

Reimbursement Recommendation

Mosunetuzumab IV (Lunsumio)

Indication: As monotherapy for the treatment of adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy

Sponsor: Hoffmann-La Roche Limited

Recommendation: Reimburse with conditions

Summary

What Is the Reimbursement Recommendation for Lunsumio?

Canada's Drug Agency (CDA-AMC) recommends that Lunsumio be reimbursed by public drug plans "as monotherapy for the treatment of adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy," if certain conditions are met.

Why Did CDA-AMC Recommend Reimbursement?

The pan-Canadian Oncology Drug Review Expert Review Committee (pERC) determined that it is uncertain whether Lunsumio demonstrates acceptable clinical value in "adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy." Given that Lunsumio is expected to be an alternative option for third-line and beyond therapy, acceptable clinical value refers to at least comparable value relative to other third-line and beyond therapies relevant in the context in Canada. Direct evidence from 1 clinical trial (GO29781) showed that treatment with Lunsumio resulted in response rate benefits considered clinically meaningful and durable by the CDA-AMC consulted experts and suggested potential survival benefits. Evidence from an indirect treatment comparison (ITC) suggested that overall survival (OS) and response outcomes with Lunsumio may be broadly comparable to other third-line and beyond therapies, although results were uncertain and mixed across comparisons. Uncertainty remains due to the single-arm study design, limited comparative evidence, and imprecision in indirect estimates. pERC concluded that, although the evidence suggests mosunetuzumab monotherapy has uncertain clinical value, given the rarity and severity of the condition the drug may address a significant unmet clinical need to a degree that justifies a positive recommendation despite the uncertainty in the clinical value.

pERC discussed the direct and indirect evidence and the clinical experts' input and noted that the overall evidence suggested that Lunsumio may address a significant unmet clinical need, offering a chemotherapy-free, fixed-duration treatment with manageable safety profile that is readily available, particularly for patients with limited access to existing therapies.

pERC noted that there are significant unmet nonclinical needs and health inequities for patients with relapsed or refractory follicular lymphoma (r/r FL). pERC considered the IV and subcutaneous (SC) formulations of Lunsumio to have similar efficacy and safety, and therefore preferred the

Summary

SC formulation, while allowing flexibility for patient preference and for those who may need IV due to significant injection site reactions.

Based on all of the preceding considerations, pERC recommended that Lunsumio be reimbursed.

Which Patients Are Eligible for Coverage?

Lunsumio should only be covered for adults with histologically confirmed r/r FL (grades 1 to 3a) who have received at least 2 prior lines of systemic therapy, including an anti-CD20 therapy and an alkylating agent, and who have good performance status. Lunsumio should not be covered for patients with nonfollicular indolent lymphoma or a disease with central nervous system involvement.

What Are the Conditions for Reimbursement?

Lunsumio should be prescribed by clinicians experienced in managing hematologic malignancies and bispecific antibody-related complications, and given in settings with access to tocilizumab and appropriate supportive care. Reimbursement should be for a fixed duration of 8 or 17 cycles as per the drug's product monograph and should be discontinued upon the occurrence of complete response, unacceptable toxicity, or disease progression. Re-treatment may be considered for patients whose disease relapses after a treatment-free interval of at least 6 months following completion of the initial treatment course.

The total cost of Lunsumio should not exceed the total cost of treatment with the least costly relevant chemotherapy comparator for the same indication.

Important budget impact considerations and organizational implications must be addressed for health systems to be able to adopt Lunsumio.

