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

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

brentuximab vedotin (Adcetris)

(Seagen Canada Inc.)

Indication: Brentuximab vedotin in combination with doxorubicin, vincristine, etoposide, prednisone and cyclophosphamide in previously untreated high-risk HL in the pediatric population. Brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine for the treatment of previously untreated patients with advanced stage Hodgkins Lymphoma

May 02, 2023

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

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CDA-AMC and do not necessarily represent or reflect the views of CDA-AMC. No endorsement by CDA-AMC is intended or should be inferred.

By filing with CDA-AMC, the submitting organization or individual agrees to the full disclosure of the information. CDA-AMC does not edit the content of the submissions received.

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Patient Input

Name of Drug: <Brentuximab vedotin>

Indication: <For the treatment of previously untreated patients with advanced stage HL, in combination with doxorubicin, vinblastine, and dacarbazine.>

Name of Patient Group: <Lymphoma Canada>

Author of Submission: <Sarah Eisinga, Manager of Patient Programs, Research & Advocacy>

1. About Your Patient Group

Lymphoma Canada (LC) 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 March 14 to May 2, 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. 26 responses were collected. Information from this survey was used to identify the main areas of concern for patients with Hodgkin Lymphoma, in particular those with advanced stage disease (3 or 4). Three of these patients indicated they received A+AVD treatment (Adcertis or Brentuximab vedotin + AVD chemotherapy). Please see tables 1-5 below for demographic and relevant information of all survey respondents. The majority of patients lived in Canada (83%), were between the age of 35 and 44 (50%), female (50%), and diagnosed 1- 2 years ago (26%) with classical Hodgkin lymphoma subtype (47%).

Table 1: Country of respondents from Lymphoma Canada survey

Respondents	CAN	Nigeria	Skipped	Total
Patients with Hodgkin lymphoma	5	1	20	6

Table 2: Age range of respondents from Lymphoma Canada survey

Respondents	Age (years old)				
	35-44	45-54	65-74	Skipped	Total
Patients with Hodgkin lymphoma	3	2	1	20	26

Table 3: Gender of respondents from Lymphoma Canada survey

Respondents	Gender			
	Female	Male	Skipped	Total
Patients with Hodgkin lymphoma	3	3	20	26

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

Respondents	Years					Skipped	Total
	<1	1-2	3-5	5-8	9-10		
Patients with Hodgkin lymphoma	4	5	4	3	3	7	26

Table 5: Subtype of Hodgkin lymphoma of survey respondents

Subtype of Hodgkin Lymphoma	Number of respondents
Classical Hodgkin Lymphoma (cHL) – Nodular Sclerosis	9
Hodgkin Lymphoma – not sure of specific subtype	7
cHL – Lymphocyte-rich	3
Skipped	7
Total	19

Table 6: Subtype of Hodgkin lymphoma of survey respondents

Subtype of Hodgkin Lymphoma	Number of respondents
Stage 2	8
Stage 3	6
Stage 4	5
Skipped	7
Total	19

3. Disease Experience

Hodgkin lymphoma (HL) patients who completed Lymphoma Canada's survey were asked numerous questions regarding the physical and psychosocial symptoms experience at the time of diagnosis, current quality of life, and how these symptoms impacted their daily activities.

Survey respondents were asked to select symptoms (from a list) that they experienced at the time of their lymphoma diagnosis and rate their impact on quality of life, from 1 (no impact) to 5 (significant negative impact). 79% of patients reported fatigue as the most impactful symptoms (5 out of 5), followed by enlarged lymph nodes (58%), shortness of breath (63%), and weight loss (47%). During this time 74% of patients experienced anxiety/worry, 68% were stressed about their diagnosis, 63% had difficulty sleeping, and 58% feared progression of their lymphoma.

In this section, HL patients were also asked to select and rate the physical symptoms that currently impact their quality of life. 7 responses were collected from this question and the most significant factors which have a negative impact (5 out of 5) on their lives include fatigue (29%) and headaches (14%). A large majority of patients are no longer impacted by physical symptoms of their disease, such as leukocytosis (29%), frequent infections (29%), persistent cough (29%), weight loss (29%), enlarged lymph nodes (14%), nausea/vomiting (14%), night sweats (14%), chest pain (14%), and reduced appetite (14%). The most impactful psychosocial factors impacting HL patients during their current quality of life are the stress of having cancer (71%), fear of progression (71%), anxiety/worry (71%), difficulty sleeping (43%), problems concentrating (43%) and inability to attend work/school (43%).

