



# Provisional Funding Algorithm

Indication: Large B-cell lymphoma

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**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

## Background

Following a request from jurisdictions, CADTH will design or update an algorithm depicting the sequence of funded treatments for a particular tumour type. These algorithms are proposals for the jurisdictions to implement and adapt to the local context. As such, they are termed “provisional.” Publishing of provisional algorithms is meant to improve transparency of the oncology drug funding process and promote consistency across jurisdictions.

Provisional funding algorithms are based on 3 principal sources of information:

- CADTH pCODR Expert Review Committee (pERC) reimbursement recommendations and/or implementation guidance regarding drug place in therapy and sequencing
- implementation advice from panels of clinicians convened by CADTH concerning sequencing of drugs in the therapeutic space of interest
- existing oncology drug reimbursement criteria and legacy funding algorithms adopted by jurisdictional drug plans and cancer agencies.

Note that provisional funding algorithms are not treatment algorithms; they are neither meant to detail the full clinical management of each patient nor the provision of each drug regimen. The diagrams may not contain a comprehensive list of all available treatments, and some drugs may not be funded in certain jurisdictions. All drugs are subject to explicit funding criteria, which may also vary between jurisdictions. Readers are invited to refer to the cited sources of information on the CADTH website for more details.

Provisional funding algorithms also delineate treatment sequences available to patients who were never treated for the condition of interest (i.e., incident population). Time-limited funding of new options for previously or currently treated patients (i.e., prevalent population) is not detailed in the algorithm.

Provisional funding algorithms may contain drugs that are under consideration for funding. Algorithms will not be dynamically updated by CADTH following changes to drug funding statuses. Revisions and updates will occur only upon request by jurisdictions.

**Jurisdictional cancer drug programs requested a CADTH provisional funding algorithm on large B-cell lymphoma. However, no outstanding implementation issues were identified, and no additional implementation advice is provided in this report. The algorithm depicted herein is meant to reflect the current and anticipated funding landscape based on the previously mentioned sources of information.**

## History and Development of the Provisional Funding Algorithm

This is the first rapid provisional funding algorithm report by CADTH for large B-cell lymphoma (LBCL) to incorporate CADTH recommendations for the following drug products:

- axicabtagene ciloleucel or *axi-cel* (Yescarta)
- lisocabtagene maraleucel or *liso-cel* (Breyanzi)
- polatuzumab vedotin or *pola* (Polivy).

In addition, this algorithm for LBCL will also incorporate the relevant Health Technology Expert Review Panel (HTERP) recommendations for the following drug products:

- tisagenlecleucel or *tisa-cel* (Kymriah)
- axi-cel (Yescarta).

**Table 1: Relevant CADTH or HTERP Recommendations**

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Axicabtagene ciloleucel (Yescarta)	<a href="#">February 22, 2023</a>	<p>pERC recommends that axicabtagene ciloleucel (axi-cel) be reimbursed for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL) that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy, who are eligible for autologous stem cell transplant (ASCT) only if the following conditions are met:</p> <p><b>Initiation:</b></p> <ol style="list-style-type: none"> <li>1. Axi-cel should be reimbursed in adult patients with DLBCL or HGBL only if all of the following criteria are met:               <ol style="list-style-type: none"> <li>1.1. refractory to first-line chemoimmunotherapy or relapsed within 12 months of first-line chemoimmunotherapy</li> <li>1.2. eligible for ASCT</li> <li>1.3. have a good performance status.</li> </ol> </li> <li>2. Axi-cel should not be reimbursed for patients who have had previous CAR T-cell therapy.</li> </ol> <p><b>Renewal:</b></p> <ol style="list-style-type: none"> <li>3. Treatment with axi-cel is a 1-time therapy.</li> </ol> <p><b>Prescribing:</b></p> <ol style="list-style-type: none"> <li>4. Axi-cel should be prescribed by clinicians with expertise in the management of lymphomas and CAR T-cell toxicities. Axi-cel should be administered in a hospital setting with adequate infrastructure,</li> </ol>