Review Background

- **Disease background:** FL is a systemic malignancy of lymphoid tissue characterized by germinal-centre B cell differentiation, typically presenting as a slow-progressing indolent non-Hodgkin lymphoma associated with common relapse and long survival measured in years. In Canada, it is estimated that more than 22,000 people were diagnosed with FL from 1992 to 2010, corresponding to an age-standardized incidence rate of 38 cases per million persons per year.
- **Indication and reimbursement request:** Mosunetuzumab for IV injection (Lunsumio) has received a Notice of Compliance with Conditions (NOC/c) from Health Canada as a monotherapy for “adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy.” The sponsor is seeking reimbursement for this patient population.
- **Drug under review:** Mosunetuzumab IV is a bispecific antibody inducing T cell-mediated B cell lysis. It is a 1 mg/mL solution for IV infusion available as 1 mg/mL in a 2 mL vial, or as 30 mg/30 mL in a 50 mL vial. Mosunetuzumab IV should be administered for a fixed duration of 8 or 17 cycles based on tumour response, unless the patient experiences unacceptable toxicity or disease progression. The recommended dose for each 21-day cycle follows a step-up dosing regimen, consisting of 1 mg on cycle 1 day 1, 2 mg on cycle 1 day 8, and 60 mg on cycle 1 day 15, followed by 60 mg on cycle 2 day 1. Beginning in cycle 3, 30 mg is administered on day 1 through cycle 8 if a complete response is achieved, or up to cycle 17 if disease stability or a partial response is observed.
- **Treatment costs:** At the submitted price of \$411.00 per 1 mg vial, the cost of mosunetuzumab IV is expected to be \$34,524 per patient for the first 28-day cycle, \$32,880 for the second 28-day cycle, and \$16,440 for subsequent 28-day cycles, based on the Health Canada–recommended dosage.

Highlights of Input From Interested Parties

The patient group (Lymphoma Canada) noted the following regarding impacts of the disease, unmet needs, and important outcomes:

- FL is associated with physical symptoms such as fatigue, lymph node swelling, abdominal discomfort, night sweats, and body pain, along with psychological and practical impacts including stress and anxiety, fear of progression, sleep difficulties, frequent health care visits, and reduced daily functioning.
- Important treatment outcomes for patients include prolonged survival, durable disease and symptom control, longer remission, improved quality of life, fewer side effects, and predictable benefits.

The clinician groups (Leukemia and Lymphoma Society Nurses Network, Ontario Health [Cancer Care Ontario] Hematology Cancer Drug Advisory Committee, and Lymphoma Canada) and the clinical experts consulted by CDA-AMC noted the unmet needs arising from the disease as follows:

- There is an ongoing need for effective, well-tolerated, chemotherapy-free, and time-limited outpatient treatment options for r/r FL, particularly in later lines of therapy and for patients with limited tolerance for intensive treatments or barriers to access.

Regarding place in therapy, the clinician groups noted that mosunetuzumab IV is anticipated to be used primarily as a later-line outpatient treatment option for adults with r/r FL, including patients who are ineligible for, unable to access, or prefer to avoid CAR T-cell therapy, and as a potential option following disease relapse after CAR T-cell treatment.

The participating public drug programs raised potential implementation issues related to relevant comparators, considerations for initiation and prescribing of therapy, generalizability of trial populations to broader populations, potential need for a provisional funding algorithm, care provision issues, and system and economic issues.

Recommendation

With a vote of 12 in favour to 4 against, pERC recommends that mosunetuzumab IV be reimbursed “as monotherapy for the treatment of adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy” only if the conditions listed in [Table 1](#) are met.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Mosunetuzumab IV should be reimbursed in adults with r/r FL (grades 1 to 3a) who meet all the following criteria: 1.1. histologically confirmed FL (grades 1 to 3a) 1.2. r/r to 2 or more previous lines of treatment, including an anti-CD20 therapy and an alkylating agent 1.3. have a good performance status.	Evidence from the GO29781 study demonstrated (and clinical experts consulted by CDA-AMC indicated) that treatment with mosunetuzumab IV may provide a clinical benefit in patients with the characteristics listed in this condition. The GO29781 study enrolled patients who had an ECOG PS score of 0 or 1.	Condition 1.2: • pERC confirmed that jurisdictions can use the existing definition of rituximab refractory, which is defined as having no response to or progression during or within 6 months after treatment with rituximab or a rituximab-containing regimen. • pERC confirmed that single-agent rituximab, with or without maintenance, should be counted as 1 line of therapy. • pERC agreed with the clinical experts that patients who have previously received CAR T-cell therapy may be eligible for mosunetuzumab IV if they meet the criteria in the first column. As mosunetuzumab and CAR T-cell therapies target different antigens, prior CAR T-cell therapy should not be considered a basis for exclusion. Condition 1.3: Based on the clinical experts' input, selected patients with an ECOG PS score of 2 could be considered for treatment

