patients experienced on Pola-R-CHP included: fatigue (3), neutropenia (2), thrombocytopenia (2), decreased appetite (2), diarrhea (2), cytokine release syndrome (1), fever (1), febrile neutropenia (1), low blood pressure (1), infections (1), nausea/vomiting (1), and joint or muscle pain (1).

Summary of Drug Under Review

- Overall, the experience of Pola-R-CHP from LBCL patients was positive with minimal negative comments left about the ability to access treatment, financial implications, or challenges tolerating side effects.

7. Companion Diagnostic Test

N/A

8. Anything Else?

Lymphoma Canada is a strong advocate for ensuring that lymphoma patients and their caregivers have access to the most innovative lymphoma therapies. A broader range of treatment options empowers patients to work with their medical care team to select therapies that align with their personal goals and individual needs.

Patients with activated B-cell (ABC) subtype of diffuse large B-cell lymphoma (DLBCL) are at particularly high risk of relapse or refractory disease following R-CHOP treatment. This underscores the urgent need for innovative therapies to address this high-risk group. Additionally, a significant number of patients with large B-cell lymphoma (LBCL) experience relapse after first-line therapy, highlighting the necessity for more effective and novel treatment options for these individuals. This is reflective in the survey data above as most patients relapsed and received second or third line therapy (53%).

All in all, in the first-line treatment setting for DLBCL, it is critical to ensure that patients, especially those in the ABC subgroup, receive the most effective available therapy at the outset. Early and optimal treatment can prevent poor prognoses and the development of aggressive disease later on.

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
Roche			X	
Gilead				X
Incyte			X	
Novartis			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 and Sarah Eisinga
Position: Manager of Patient Programs, Research, and Advocacy
Patient Group: Lymphoma Canada
Date: Dec 1, 2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0397-000

Generic Drug Name (Brand Name): Polatuzumab vedotin (POLIVY), in combination with rituximab, cyclophosphamide, doxorubicin and prednisone (Pola RCHP)

Indication: Polivy (polatuzumab vedotin) plus rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult patients with previously untreated large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma, Epstein-Barr virus-positive (EBV+) DLBCL NOS, and T-cell/histiocyte rich LBCL, that are classified as activated B-cell-like (ABC) lymphoma subtype

Name of Clinician Group: Lymphoma Canada Scientific Advisory Board

Authors of Submission: Dr Pam Skrabek, John Kuruvilla, Caorlyn Owen, David Szwajcer, Chantalle Menard, Versha Banerji, Kristjan Paulson, Craig Speziali, Leonard Minuk

1. About Your Clinician Group

Lymphoma Canada Scientific Advisory Board

2. Information Gathering

Data sources included the previous CADTH review, the randomized trial of the treatment in question (POLARIX). In addition, an online search for published abstracts and articles pertaining to Pola RCHP in LBCL was performed and included cell of origin data and Polatuzumab vedotin as search terms.

See list of references provided.

3. Current Treatments and Treatment Goals

At present, initial therapy for most LBCL is R-CHOP every 21 days for 6 cycles. The goal of therapy is curative with an early indication of success being the demonstration of complete remission. With current therapy, a significant portion of patients may not achieve a complete remission or can develop disease progression after an initial response of remission. Treatment at time of relapse is associated significant cost and toxicity with many patients dying of LBCL even if eligible for intensive therapies.

Initial therapy that is associated with decrease relapse risk / improvement in progression free survival is needed, particularly for high risk patients. Patients activated B cell type (ABC) cell of origin subtype are particularly high risk of having relapsed/ refractory disease post RCHOP. These are the patients for which we suggest a change in therapy to Pola RCHP, as opposed to RCHOP, first line as in the POLARIX trial.