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		<p>resources, and expertise to perform the procedure and manage side effects.</p> <p><b>Pricing:</b></p> <p>5. A reduction in price.</p> <p><b>Feasibility of adoption:</b></p> <p>6. The feasibility of adoption of axi-cel must be addressed.</p> <p><b>Guidance on sequencing:</b></p> <ul style="list-style-type: none"> <li>• With regards to DLBCL arising from FL, pERC agreed with the clinical experts, who indicated that in clinical settings, the diagnosis of transformation may be clinically driven, based on patient symptoms and signs, rather than pathologically driven. In some cases, biopsy is unavailable or risky to obtain. Therefore, a high clinical suspicion of transformation is sufficient and biopsy-proven DLBCL is not necessary to confirm transformation to DLBCL.</li> </ul> <p>The clinical experts indicated that, generally, once the diagnosis of transformation is made, line of therapy for the transformation (i.e., disease eligible for CAR T-cell therapy) starts at that point. However, the clinical experts noted that if a patient with FL has already been given therapy that is an active regimen for high-grade lymphoma including DLBCL that includes a rituximab-containing regimen with anthracycline (e.g., R-CHOP), especially when treatment is recent, the patients should be regarded as having failed first-line therapy and should be eligible for second-line CAR T-cell therapy.</p> <p>To be considered for second-line CAR T-cell therapy, the clinical experts noted that patients should have been exposed to a rituximab-containing regimen with an anthracycline as in the ZUMA-7 trial (or etoposide if an anthracycline was unavailable) whether for DLBCL or FL transformed into LBCL.</p> <ul style="list-style-type: none"> <li>• The clinical experts clarified that the definition of relapsed disease used in the ZUMA-7 trial is reasonable and indicated this definition could be applied to eligibility criteria for axi-cel (i.e., relapse, within 12 months from date of last exposure to active therapy). pERC noted that this is specified in the Health Canada indication.</li> <li>• pERC agreed with the clinical experts, who indicated patients with ECOG performance status <math>\leq 2</math> can be considered for CAR T-cell therapy.</li> </ul>



Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		<p>pERC noted that there is no evidence to support using axi-cel in patients who received prior CD-19–targeted therapy.</p> <ul style="list-style-type: none"> <li>• pERC noted that patients with a history of a Richter’s transformation of chronic lymphocytic leukemia are managed differently than patients with LBCL. The clinical experts indicated that patients with PMBCL should be eligible for CAR T-cell therapy.</li> <li>• pERC noted that there is currently no evidence to support CAR T-cell re-treatment in patients who had received a prior CAR T-cell therapy.</li> <li>• pERC agreed with the clinical experts, who indicated that as long as the CNS disease is treated and the patient is neurologically stable, they should be eligible for CAR T-cell therapy.</li> <li>• pERC agreed with the clinical experts, who indicated that bridging therapies other than corticosteroids can be used. Any standard salvage chemotherapy regimen (e.g., R-GemOx, R-GDP, R-ICE, R-DHAP, R-ESHAP, pola-BR) could be used as bridging therapy.</li> <li>• The clinical experts indicated that depending on where the patient is in the course of treatment (e.g., completed salvage chemotherapy and a plan is in place for transplant), they should be allowed to switch to CAR T-cell therapy. pERC agreed that the decision to have CAR T-cell therapy rather than ASCT would be at the discretion of the treating hematologist in discussion with the patient.</li> <li>• pERC agreed with the clinical experts, who reported that other treatments may be used to manage cytokine release syndrome. These include siltuximab, a next-generation IL-6 inhibitor, and steroids if an IL-6 inhibitor is unavailable.</li> </ul>
Tafasitamab (Minjuvi)	<a href="#">October 13, 2022</a>	pERC recommends that tafasitamab not be reimbursed in combination with lenalidomide for the treatment of adult patients with R/R DLBCL not otherwise specified, including DLBCL arising from low-grade lymphoma, who are not eligible for ASCT.
Lisocabtagene maraleucel (Breyanzi)	<a href="#">June 29, 2022</a>	pERC recommends that lisocabtagene maraleucel (liso-cel) be reimbursed for the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified,