Reimbursement condition	Reason	Implementation guidance
		with mosunetuzumab IV at the discretion of the treating physician.
2. Patients are ineligible for treatment with mosunetuzumab if they have any of the following criteria: 2.1. nonfollicular indolent lymphoma 2.2. CNS involvement.	Patients with nonfollicular indolent lymphoma or CNS involvement were not included in the GO29781 study. The clinical experts noted that conditions such as marginal zone lymphoma and chronic lymphocytic leukemia have biological behaviour that differs from FL, and that FL rarely involves the CNS. As a result, these patient populations were excluded from the study, and the evidence is therefore not generalizable to these groups.	pERC considered mosunetuzumab appropriate for patients who are ineligible for, unable to access, or decline CAR T-cell therapy, but not as a preferred alternative for eligible patients with adequate access to CAR T-cell therapy.
Renewal		
3. Reimbursement of re-treatment with mosunetuzumab IV could be considered if a patient experiences r/r FL after a treatment-free interval of at least 6 months following the initial 8 or 17 cycles of treatment.	Re-treatment after a complete response and discontinuation at 8 cycles was allowed in the GO29781 study. pERC confirmed that a minimum disease-free interval (remission) of at least 6 months is required. The clinical experts emphasized that CD20 expression should be reassessed at disease relapse, as a biopsy is standard practice and CD20 down regulation may occur under selective pressure from CD20 targeted therapies. Re-treatment after completing 17 cycles may also be considered, depending on clinical context and prior tolerability.	The clinical experts noted that response should be assessed using imaging (CT or PET) after 8 cycles and again at the end of therapy, consistent with trial practice and routine standards in Canada. Interim imaging before the end of cycle 8 is recommended to determine whether treatment should stop at 8 cycles for patients who achieve a complete response or continue to 17 cycles for patients who achieve a partial response. The clinical experts indicated that these assessments align with the clinical practice in Canada and are feasible to implement.
Discontinuation		
4. Reimbursement of mosunetuzumab IV should be discontinued upon occurrence of any of the following: 4.1. complete response 4.2. unacceptable toxicity 4.3. disease progression.	In the GO29781 study, mosunetuzumab IV treatment was discontinued if a patient experienced disease progression or intolerable AEs.	Per the drug's product monograph, for patients who achieve a complete response, no further treatment beyond 8 cycles is required, and for patients who achieve a partial response or have disease stability in response to treatment with mosunetuzumab IV after 8 cycles, an additional 9 cycles of treatment (17 cycles total) could be administered, unless a patient experiences unacceptable toxicity or disease progression.
Prescribing		
5. Mosunetuzumab IV should only be prescribed by clinicians experienced in managing hematologic malignancies and the complications of bispecific antibody therapy (e.g., CRS and ICANS) and administered in a setting with access to	This is meant to ensure that mosunetuzumab IV is prescribed for appropriate patients and that adverse effects are managed in an optimized and timely manner.	pERC considered that the IV and SC formulations of mosunetuzumab have comparable efficacy and safety. The committee discussed clinical experts' input indicating that SC administration is generally preferred by patients and health care systems due to reduced health