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 main treatment goal that is unmet with current therapy is a need for less patients with relapse/ or progression after initial therapy. Pola R-CHP is associated with significantly lower need for second line or subsequent therapy compared to RCHOP [7]. Two different clinician groups provided feedback on the original CADTH submissions and highlighted these needs [7]. The POLARIX trial has a significant magnitude of clinical benefit overall and the primary endpoint of improvement in PFS was highlighted as suitable surrogate for cure in DLBCL. Thus, this trial has achieved the most important goal in DLBCL with the additional benefit that Pola-R-CHP adds minimal toxicity. The magnitude of benefit was most in patients with higher risk disease (including ABC subtype) making these the patients who are most suitable to receive Pola-RCHP instead of RCHOP. It is important to note that relapse of DLBCL is associated with significant morbidity as well as the risk of mortality. From a patient perspective, the need for second line therapy not only increases the risk of dying of lymphoma but leads to loss of work, time away from family and activities, risks of hospitalization for intensive curative-intent relapsed therapies and/or toxicities of relapse treatments.

5. Place in Therapy

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

Pola-R-CHP would replace of R-CHOP as initial therapy for patients meeting the indication described. While the POLARIX study was tested in a specific population defined by the IPI and other inclusion/exclusion factors, we feel that a subset of patients, those classified as ABC subtype appear to derive a significant magnitude of benefit from the addition of polatuzumab to primary treatment. Given the significant PFS benefit in ABC-LBCL, continuing to treat these patients with RCHOP would be associated with significantly higher relapse and need for subsequent therapies compared to the requested switch to Pola-RCHP.

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?

Adult patients with Advanced Stage LBCL, IPI 2-5 that have not yet been treated, eligible for multiagent chemoimmunotherapy would be eligible if they are classified as ABC subtype. In the POLARIX trial this was done using gene expression profiling however standard of care in most Canadian centers would be to classify via standard IHC algorithms (which has ~ 80-90% agreement with gene expression profiling). Both methods of classification would be acceptable. The efficacy of Polatuzumab vedotin in ABC LBCL has been established in several studies highlighted below and supported by results of the POLARIX study.

DLBCL patients with ABC subtype cell of origin have a worse prognosis than those with GCB DLBCL. This is a patient population where better treatments are needed, as such, cell of origin (COO) has informed several clinical trial designs all of which have been negative to date. The POLARIX trial was not specifically designed to test efficacy by LBCL subtypes however it did meet its primary endpoint of improvement in progression free survival (PFS). ABC tumors in the POLARIX trial benefited profoundly from polatuzumab vedotin: the hazard ratio for disease progression, relapse, or death in those treated with pola-R-CHP compared with R-CHOP was 0.34 (95% confidence interval [CI], 0.13 to 0.85), and the hazard ratio for death was 0.27 (95% CI, 0.06 to 1.26) [as presented to FDA March 2023, 5]. Data in relapsed and refractory DLBCL supports this interaction with efficacy [4,5]. Morschhuaser et al analyzed baseline biopsies from 689 patients in the POLARIX trial using digital gene expression (NanoString Lymph2Cx) to determine COO. They found that 235 patients were classified as ABC subtype with the remainder being GCB (357) and unclassified (97). For ABC-DLBCL treated with Pola-R-CHP the two-year PFS was 85% compared to 56% in patients treated with RCHOP (HR 0.34 CI 0.21-0.56). The previous review of Pola-R-CHP by CADTH stated the magnitude of benefit was not felt to be sufficiently clinically significant. In ABC-LBCL, a 29% absolute difference in PFS would be substantially beneficial and clinically significant.

Over years multiple trials have aimed to improve on results of RCHOP in LBCL. Sheng et al. performed a network meta-analysis of 20 randomized control trials. They confirmed that Pola-RCHP had significant improvement in PFS compared to RCHOP. Looking at PFS of ten first line treatment regimens they found Pola-RCHOP to be the best first line intervention. For ABC-DLBCL, treated with Pola-R-CHP there was a significant PFS benefit compared to R-CHOP+Bort (HR: 0.52, *P*=0.02), R-CHOP+Ibru (HR: 0.43, *P*=0.001), R-CHOP+Lena (HR: 0.51, *P*=0.009), G-CHOP (HR: 0.46, *P*=0.008), and **R-CHOP (HR: 0.40, *P*<0.001)**.

It is known that a portion of patients can be misclassified by IHC however this is the method most commonly used at present in Canada. A real-world study of patients classified by the Hans algorithm confirmed that using this method to classify patients the

differential benefit of Polatuzumab vedotin in non-GCB COO compared to GCB was verified [6]. A misclassified patient with GCB-DLBCL will not be harmed by receiving Pola-RCHP as there was an overall benefit in the POLARIX trial.