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		<p>primary mediastinal large B-cell lymphoma (PMBCL), high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma, only if the following conditions are met.</p> <p><b>Initiation:</b></p> <ol style="list-style-type: none"> <li>1. Liso-cel should be reimbursed in adult patients with relapsed or refractory LBCL according to the following criteria:               <ol style="list-style-type: none"> <li>1.1. DLBCL not otherwise specified, HGBCL, PMBCL, DLBCL arising from follicular lymphoma AND</li> <li>1.2. relapsed or refractory to at least 2 prior lines of systemic therapy including a CD20-targeted agent.</li> </ol> </li> <li>2. Patients must have a good performance status.</li> <li>3. Liso-cel should not be reimbursed for patients who have had a previous CAR T-cell therapy.</li> <li>4. Liso-cel should be reimbursed in patients with secondary CNS involvement as long as they fulfill all other criteria.</li> </ol> <p><b>Renewal:</b></p> <ol style="list-style-type: none"> <li>5. Treatment with liso-cel is a 1-time therapy.</li> </ol> <p><b>Prescribing:</b></p> <ol style="list-style-type: none"> <li>6. Liso-cel should be prescribed by clinicians with expertise in the management of lymphomas and CAR T-cell toxicities. It should be administered at manufacturer-certified transplant centres with the necessary resources and human expertise to perform the procedure and manage side effects.</li> </ol> <p><b>Pricing:</b></p> <ol style="list-style-type: none"> <li>7. Liso-cel should be negotiated so that it does not exceed the drug program cost of treatment with the least costly CAR T-cell therapy reimbursed for the treatment of relapsed or refractory LBCL.</li> </ol> <p><b>Feasibility of adoption:</b></p> <ol style="list-style-type: none"> <li>8. The feasibility of adoption of liso-cel must be addressed.</li> </ol> <p><b>Guidance on sequencing:</b></p> <ul style="list-style-type: none"> <li>• pERC noted that PET results are not required before lymphodepleting therapy or cell infusion because PET results are expected to be positive in most patients whether or not bridging therapy is used.</li> <li>• pERC noted that patients would need at least 2 lines of systemic therapy from the time of diagnosis of the transformed DLBCL.</li> </ul> <p>Potential exception may include individuals with follicular lymphoma for which they already have received induction</p>

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		<p>chemotherapy followed by ASCT, but then transformed to DLBCL/HGBCL. For these cases, clinicians may want to move directly to offer CAR T-cell therapies because other options are limited. Clinical experts suggest criteria could stipulate the minimum types of therapy required in these situations.</p> <ul style="list-style-type: none"> <li>• Eligibility criteria for liso-cel would overlap with axi-cel and tisa-cel. The approved indication aligns with the axi-cel indication and does not include DLBCL from indolent lymphomas and follicular lymphoma grade 3B; therefore, pERC cannot provide guidance on these populations.</li> <li>• pERC and clinical experts indicated that liso-cel would be considered for use in patients who are aged &gt; 75 years, have ECOG PS &gt; 2, or have CNS involvement. pERC and clinical experts emphasized the need for more data, especially comparative data. TRANSCEND is the first study to include the patients with CNS involvement and prior allo-SCT. pERC and clinical experts noted that both of these subgroups of patients represent a small proportion of the population in practice, making it difficult for studies to be conducted with these subgroups specifically.</li> <li>• Patients with comorbidities are eligible, but patients require sufficient cardiac function to survive CRS or sepsis, and renal function to tolerate fludarabine. Currently, there is variability on the approach to patients with comorbidities by Canadian centres.</li> <li>• There are currently no data to support that patients who have received previous CAR T-cell therapies for DLBCL should receive liso-cel. Responses to a second (different) CAR T-cell product is unknown and should be studied independently.</li> <li>• A small proportion of patients in TRANSCEND were re-challenged with liso-cel. According to the clinical experts and pERC, there remains insufficient data on the outcome of such a scenario to support re-treatment.</li> <li>• pERC and the experts agreed that patient with secondary CNS involvement can be eligible as per the clinical trial eligibility criteria. This population is in great need of better therapies.</li> <li>• According to experts and pERC, it is not expected that liso-cel would be better than other CAR T-cell therapies, but it may be offered to a broader population of patients with CNS disease.</li> </ul>