Reimbursement condition	Reason	Implementation guidance
tocilizumab and appropriate supportive care.		system resource use (e.g., chair time, compounding time) and a more favourable safety profile. Accordingly, pERC determined that the mosunetuzumab SC be prioritized over the IV formulation, with flexibility for patients' preference and the occasional patient who may experience significant injection site reactions, for whom IV administration may be more suitable.
6. Mosunetuzumab IV should be administered as monotherapy.	In the GO29781 study, mosunetuzumab IV was administered as a monotherapy.	—
Pricing		
7. The total cost of mosunetuzumab IV should be negotiated so that it does not exceed the total cost of treatment with the least costly relevant chemotherapy comparator for the same indication.	Based on the committee's assessment of the evidence, mosunetuzumab IV is expected to have similar clinical benefits and harms compared with relevant comparators. Therefore, the total cost of mosunetuzumab IV should be no more than the least costly relevant chemotherapy regimen.	—
Feasibility of adoption		
8. The economic feasibility of adoption of mosunetuzumab IV must be addressed.	At the submitted price, the magnitude of uncertainty in the budget impact must be addressed to ensure the feasibility of adoption, given the difference between the sponsor's estimate and the estimate from CDA-AMC.	—

AE = adverse event; CDA-AMC = Canada's Drug Agency; CNS = central nervous system; CRS = cytokine release syndrome; ECOG PS = Eastern Cooperative Oncology Group Performance Status; FL = follicular lymphoma; ICANS = immune effector cell associated neurotoxicity syndrome; pERC = pan-Canadian Oncology Drug Review Expert Review Committee; r/r = relapsed or refractory; SC = subcutaneous.

Rationale for the Recommendation

Clinical Value

Based on the totality of the clinical evidence, pERC noted that it is uncertain whether mosunetuzumab IV monotherapy demonstrates acceptable clinical value in “adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy.” Given that mosunetuzumab IV is expected to be an alternative option for third-line and beyond therapy, acceptable clinical value refers to at least comparable value relative to other third-line and beyond therapies relevant in the context in Canada. pERC concluded that, although the evidence suggests mosunetuzumab IV monotherapy has uncertain clinical value, given the rarity and severity of the condition the drug may address a significant unmet clinical need to a degree that justifies a positive recommendation despite the uncertainty in the clinical value.

One phase I (1b)/II, single-arm, open-label study (GO29781; N = 90) demonstrated that treatment with mosunetuzumab IV resulted in benefits in the primary end point of complete response rate (CRR) for “adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy.” In a median observation time of 18.3 months, the CRR was 60.0% (95% confidence interval [CI], 49.1% to 70.2%), and the overall response rate (ORR) (partial or complete response) was 80.0% (95% CI, 70.3% to 87.7%). The clinical experts consulted by CDA-AMC considered the response rates observed in the GO2981 study to be clinically meaningful in the context of expected outcomes for adult patients with r/r FL (grades 1 to 3a) undergoing third-line and beyond therapy. Mosunetuzumab IV was associated with potential benefits in survival outcomes; at the 48-month follow-up analysis, median OS was not reached, while the median progression-free survival (PFS) was 24.0 months (95% CI, 12.0 months to not estimable). The Kaplan-Meier survival probability at 48 months was 82.7% (95% CI, 74.7% to 90.7%). Cytokine release syndrome was among the notable harms and aligned with the known safety profile of mosunetuzumab. Overall, the safety findings from the GO29781 study were consistent with the established risks of the bispecific antibody drug class, with no unexpected signals identified.

Evidence from the sponsor-submitted ITC evaluating the effects of mosunetuzumab IV monotherapy versus relevant comparators, indicated some uncertainty in the OS and ORR results across comparisons, with estimates suggesting that outcomes may be comparable between treatments. Results for PFS, CRR, and treatment discontinuation due to adverse events (AEs) showed mixed results across comparisons, with some analyses favouring comparator therapies (e.g., axicabtagene ciloleucel, tisagenlecleucel, or obinutuzumab plus bendamustine for PFS; axicabtagene ciloleucel for CRR), others favouring mosunetuzumab IV (e.g., compared to rituximab plus lenalidomide and obinutuzumab plus bendamustine for CRR, and compared to obinutuzumab plus bendamustine for treatment discontinuation due to AEs), and several comparisons remaining uncertain. Overall, the ITC evidence was very uncertain due to imprecision, limited sample size, and limitations in the assumptions underlying the model.