When asked how HL symptoms have impacted or limited one's daily activities, survey respondents rated the following factors as having a very negative impact (5 out of 5): ability to travel (n = 2), ability to go to work/school/volunteer (n = 2), ability to fulfill family obligations (n = 2), ability to exercise (n = 1) and ability to contribute to finances (n = 1).

Patient quotes

- "Very low energy and I would sweat like mad with any exertion. I work a physical job and usually keep up well."
- "I find I have zero energy sometimes for absolutely no reason. My household chores are mostly done by my husband and I feel guilty that he has to burden that. Sometimes, I feel I want to volunteer but I have no energy so I fear letting the organization down and end up not volunteering."

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 Hodgkin Lymphoma. The majority of 7 patients indicated they received 1 (29%) or 3 (57%) lines of treatment, see Table 7. As the indication for this CADTH submission is for previously untreated Hodgkin Lymphoma, patient experiences were focused on those that only received one line of treatment.

Table 7: Number of lines of therapy survey respondents received

Respondents	Have not received therapy	1	3+	Skipped	Total

Patients with Hodgkin lymphoma	1	2	4	19	7

Survey respondents were asked in a separate question to provide the name of the treatment they received in the frontline setting. 3 HL patients indicated ABVD, 2 were treated with other forms of chemotherapy, and 1 was treated with the chemoimmunotherapy R-CHOP. Overall, 2 patients were satisfied with the frontline treatment options provided to them, and 3 were very satisfied (total of 7 respondents).

In one section of the LC survey patients were asked about their experience accessing their current or most recent HL therapy. 6 of 7 respondents indicated they did not have any difficulty accessing treatment, 1 patient found it very difficult and did not leave any additional comments as to why. When asked about financial challenges when accessing current HL treatments, 2 patients claimed challenges due to drug costs, 4 patients reported impact from supplementary drug costs, 2 selected medical supply costs and 5 reported difficulties due to absence from work. A few patients left comments about their HL treatment:

- "I was only able to access Brentuximab through a clinical trial. Lucky it was available and hopefully will becoming a standard option for patients in Nova Scotia."
- "It is everything that accompanies the main treatment that is hard like drugs for symptoms, drugs for young women to preserve fertility that are very expensive."

5. Improved Outcomes

In LC's survey, patients were asked "how important is it for a new drug to be able to control the following aspects of you HL?" The following factors were rated as 5 out of 5 (very important) by patients for a novel lymphoma therapy to control disease symptoms, longer disease remission, allow me to live longer and improved quality of life. A few patients left comments about their HL treatment experience and how important novel therapies are for them:

- "I was told I still have treatment options to go. I am not sure about my current situation but I believe more is always better. Not everyone respond well or equal to a treatment. So new therapies are extremely important for us."
- "I was told I still have treatment options to go. I am not sure about my current situation but I believe more is always better. Not everyone respond well or equal to a treatment. So new therapies are extremely important for us."

6. Experience With Drug Under Review

Of the three HL patients which received Brentuximab vedotin + AVD chemotherapy, 1 patient was treated

<6 months ago, another was treated 1 year ago, and the third was treated 3-5 years ago. 2 patients accessed this therapy through medicare/public care, and the other accessed the therapy through a clinical trial. One of these patients indicated they have been in-remission for 6 months up to a year, another in remission longer than a year, and the other patient is in post treatment (not sure about remission status).

Side effects which patients reported while on A+AVD treatment were fatigue (n = 3), neutropenia (n = 2), constipation (n = 2), joint or muscle pain (n = 2), low platelet count (n = 1), decreased appetite (n = 1), low blood pressure (n = 1), and decreased appetite (n = 1). Psychosocial impacts patients experience during treatment were like factors HL patients reported at diagnosis, including fear of progression, anxiety/worry, difficulty sleeping and difficulty concentrating.