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		<p>Although there is a perception of a better safety profile, experts agreed that it may be a result of clinicians having a better understanding on how to better manage CRS and ICANS, which would lead to more favourable outcomes, although the evidence is still uncertain to support any assumption.</p> <p>Another expert mentioned that there is no clear clinical evidence to favour 1 CAR T-cell therapy over another for the overlapping indications. However, in practice, some centres may choose to align with a limited number of manufacturers to minimize contractual and manufacturer-specific requirements (i.e., it is possible 1 will be favoured for logistical reasons).</p> <ul style="list-style-type: none"> <li>• pERC and clinical experts agree that liso-cel may have a better safety profile, but there is still uncertainty around this issue. For now, it would be important to focus on the proportion treated as outpatients in the TRANSCEND study.</li> </ul> <p>The use of tocilizumab and possible drug shortages is a concern because the companies require 2 doses on hand for each patient. The use of siltuximab has been considered by some clinicians if there is a severe shortage. A biosimilar tocilizumab would be helpful in the future.</p>
Polatuzumab vedotin (Polivy)	<a href="#">April 21, 2021</a>	<p>pERC conditionally recommends the reimbursement of polatuzumab vedotin in combination with bendamustine and rituximab (pola-BR) for the treatment of adult patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL), not otherwise specified, who are not eligible for autologous stem cell transplant (ASCT), if the following conditions are met:</p> <ul style="list-style-type: none"> <li>• cost-effectiveness is improved to an acceptable level</li> <li>• feasibility of adoption (budget impact) is addressed.</li> </ul> <p>Eligible patients should have good performance status (PS) and a life expectancy greater than or equal to 24 weeks. Patients must have received at least 1 prior therapy. Treatment with pola-BR should continue for a maximum of 6 cycles (21 days per cycle) or until unacceptable toxicity or disease progression, whichever comes first.</p> <p><b>Guidance on sequencing:</b> Based on the GO29365 trial eligibility criteria, pERC agreed with the CGP on the eligibility of the following groups of patients:</p>

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		<ul style="list-style-type: none"> <li>• Pediatric patients: Pediatric patients were not included in the trial, and thus would not be eligible for pola-BR.</li> <li>• Prior ASCT: Patients with prior ASCT were eligible for the GO29365 trial, and thus would be eligible for pola-BR.</li> <li>• Progression on CAR T: Patients with prior CAR T-cell therapy were eligible for the trial, and thus would be eligible for pola-BR.</li> <li>• Failed vs. ineligible for ASCT: Per the inclusion criteria, patient who were ineligible for or failed ASCT were eligible for the trial, and thus would be eligible for treatment with pola-BR.</li> </ul> <p>pERC agreed with the CGP on the following sequencing scenarios:</p> <ul style="list-style-type: none"> <li>• Options after failure on pola-BR: Treatment options after progression on pola-BR should be up to the treating clinician; however, options such as anti-CD19 or CAR T-cell therapies could be considered.</li> <li>• Use of pola-BR as a bridge to CAR T-cell therapy and omitting bendamustine: Bendamustine can be omitted if appropriate based on clinical judgment. However, there is no evidence to support its use in this way.</li> <li>• Number and types of prior therapies: Consistent with the GO29365 trial, patients who were R/R after at least 1 prior line of therapy and were transplant ineligible would be eligible for pola-BR.</li> <li>• Switching to polatuzumab vedotin plus other chemo-immunotherapies if BR is not tolerated: As previously noted, there is no evidence to support the safe use of polatuzumab vedotin in combination with other chemo-immunotherapies.</li> </ul>
<p>Axicabtagene ciloleucel (Yescarta)</p>	<p><a href="#">August 2019</a></p>	<p>On the condition that there is a substantial reduction in price, HTERP recommends the provision of axicabtagene ciloleucel for adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. Regarding implementation of this therapy, HTERP recommends:</p> <ul style="list-style-type: none"> <li>• the creation of interprovincial agreements to ensure equitable access to eligible patients in all jurisdictions, including consideration of financial and logistic support for required travel and short-term relocation</li> </ul>



Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		<ul style="list-style-type: none"><li>• the development of clear and transparent eligibility criteria that are acceptable to patients’ and clinicians’ needs, based on the approved indications</li><li>• the collection of standardized outcomes data in a pan-Canadian registry of patients, which uses a defined set of outcomes and definitions to generate additional real-world evidence, for consideration in future reassessments of longer-term effectiveness, safety, and cost-effectiveness.</li></ul> <p><b>Implementation analysis:</b> The implementation analysis was guided by 2 research objectives:</p> <ul style="list-style-type: none"><li>• Provide a detailed description of potential pathways of care for patients to receive axicabtagene ciloleucel, and the resources (e.g., health and human resources, training, organizational) needed to do so.</li><li>• Provide an overview of feasibility and capacity considerations relating to the provision of axicabtagene ciloleucel at the level of the individual patient and provider (i.e., micro level); hospital or health care organization such as health authority or region (i.e., meso level); and the provincial, territorial, and federal levels (i.e., macro level).</li></ul> <p>Structuring the provision of axicabtagene ciloleucel raises several challenges. The management of toxicities and potential for severe AEs, coupled with the need for ongoing data collection, help shape potential models of delivery. The proposed model of delivery is that axicabtagene ciloleucel be delivered at manufacturer-trained and qualified hematopoietic stem cell transplant sites. The process for onboarding of sites across Canadian jurisdictions may take time, and supporting treatment across and within jurisdictions through reimbursement mechanisms and resources for patient travel (financial and logistical) may mitigate potential geographic inequalities. As treatment sites grapple with several levels of oversight and gaining accreditation for multiple products, deciding which organizations are most suited to provide treatment sites’ oversight, as well as the roles of the Foundation for the Accreditation of Cellular Therapies accreditation and of the manufacturer, involves complex considerations. Patient selection will likely involve the selection of patients who are less stable than those in the pivotal trial supporting regulatory approval of axicabtagene ciloleucel, and bridging</p>