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?

In clinical practice improved symptoms is assessed throughout treatment course in addition to examination of palpable lymph nodes or organomegaly. Repeat imaging with CT and PET/CT is used to compare to baseline to determine response as per Lugano criteria. This is generally considered after 3-4 cycles of therapy (CT) and standard at end of treatment (PET /CT with completion of 6 cycles) which is similar to clinical trials. A switch to Pola-RCHP would not impact on response assessment as the same standard of care procedures would be followed with Pola-RCHP as currently with RCHOP. No additional tests would be implemented.

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

Patients with disease progression or lack of response on Pola RCHP should be discontinued and treated with appropriate second line therapy. Development of peripheral neuropathy should be managed as per the clinical trial, if severe then Polatuzumab vedotin would need to be discontinued.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

This regimen could be administered by any site or practitioner that currently gives RCHOP chemotherapy due to similar toxicity profiles. Polatuzumab vedotin has been approved in combination with bendamustine and rituximab for the treatment of relapsed/refractory DLBCL for several years in the majority of provinces in Canada. There is broad experience with the drug and in a combination chemotherapy regimen.

6. Additional Information

List of References:

1. Deciphering the Clinical Benefit of Pola-R-CHP versus R-CHOP in Different Genetic Subtypes Beyond Cell of Origin in the POLARIX Study. Abstract 621. Morschhauser, et al. *Blood* (2023) 142 (Supplement 1): 3000.
2. Tilly H, et al. N Engl J Med 2022;386:351–363.
3. Sheng Z, Li D, Chen B, Zhao C, Zhang W, Ding B, Wang L. Superiority of polatuzumab vedotin over other novel agents in previously untreated ABC-type diffuse large B-cell lymphoma: a network meta-analysis of 20 RCTs. Ann Hematol. 2023 May;102(5):1011-1017.
4. Russler-Germain D, . Scheffer Cliff E, Bartlett N. Cell-of-origin effect of polatuzumab vedotin in diffuse large B-cell lymphoma: no ordinary subgroup analysis. Blood. 2023 Dec 21;142(25):2216-2219.
5. Palmer AC, Kurtz DM, Alizadeh AA. Cell-of-Origin Subtypes and Therapeutic Benefit from Polatuzumab Vedotin. N Engl J Med. 2023 Aug 24;389(8):764-766.
6. Edward R Scheffer Cliff, et al. The Predictive Value of Cell-of-Origin Subtype by Hans Algorithm in 718 Patients with Large B cell Lymphoma Receiving Polatuzumab Vedotin. Abstract 652. https:// ash.confex.com/ash/2024/webprogram/Paper202153.html
7. CADTH Reimbursement Review Stakeholder Feedback on Draft Recommendation. Polatuzumab vedotin in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult patients with previously

untreated large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma, Epstein-Barr virus-positive (EBV+) DLBCL NOS, and T-cell/histiocyte rich LBCL. September 15, 2023

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 Pam Skrabek
Position: Associate Professor, Max Rady College of Medicine, Department of Internal Medicine
Section of Hematology and Medical Oncology, Cancer Care Manitoba

Date: 27-11-2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Hoffmann-La Roche Ltd.	X			

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

Declaration for Clinician 2

Name: Carolyn Owen

Position: Associate Professor
Date: 02-12-2024

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

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Hoffman La Roche	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. John Kuruvilla
Position: Chair, Lymphoma Canada SAB, Lymphoma/Myeloma Disease Site Lead, Princess Margaret Cancer Centre.
Date: 4-Dec-2024

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

Table 3: Conflict of Interest Declaration for Clinician 3

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

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

Declaration for Clinician 4

Name: Dr. David Szwajcer
Position: Associate Professor, Hematologist CCMB
Date: Dec 4, 2024

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

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
No COI				

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

Declaration for Clinician 5

Name: Dr. Chantalle Menard
Position: Hematologist, CanCercare Manitoba
Date: Dec 4, 2024