pERC acknowledged that patients identified a need for more effective, well-tolerated, and accessible treatment options in later lines of therapy, particularly those that reduce cumulative toxicity, treatment burden, and barriers related to travel and availability. The committee also noted clinicians emphasized the need for novel, noncross-resistant therapies that can provide durable responses, are chemotherapy-free, and can be delivered conveniently in outpatient or community settings, given the limitations and restricted accessibility of CAR T-cell therapy. pERC considered the uncertainties in the evidence due to the limitations in the studies, including the single-arm design of the GO29781 trial. The committee also considered the clinical experts’ observation that the CRR and ORR were clinically meaningful for the population of patients, especially those with limited access to or for whom other options are less suitable. Therefore, pERC determined that mosunetuzumab IV represents an alternative immunotherapy option for “adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy” that may address some of these unmet needs by offering a fixed-duration, outpatient treatment with a manageable safety profile.

Further information on the committee’s discussion around clinical value is provided in the Summary of Deliberation section.

Considering Significant Unmet Clinical Need

pERC acknowledged that there is a significant unmet clinical need for patients with r/r FL (grades 1 to 3a), particularly in the third-line setting and beyond. This reflects the incurable and relapsing nature of the disease, diminishing effectiveness and durability of available treatments with successive lines, cumulative toxicities, and limited access to certain therapies (e.g., CAR T-cell therapy) due to eligibility, logistical, and geographic constraints. Patients and clinicians emphasized the need for effective, well-tolerated, chemotherapy-free, and accessible outpatient treatment options that can provide durable disease control and reduce treatment burden.

Further information on the committee's discussion around unmet clinical need is provided in the Summary of Deliberation section.

Considering Significant Unmet Nonclinical Need or Health Inequity

pERC noted that there are significant unmet nonclinical needs and health inequities for patients with r/r FL. These include barriers to accessing specialized treatments (e.g., CAR T-cell therapy), particularly for patients who are older, experiencing frailty, or living in rural or remote areas, as well as the logistical burden of frequent clinic visits, travel to tertiary centres, and prolonged treatment administration. The committee observed that socioeconomic factors and geographic distance disproportionately limit access for marginalized populations who face barriers to care or are at increased risk for r/r FL.

pERC considered that the fixed-duration, outpatient administration and off the shelf availability of mosunetuzumab IV may help address unmet nonclinical needs and inequities by reducing treatment burden and improving access, particularly for patients in rural or remote areas.

Further information on the committee's discussion around unmet nonclinical need is provided in the Distinct Social and Ethical Considerations domain in the Summary of Deliberation section.

Developing the Recommendation

Due to the uncertainty in clinical value, pERC could not recommend whether to reimburse mosunetuzumab IV or not based on clinical value alone. Therefore, they also considered whether mosunetuzumab IV addresses a significant unmet clinical need. pERC concluded that mosunetuzumab IV addresses a significant unmet clinical need with an acceptable level of certainty. Based on the preceding considerations, pERC recommended that mosunetuzumab IV be reimbursed. As part of the deliberation on whether to recommend reimbursement or not, the committee also considered unmet nonclinical need and health inequity. Information on this discussion is provided in the Distinct Social and Ethical Considerations domain in the Summary of Deliberation section.

Because pERC recommended that mosunetuzumab IV be reimbursed, the committee also deliberated on whether reimbursement conditions should be added to address important economic considerations, health system impacts, or social and ethical considerations, or to ensure clinical value is realized. The resulting reimbursement conditions, with accompanying reasons and implementation guidance, are stated in [Table 1](#).

Summary of Deliberation

pERC considered all domains of value of the deliberative framework before developing its recommendation: clinical value, unmet clinical need, distinct social and ethical considerations, economic considerations, and impacts on health systems. For further information on the domains of value, refer to [Expert Committee Deliberation at Canada's Drug Agency](#).