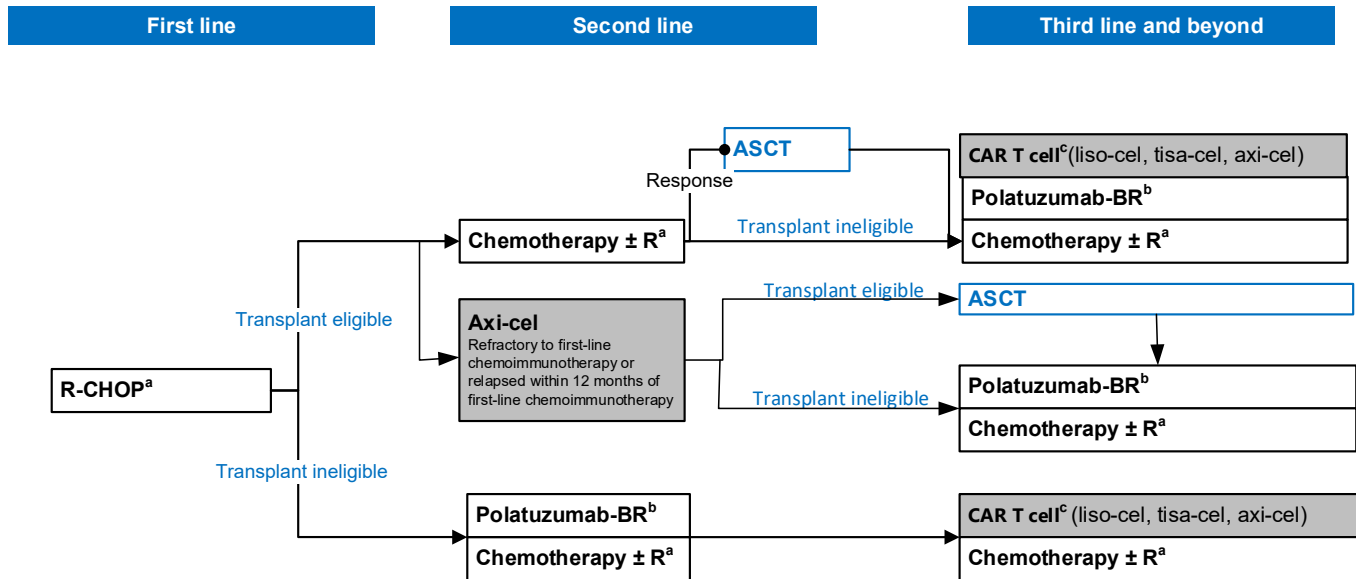
Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		<p>therapy will also likely be used in practice. Patient selection may occur across the process of receiving the therapy, and processes for allocating manufacturing slots as they become available will be needed. Uncertainty around long-term clinical effectiveness, cost-effectiveness, and safety raises challenges for regulatory agencies and payers when making decisions, highlighting the need for long-term data collection.</p>
Tisagenlecleucel (Kymriah)	<p><a href="#">January 2019</a></p>	<p>On the condition that there is a substantial reduction in price, HTERP recommends the provision of tisagenlecleucel for adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. With regard to implementation of this therapy, HTERP recommends:</p> <ul style="list-style-type: none"> <li>• the creation of interprovincial agreements to ensure equitable access to eligible patients in all jurisdictions, including consideration of financial and logistic support for required travel and short-term relocation</li> <li>• the development of clear and transparent eligibility criteria that are acceptable to patients' and clinicians' needs, based on the approved indications</li> <li>• the collection of standardized outcomes data in a pan-Canadian registry of patients, which uses a defined set of outcomes and definitions to generate real-world evidence, for consideration in future reassessments to assess longer-term effectiveness, safety, and cost-effectiveness.</li> </ul> <p><b>Implementation analysis:</b> The implementation analysis had the following objectives:</p> <ul style="list-style-type: none"> <li>• to provide a detailed description of potential pathways of care for patients to receive tisagenlecleucel, and the resources (e.g., health and human resources, training, organizational) needed to do so</li> <li>• to provide an overview of feasibility and capacity considerations relating to the provision of tisagenlecleucel at the level of the individual patient and provider (i.e., micro level); via hospital or health care organizations such as regional health authorities (i.e., meso level); and at the provincial, territorial, and federal levels (i.e., macro level).</li> </ul>

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		<p>The analysis described the proposed model of access within Canada and across jurisdictions. A centralized model of access with manufacturer-trained sites is required by the FDA and the European Medicines Agency to address key safety concerns about the management of potential AEs. Many stakeholders see accreditation by FACT as ensuring the necessary resources, experience, policies, and procedures to safely deliver CAR T-cell therapy and collect long-term data.</p> <p>The ability to deliver effectiveness therapy is dependent on timely access and provision. However, providing tisagenlecleucel may exacerbate existing capacity issues (such as treatment and clinical resources, space, and workforce) related to provision of hematopoietic SCT. Within Canada, a centralized model may create geographic inequities. Travel and relocation to receive treatment has economic, social, physical, and psychological impacts for patients and carers. Similar to other therapies delivered using a centralized model, consideration should be given to support services for patients, carers, and families, including travel support, lodging, and psychosocial support.</p> <p>The analysis also found that developing and applying eligibility criteria is a key implementation challenge. Clear and transparent eligibility criteria that are based on approved indications and that are acceptable to clinicians and patients are needed. Interprovincial agreements on the appropriate eligibility criteria will be required to ensure equitable access.</p>