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

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NO COI				

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

Declaration for Clinician 6

Name: Dr. Craig Speziali
Position: Hematologist, CancerCare Manitoba, Assistant Professor, Max Rady College of Medicine, University of Manitoba
Date: Dec 4, 2024

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

Table 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**

NO COI				

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

Declaration for Clinician 7

Name: Dr. Kristjan Paulson
Position: Chair, Leukemia Disease Site Group, CancerCare Manitoba, Assistant Professor, Max Rady College of Medicine, University of Manitoba
Date: Dec 4, 2024

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

Table 7: 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**
NO COI				

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

Declaration for Clinician 8

Name: Dr. Leonard Minuk
Position: Co-Head, Department of Medical Oncology and Hematology and Section of Hematology/Oncology, CancerCare Manitoba
Date: Dec 4, 2024

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

Table 8: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NO COI				

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

Declaration for Clinician 9

Name: Versha Banerji

Position: Director, CLL Clinical Care, Education and Translational Research Unit
Date: Dec 4, 2024

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

Table 9: Conflict of Interest Declaration for Clinician 9

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NO COI				

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

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0397-000
Generic Drug Name (Brand Name): Polatuzumab vedotin (Polivy)
Indication: Polivy (polatuzumab vedotin) plus rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult patients with previously untreated large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high grade B-cell lymphoma, Epstein-Barr virus-positive (EBV+) DLBCL NOS, and T-cell/histiocyte rich LBCL, that are classified as activated B-cell-like (ABC) lymphoma subtype.
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis and members of the OH-CCO Hematology Cancer Drug Advisory Committee

1. About Your Clinician Group

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

2. Information Gathering

Information is gathered via video conferencing and emails.

3. Current Treatments and Treatment Goals

Current standard of care is R-CHOP.

Treatment goals: Cure and prevent need for salvage treatment (e.g., transplant and CAR-T)

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.

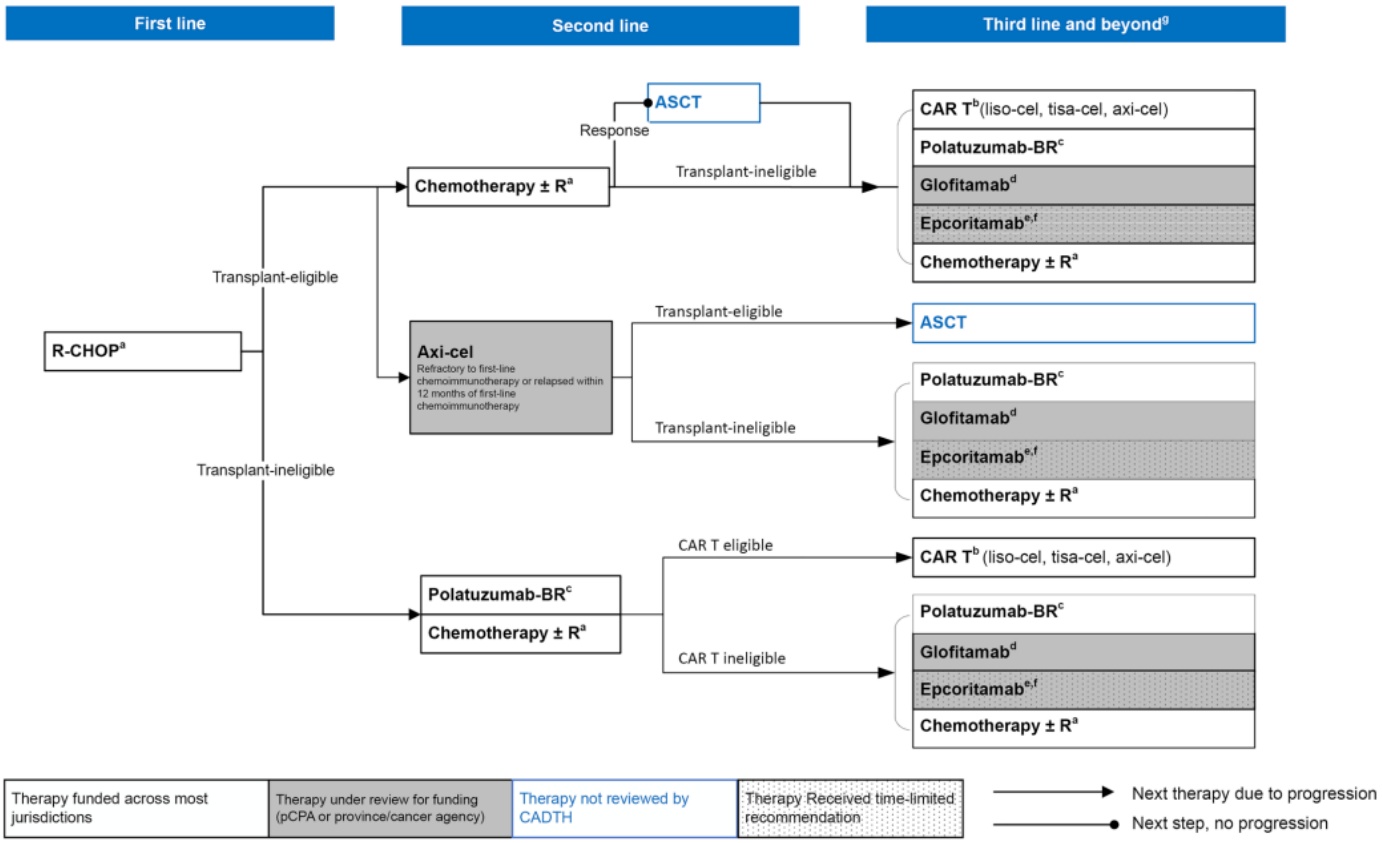
A good proportion of patients still fails first-line therapy.