The committee considered the following key discussion points, organized by the 5 domains of value.



Clinical Value

- **Appropriate comparators:** pERC noted that axicabtagene ciloleucel and tisagenlecleucel are the most relevant treatment options, as CAR T-cell therapy is the standard of care in the third-line setting and beyond. Other treatments considered relevant comparators were rituximab, rituximab plus bendamustine, rituximab plus lenalidomide, obinutuzumab plus bendamustine, idelalisib, a combination of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, and a combination of rituximab, cyclophosphamide, vincristine, and prednisone.
- **Efficacy from a single-arm study:** Evidence from the GO29781 study showed that after a median observation time of 18.3 months, the CRR was 60.0% (95% CI, 49.1% to 70.2%), and the ORR was 80.0% (95% CI, 70.3% to 87.7%). At the 48-month follow-up analysis, OS was not reached, while the median PFS was 24.0 months (95% CI, 12.0 months to not estimable). The Kaplan-Meier survival probability at 48 months was 82.7% (95% CI, 74.7% to 90.7%). At cycle 8, 41% of patients in the IV cohort and 35% of patients in the SC cohort achieved an improvement of at least 3 points from baseline in the Functional Assessment of Cancer Therapy–Lymphoma subscale score. The notable harm (cytokine release syndrome) was consistent with the known safety profile of mosunetuzumab. Immune effector cell associated neurotoxicity syndrome was reported by 4 patients (4.4%), and the risk of immune effector cell associated neurotoxicity syndrome remains uncertain due to the small sample size.
- **Clinical importance of treatment effects:** Patients identified longer survival, durable disease and symptom control, longer remission, improved quality of life, and fewer side effects as the most important treatment outcomes. Patients also emphasized the importance of having treatment choice, predictable benefits, and therapies that balance effectiveness with tolerability to minimize treatment burden and preserve daily functioning. Based on expert input, the response rates were clinically meaningful in the context of expected outcomes for adult patients with r/r FL (grades 1 to 3a) undergoing third-line or later therapy. The health-related quality of life results in the GO29781 study were inconclusive because of its single-arm design and missingness of data. pERC considered that despite the uncertainty in the evidence from the GO29781 study, mosunetuzumab IV represents an alternative immunotherapy option for patients with r/r FL (grades 1 to 3a), particularly in the third-line setting and beyond.
- **Certainty of the evidence:** In the absence of a comparator group in the GO29781 study, a Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment rated

the certainty of evidence from the study as very low and a conclusion regarding the efficacy of mosunetuzumab IV relative to other treatments could not be drawn.

- **Efficacy versus relevant third-line and beyond therapies:** Three matching-adjusted indirect comparisons and 4 propensity score analyses showed uncertainty in the OS and ORR results across comparisons, with estimates suggesting that outcomes may be comparable between treatments. Results for PFS, CRR, and treatment discontinuation due to AEs were inconclusive due to limitations such as small sample sizes and analytical assumptions. Across all comparisons, it remains unclear whether the assumptions underlying these analyses were met and whether treatment effect modifiers and prognostic variables were adequately adjusted for. Considering the limitations noted in the ITCs, including serious imprecision, small sample sizes, decreases in the number of patients at risk over follow-up, and violations of model assumptions for some comparisons, pERC considered the findings insufficient to draw firm conclusions on the relative efficacy or safety of mosunetuzumab compared with the comparators. pERC agreed with clinical experts that mosunetuzumab may be offered to patients who are ineligible for CAR T-cell therapy or face barriers to access. However, pERC agreed with clinical experts that in eligible patients with reasonable access, CAR T-cell therapy would be preferred over mosunetuzumab in the third-line setting and beyond.
- **Clinical value:** Based on the preceding considerations, pERC determined that mosunetuzumab IV would provide an alternative treatment option in “adult patients with relapsed or refractory follicular lymphoma (Grades 1 – 3a) who have received at least two prior lines of systemic therapy,” especially in those for whom current treatments are inaccessible or unsuitable.