AE = adverse event; ASCT = autologous stem cell transplant; CAR = chimeric antigen receptor; CNS = central nervous system; CRS = cytokine release syndrome; DLBCL = diffuse large B-cell lymphoma; ECOG = Eastern Cooperative Oncology Group; FACT = Foundation for the Accreditation of Cellular Therapy; HGBCL = high-grade B-cell lymphoma; HTERP = Health Technology Expert Review Panel; ICANS = immune effector cell-associated neurotoxicity syndrome; LBCL = large B-cell lymphoma; PMBCL = primary mediastinal large B-cell lymphoma; R/R = relapsed or refractory; SCT = stem cell transplant.

## Provisional Funding Algorithm

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



### Legend

Therapy funded across most jurisdictions	Therapy under review for funding (pCPA or province/cancer agency)	→	Next therapy due to progression
		●	Next step, no progression

ASCT = autologous stem cell transplant; axi-cel = axicabtagene ciloleucel; BR = bendamustine and rituximab; CAR = chimeric antigen receptor; CNS = central nervous system; DLBCL = diffuse large B-cell lymphoma; HGBCL = high-grade B-cell lymphoma; LBCL = large B-cell lymphoma; liso-cel = lisocabtagene maraleucel; pCPA = pan-Canadian Pharmaceutical Alliance; PMBCL = primary mediastinal large B-cell lymphoma; R = rituximab; R-CHOP = rituximab in combination with cyclophosphamide, doxorubicin, vincristine sulphate (Oncovin), and prednisone; tisa-cel = tisagenlecleucel.

<sup>a</sup> Alternative rituximab chemotherapy regimens available.

<sup>b</sup> Polatuzumab-BR is only funded for patients who are ineligible for ASCT and have received at least 1 prior therapy.

<sup>c</sup> If not received previously, polatuzumab-BR can be offered for bridging to CAR T-cell therapy.

## Description of the Provisional Funding Algorithm

### First-Line Therapy for All Patients

Currently, the first-line treatment for LBCL is R-CHOP chemotherapy, which is the combination of the following drugs:

- R for rituximab
- C for cyclophosphamide

- *H* for doxorubicin hydrochloride or hydroxydaunomycin
- *O* for vincristine sulphate (Oncovin)
- *P* for prednisone

### **Subsequent-Line Therapies for Transplant-Eligible Patients**

Second-line treatment options for patients eligible for ASCT include axi-cel, as well as salvage chemotherapy regimens with or without rituximab followed by high-dose therapy and ASCT.

For patients who have received salvage chemotherapy and ASCT as second-line therapy, the third-line options are chimeric antigen receptor (CAR) T-cell therapies, pola-BR, or a chemotherapy regimen with or without rituximab. CAR T-cell therapy options include axi-cel, tisa-cel, and liso-cel. If the patient has not previously received pola-BR, it can be offered for bridging to CAR T-cell therapy.

For patients who have received axi-cel as a second-line option, their third-line options are either:

- ASCT if they are transplant eligible
- pola-BR, a chemotherapy regimen with or without rituximab if they are transplant ineligible.

### **Subsequent-Line Therapies for Transplant-Ineligible Patients**

Second-line treatment options for patients who are not eligible for ASCT include pola-BR and chemotherapy regimens with or without rituximab. Third-line treatments include CAR T-cell therapies or a chemotherapy regimen with or without rituximab. CAR T-cell therapy options include axi-cel, tisa-cel, and liso-cel. If the patient has not previously received pola-BR, it can be offered for bridging to CAR T-cell therapy.