5. Place in Therapy

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

Pola-R-CHP will be an alternative to 1L R-CHOP, as per POLARIX, for the ABC subtype.

Figure 1: Provisional Funding Algorithm Diagram for Large B-Cell Lymphoma



ASCT = autologous stem cell transplant; axi-cel = axicabtagene ciloleucel; BR = bendamustine and rituximab; CAR = chimeric antigen receptor; liso-cel = lisocabtagene maraleucel; pCPA = pan-Canadian Pharmaceutical alliance; R = rituximab; R-CHOP = rituximab in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone; tisa-cel = tisagenlecleucel.

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 study inclusion criteria, for the ABC subtype

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?

Per standard lymphoma response criteria and testing.

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

Disease progression, adverse events

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

6. Additional Information

The study used molecular profiling for ABC subtype that is not routinely available. Current standard of care in Canada is to use IHC testing to determine ABC subtype.

There should be allowance for time-limited switching for patients being treated with R-CHOP at the time of implementation.

There should be allowance for re-treatment with polatuzumab-BR as long as the patient is not polatuzumab refractory.

7. Conflict of Interest Declarations

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

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

   OH-CCO provided secretariat function to the group.

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

   No.

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

Declaration for Clinician 1

Name: Dr. Tom Kouroukis
Position: Lead, OH-CCO Hematology Cancer Drug Advisory Committee ("Hem DAC")
Date: Oct 24, 2024

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

Table 1: Conflict of Interest Declaration for Clinician 1

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

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

Declaration for Clinician 2

Name: Dr. Christopher Cipkar
Position: Member, OH-CCO Hem DAC
Date: Nov 7, 2024

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

Table 2: Conflict of Interest Declaration for Clinician 2

	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: Dr. Lee Mozessohn
Position: Member, OH-CCO Hem DAC
Date: Nov 7, 2024

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

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
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. Selay Lam
Position: Member, OH-CCO Hem DAC
Date: Nov 7, 2024

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

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche	x			
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: Member, OH-CCO Hem DAC
Date: Nov 7, 2024

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

Table 5: Conflict of Interest Declaration for Clinician 5

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

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

Declaration for Clinician 6

Name: Dr. Joanna Graczyk
Position: Member, OH-CCO Hem DAC
Date: Nov 7, 2024

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

Table 6: Conflict of Interest Declaration for Clinician 6

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

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

Declaration for Clinician 7

Name: Rami El-Sharkaway
Position: Member, OH-CCO Hem DAC
Date: Nov 7, 2024

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

Table 7: Conflict of Interest Declaration for Clinician 7

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

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

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