Unmet Clinical Need

- **Input on unmet clinical need:** Patients identified a need for more effective, durable, and well-tolerated treatment options in later lines of therapy, along with improved access and reduced treatment burden. They highlighted challenges related to side effects, frequent hospital visits, and travel, which affect quality of life. Clinical experts and clinician groups similarly emphasized the need for therapies that provide longer remission, limit cumulative toxicity, and offer options for patients who are ineligible for or unable to access CAR T-cell therapy. These unmet needs contribute to declining response rates, shorter remissions, reduced quality of life, and inequitable access to care, particularly for those living in rural or remote areas.
- **Severity of the disease:** pERC acknowledged that FL is an incurable, indolent malignancy that typically requires ongoing treatment, with many patients receiving multiple lines of therapy that become progressively less effective and less durable over time. Clinical experts consulted by CDA-AMC noted that FL accounts for approximately 20% to 30% of non-Hodgkin lymphoma, which is the fifth most common cancer in Canada.
- **Availability of treatment options:** Available treatments for r/r FL in the third-line and later setting include chemoimmunotherapy regimens (e.g., rituximab-based combinations), rituximab plus lenalidomide, obinutuzumab plus bendamustine, and CAR T-cell therapies (axicabtagene ciloleucel and tisagenlecleucel). Clinical experts and clinician group input indicated that the effectiveness

of these options declines with successive lines of therapy, with shorter remission durations and increasing toxicity. Patients, clinicians, and clinical experts identified important gaps, including limited durability of response, cumulative treatment burden, access barriers (particularly for CAR T-cell therapy and for those living in rural or remote areas), and the lack of well-tolerated, chemotherapy-free, fixed-duration outpatient options that preserve quality of life.



Distinct Social and Ethical Considerations

- **Input on unmet nonclinical need:** Patient and clinician groups identified important unmet nonclinical needs and health inequities for patients with r/r FL. These include barriers to accessing specialized therapies (e.g., CAR T-cell therapy), particularly for patients who are older, experiencing frailty, or living in rural or remote areas, as well as the burden associated with frequent clinic visits, travel to tertiary centres, and prolonged treatment administration. Socioeconomic and geographic factors were noted to further limit access for marginalized populations who face barriers to care or are at increased risk for r/r FL. pERC acknowledged that mosunetuzumab IV may help address some of these needs by offering a fixed-duration, outpatient treatment; however, uncertainty regarding its comparative benefit remains due to the lack of head-to-head evidence.
- **Equity considerations:** pERC noted that geographic location, particularly residence in rural or remote areas, along with socioeconomic status, may limit access to specialized therapies and contribute to inequities in care. pERC concluded that treatments that can be delivered in outpatient or community settings may help reduce travel burden and improve access, although persistent system-level barriers may continue to affect equitable access across patient populations.
- **Significant unmet nonclinical need or health inequity:** pERC observed that barriers to access for some specialized therapies (e.g., CAR T-cell therapy), as well as the logistical burden of frequent clinic visits, travel to tertiary centres, and prolonged treatment administration due to socioeconomic factors and geographic distance disproportionately affect marginalized populations who face barriers to care or are at increased risk for r/r FL. pERC acknowledged that the fixed-duration, outpatient administration and off the shelf availability of mosunetuzumab IV may help address certain unmet nonclinical needs and inequities.



Economic Considerations

- **Health impacts of mosunetuzumab IV versus relevant comparators:** The relative impact of mosunetuzumab IV on patient health is very uncertain due to uncertainty in the findings from the ITCs. Based on evidence reviewed for this submission, there is no robust evidence to suggest that mosunetuzumab IV provides greater health benefit than rituximab plus lenalidomide, obinutuzumab plus bendamustine, rituximab plus bendamustine, axicabtagene ciloleucel, or tisagenlecleucel.
- **Cost of mosunetuzumab IV versus relevant comparators:** Based on the submitted price of mosunetuzumab IV, it is expected to increase health care system costs if reimbursed by public drug plans when compared to rituximab plus lenalidomide, obinutuzumab plus bendamustine,

and rituximab plus bendamustine. Drug acquisition costs were the primary driver of incremental costs between mosunetuzumab IV and these comparators. Relative to axicabtagene ciloleucel and tisagenlecleucel, the committee discussed that the impacts to health system costs are very uncertain due to the one-time cost of CAR T-cell treatment and will depend on length of treatment of mosunetuzumab IV.