A few patients experience financial setbacks due to absence from work (n = 2), cost of other medications (n =1). One of these patients had a poor experience with Adcetris, and the other two rated their experience as very good. These two patients would recommend it to another HL patient.

A few HL patients left quotes about their treatment experience with Brentuximab vedotin:

- "I wish I could say by now that I am in remission but I can't. The treatment was very well tolerated. I could stay active for almost the whole treatment. Fatigue became worse in the end after 5 months of chemo. In my experience I was cancer free after de second treatment. My first scan showed no cancer at all. After my very first treatment I didn't have any symptoms, no night sweats, no rashes, nothing. I would say that everything was perfect if it wasn't for this little activity in my neck."
- "As it was my only chemo treatment to date, hard to know how it would have gone on another drug. That being said, my side effects were manageable and it has apparently been effective in dealing with my cancer so it's great in my books."

7. Companion Diagnostic Test

N/A

8. Anything Else?

With the positive CADTH recommendation of Brentuximab vedotin in December 2020 for Stage IV HL, Lymphoma Canada highly encourages access to this therapy for patients with stage 3 and 4 Hodgkin lymphoma. These disease states are advanced and often have similar presentations. Based on information collected in this survey, HL patients want access to novel lymphoma which controls disease symptoms, bring a longer disease remission, allow them to live longer and improve quality of life. Lymphoma patients with aggressive subtypes, such as advanced HL, deserve access to novel treatment options including Brentuximab vedotin.

1 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
Seagen				X
Pfizer			X	
Roche			X	
Incyte			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: Sarah Eisinga

Position: Manager of Patient Programs, Research & Advocacy Patient Group: Lymphoma Canada

Date: May 2, 2023

Clinician Input

CADTH Project Number: PC0311-000

Generic Drug Name (Brand Name): brentuximab vedotin (Adcetris)

Indication: For the treatment of previously untreated patients with advanced stage HL, in combination with doxorubicin, vinblastine, and dacarbazine.

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

Author of Submission: Dr. Tom Kouroukis, Dr. Lee Mozessohn, Dr Joanna Graczyk, Dr. Selay Lam, Mark Brown, Dr. Pierre Villeneuve

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 was gathered via videoconferencing and email.

3. Current Treatments and Treatment Goals

For first-line therapy: ABVD or BEACOPP depending on their risk and in some cases depending on the results of a PET-directed therapy.

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.

To improve outcomes with first-line therapy so second line therapy is not needed.

5. Place in Therapy

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

Brentuximab vedotin will be used as first-line therapy in combination with AVD.

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 study, patients with stage III/IV disease.

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?

Typical lymphoma response measures including PET scan.

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

Significant toxicities, or progression.

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

Outpatient setting with malignant hematologists.

6. Additional Information

NA

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, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee

Date: 23-03-2023

☒ **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: Dr. Selay Lam

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee

Date: 06-04-2023

☒ 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: Dr. Lee Mozessohn

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee

Date: 06-04-2023

☒ 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: Mark Brown

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee

Date: 06-04-2023

☒ 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 Joanna Graczyk

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee

Date: 06-04-2023

☒ 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: Dr Pierre Villeneuve

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee

Date: 20-04-2023

☒ 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

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

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

CADTH Project Number: PC0311-000

Generic Drug Name (Brand Name): brentuximab vedotin (Adcetris)

Indication: Untreated Advanced Hodgkin Lymphoma

Name of Clinician Group: Pediatric Oncology Group of Ontario Author of Submission: Paul Gibson

1. About Your Clinician Group

POGO is a collaboration of Ontario's 5 specialized childhood cancer centres and the official advisor to the Ministry of Health and Long-Term Care on pediatric cancer care and control. This submission represents a collaboration of pediatric cancer clinicians from across the province with membership informed by POGO's Therapeutic and Technology Advisory Committee (TAC). For more information on POGO, please visit www.pogo.ca

2. Information Gathering

This submission was prepared in a consultative manner. Dr. Gibson discussed the indication with members of the submission panel and also sought input from the POGO TAC. Dr. Gibson subsequently drafted the initial response and all others contributing to the submission reviewed and edited the draft that has led to this final submission.