- **Key findings of the economic evaluation:** The indirect evidence for mosunetuzumab IV versus comparators is very uncertain and there is insufficient evidence to determine whether mosunetuzumab IV provides greater health benefit compared to relevant comparators. Due to the lack of robust clinical evidence, no CDA-AMC base case was performed, and therefore no incremental cost-effectiveness ratio was estimated by CDA-AMC.
- **Certainty of the evidence:** Several limitations regarding the ITC used to inform the comparison for mosunetuzumab IV versus all comparators were identified by the CDA-AMC review team such as heterogeneity, unmeasured confounding, population differences, and small sample size, in addition to residual uncertainty inherent in the indirect comparisons. For all comparisons, it is unclear whether assumptions underlying the ITCs were met and whether treatment effect modifiers and prognostic variables were appropriately adjusted for.
- **Other considerations:** Tafasitamab in combination with rituximab plus lenalidomide is currently being reviewed by CDA-AMC for the treatment of patients with r/r FL (grades 1 to 3a). Clinical experts consulted by CDA-AMC noted that it may be currently accessible to patients through compassionate use programs.



Impacts on Health Systems

- **Anticipated budget impact:** CDA-AMC estimated that in year 3 of reimbursement, 585 patients would be eligible for mosunetuzumab IV; of these, 0 patients are expected to receive mosunetuzumab IV due to a preference for the SC formulation of mosunetuzumab. As a result, there is no anticipated budget impact or expenditure associated with reimbursing mosunetuzumab IV for the first 3 years of reimbursement. The actual budget impact of reimbursing mosunetuzumab IV will depend largely on the market uptake of mosunetuzumab IV.
- **Organizational implications:** pERC acknowledged that the SC administration of mosunetuzumab would be generally preferred compared to IV administration by patients and health care systems due to reduced health system resource use (e.g., chair time, compounding time).

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information (links to the full documents for the review can be found on the [project webpage](#)):

- the CDA-AMC review of the clinical and pharmacoeconomic evidence submitted by the sponsor, as well as relevant ethical issues related to mosunetuzumab IV (refer to the Main Report and Supplemental Material document)
- the sponsor's comments on the draft report and the responses by CDA-AMC
- patients' perspectives gathered by 1 patient group, Lymphoma Canada (refer to the Patient and Clinician Group Input document)
- input from 3 clinician groups, Leukemia and Lymphoma Society Nurses Network, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee, and Lymphoma Canada (refer to the Patient and Clinician Group Input document)
- input from public drug programs that participate in the reimbursement review process (refer to the Supplemental Material document)
- input from 2 clinical experts with expertise in the management of FL consulted by CDA-AMC.

All feedback received in response to the draft recommendation is available on the CDA-AMC website.

pERC Information

Members of the Committee

Dr. Catherine Moltzan (Chair), Dr. Kelvin Chan (Vice-Chair), Paul Agbulu, Dr. Phillip Blanchette, Dr. Matthew Cheung, Dr. Michael Crump, Annette Cyr, Dr. Jennifer Fishman, Dr. Jason Hart, Terry Hawrysh, Dr. Yoo-Joung Ko, Dr. Aly-Khan Lalani, Amy Peasgood, Dr. Anca Prica, Dr. Michael Raphael, Dr. Adam Raymakers, Dr. Patricia Tang, Dr. Pierre Villeneuve, and Danica Wasney.

Meeting date: May 13, 2026

Regrets: One expert committee member did not attend.

Conflicts of interest: None



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Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

ISSN: 2563-6596

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