3. Current Treatments and Treatment Goals

Hodgkin Lymphoma is the most common lymphoma in adolescents and adults. Risk-adapted, multi-agent chemotherapy with radiotherapy in select populations is the standard of care across the country. There are, however a variety of chemotherapy and radiation approaches that vary by region and between pediatric and adult focused practitioners.

In Ontario, the standard of care front line therapy for Hodgkin Lymphoma is based on 2 primary backbones/cooperative group approaches. The first is the Children's Oncology Group (AHOD 1331-ABVE-PC backbone, Castellino, NEJM, 2022) and the other is EuroNet-PHL-C1 (OEPA-COPDAC, Mauz-Körholz, Lancet Oncology, 2022). Both approaches use response-based evaluations (metabolic response as measured by PET and anatomic size response as measured by CT) to guide the use of radiation therapy.

While even high-risk patients have generally favorable outcomes, treatment failures/relapses require more aggressive cytotoxic chemotherapy and, in most cases, autologous stem cell transplant. Therapy for Hodgkin Lymphoma is associated with substantial potential long-term morbidities including second malignancy, cardiac, pulmonary, endocrine and infertility challenges; these risks are substantially increased when patients relapse and receive intensified relapse therapy. The goal in pediatric Hodgkin Lymphoma therapy is therefore not simply cure, but cure that avoids unnecessary late effects. To that end, avoiding relapse after front line therapy is crucial.

The Echelon-1 study showed the utility of adding brentuximab vedotin (Bv) to doxorubicin, vinblastine and dacarbazine (Bv-AVD) for Hodgkin Lymphoma. The Bv-AVD arm showed superior survival in high risk (Stage III and IV) Hodgkin Lymphoma when compared to standard cytotoxic chemotherapy (ABVD). Importantly, this study limited enrollment to adult patients (> 18 years of age).

Historically, the ABVD backbone has not been favored amongst pediatric treating clinicians due to concern of higher anthracycline (doxorubicin) and bleomycin exposure and the known dose dependent cardiac and pulmonary toxicities. Thankfully, brentuximab has also been evaluated in a pediatric backbone setting.

The Children's Oncology Group (COG) studied the addition of brentuximab to a classic pediatric backbone (Castellino, NEJM, 2022). AHOD 1331 was a randomized, phase 3 trial that included patients 2 to 21 years of age with previously untreated high-risk Hodgkin lymphoma (stage IIB with bulk tumour or stage IIIB, IVA, or IVB). While both the control and treatment arms had excellent overall survival, there was a clear 3-year event free survival benefit in the brentuximab arm (92.1% vs. 82.5%). Of note, this success was achieved with substantially fewer doses of Bv in high-risk patients than in the Echelon study (5 vs. 12). Given the known significant risk of late effects from relapse

therapies, Bv-AVEPC has become standard care for high-risk pediatric patients in Ontario, despite brentuximab being unfunded. At present, pediatric clinicians are dependent on compassionate supply or the hospital global budget.

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.*

As mentioned above, the addition of Bv to standard cytotoxic therapy has shown to significantly reduce the risk of recurrence in High Risk pediatric Hodgkin Lymphoma patients. The avoidance of recurrence is crucial to minimize potential late effects which impact on quality of life and add to health care utilization costs in survivors This improved front line outcome means not only are patients and families spared the emotional distress of relapse therapy, but they are also spared the many potential late effects associated with additional cytotoxic therapy and autologous stem cell transplant.

5. Place in Therapy

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

High Risk Hodgkin Lymphoma patients (stage IIB with bulk tumour or stage IIIB, IVA, or IVB) would be best served by receiving optimal front-line therapy. We propose that Bv be included with a pediatric cytotoxic backbone (Bv-AVEPC) as the primary therapy for these newly diagnosed patients. While the proposed submission is explicitly for Bv-AVD, we think it important that the alternate backbone (with fewer Bv doses, less neurotoxicity and better progression-free survival data from a randomized trial) also be considered for funding.

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

The current pediatric evidence supports the use of Bv only in higher risk patients (stage IIB with bulk tumour or stage IIIB, IVA, or IVB). Patients with lower risk/stage disease therefore would not be suitable for this therapy in up front treatment. Furthermore, patients that progress despite receiving 2 cycles of Bv-AVEPC should not continue the same therapy.

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

The excellent survivals noted in both the Echelon-1 and COG trials are consistent with the Canadian pediatric experience (https://health-infobase.canada.ca/data-tools/cypc/survival-relapse-risk.html). While overall survival remains crucial in Hodgkin Lymphoma, particular attention should be placed on event free survival, particularly in young patients who are expected to live multiple decades after treatment and therefore will have a higher chance of experiencing late effects of therapy.

Therapy should be administered as per protocol with early PET response assessed after 2 cycles. Those with progressive disease should be offered alternative therapies. Otherwise, therapy should be completed to 5 cycles and follow-up as per institutional standards.

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

Disease progression noted clinically or by imaging assessment warrants discontinuation of the current treatment approach and consideration of alternative options.

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]?*

Pediatric Hodgkin Lymphoma patients should be cared for by a dedicated multi-disciplinary team. Therapy will primarily be delivered in ambulatory pediatric oncology clinics, however, some patients may be required to initiate therapy as an inpatient if they present with severe symptoms or organ compromise.

6. Additional Information

While the suggested regimen for evaluation is the 'adult' regimen, we implore the committee to take advantage of this submission to also consider the pediatric AHOD 1331 data. Given the much smaller annual patient population, we are unsure if this regimen will be formally submitted by the manufacturer. Given that there is a Phase 3 randomized study showing significant reduction in relapse rate using LESS of the agent in question, we feel it is important to be considered for young patients in order to provide equitable care across the age spectrum.

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.**

   None for POGO. See below for individual clinicians.

1.1.1.1 Declaration for Clinician 1

Name: Dr. Paul Gibson

Position: Associate Medical Director, POGO, Pediatric Oncologist, McMaster Children's Hospital Date: 02-05-2023

☒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 1

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

	$5,000	$10,000	$50,000	$50,000
Add company name				

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

1.1.1.2 Declaration for Clinician 2

Name: Dr. David Hodgson

Position: Medical Director, POGO, Radiation Oncologist, Princess Margaret Hospital Date: 02-05-2023

☒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 2

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

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

1.1.1.3 Declaration for Clinician 3

Name: Donna Johnston

Position: Chief, Division of Hematology/Oncology, Children's Hospital of Eastern Ontario

Date: 27-04-2023

☒**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 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
Add company name	Jazz Pharmaceuticals			

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

1.1.1.4 Declaration for Clinician 4

Name: John Wiernikowski
Position: Clinical Pharmacist
Date: 29-04-2023

☒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 4

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

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

1.1.1.5 Declaration for Clinician 5

Name: Dr. Sumit Gupta

Position: Pediatric Oncologist, The Hospital for Sick Children
Date: 02-05-2023

☒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 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				

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

1.1.1.6 Declaration for Clinician 6

Name: Dr. Angela Punnettt

Position: Pediatric Oncologist, The Hospital for Sick Children
Date: 02-05-2023

☒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

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				

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

1.1.1.7 Declaration for Clinician 7

Name: Tejinder (TJ) Bain

Position: Clinical Oncology Pharmacist, The Children's Hospital of Eastern Ontario Date: 02-05-2023

☒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

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				

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

1.1.1.8 Declaration for Clinician 8

Name: Dr. Jennifer Seelisch

Position: Pediatric Oncologist, Children's Hospital, London Health Sciences Centre Date: 02-05-2023

☒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 8

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

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

1.1.1.9 Declaration for Clinician 9

Name: Dr. Laura Wheaton

Position: Pediatric Oncologist, Kingston General Hospital Date: 02-05-2023

☒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.

1.1.1.10 Declaration for Clinician 10

Name: Dr. Vicky Breakey

Position: Pediatric Oncologist, McMaster Children's Hospital
Date: 02-05-2023

☒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 10

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

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

1.1.1.11 Declaration for Clinician 11

Name: Alicia Koo

Position: Clinical Oncology Pharmacist, McMaster Children's Hospital Date: 02-05-2023

☒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

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

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