Technology Guidance

Epcoritamab

for relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic therapy

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended epcoritamab for inclusion on the MOH List of Subsidised Drugs for treating relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic therapy. The decision for epcoritamab was based on the uncertainties surrounding its magnitude of clinical benefit, unfavourable cost-effectiveness compared with chemotherapy, and the unacceptable price-volume agreement proposed by the company.

Clinical indication, subsidy class and MediShield Life claim limit for epcoritamab are provided in the Annex.

Updated: 16 September 2025

Factors considered to inform the recommendations for funding

Company-led submission

1.1. At the March 2025 meeting, the MOH Drug Advisory Committee ("the Committee") considered the technology evaluation of epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy (i.e. third-line and beyond [3L+] setting). The evaluation included the company's evidence submission and a review by one of ACE's evidence review centres.

1.2. Expert opinion obtained from clinicians from public healthcare institutions and the MOH Cancer Drug Subcommittee, and patient experts from local patient and voluntary organisations, assisted ACE in ascertaining the clinical value of epcoritamab.

1.3. The evidence was used to inform the Committee's deliberations around four core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Clinical effectiveness and safety of the technology;
- Cost effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
- Estimated annual technology cost and the number of patients likely to benefit from the technology.

1.4. Additional factors, including social and value judgments, may also inform the Committee's funding considerations.

Clinical need

2.1. Large B-cell lymphoma is an aggressive subtype of non-Hodgkin lymphoma, of which DLBCL is the most common. Approximately 300 patients in Singapore are diagnosed with DLBCL each year. Although many patients respond to first-line multi-agent immunochemotherapy, 30–40% experience relapse or have primary refractory disease and require further treatment.

2.2. In local practice, chimeric antigen receptor T-cell (CAR-T) therapy is the preferred treatment for patients with relapsed or refractory DLBCL in the third-line (3L) setting. Following subsidy implementation from April 2025, eligible patients are also expected to receive CAR-T therapy in the second-line (2L) setting. The Committee acknowledged the clinical need for bispecific monoclonal antibodies (epcoritamab or glofitamab) in patients who are not eligible to receive CAR-T therapy at 3L or who relapse after 2L or 3L CAR-T therapy. Currently, chemotherapy is used in this 3L+ setting. The most commonly prescribed chemotherapies are rituximab, gemcitabine, oxaliplatin (R-GemOx) and rituximab, gemcitabine, dexamethasone, cisplatin (R-GDP). The Committee agreed that epcoritamab or glofitamab are expected to replace R-GemOx and R-GDP in the 3L+ setting.

2.3. The Committee considered three testimonials from local patient experts about living with lymphoma and their experience with different treatments. They heard DLBCL had a significant negative impact on patients, affecting them physically, emotionally and socially. The Committee acknowledged that these patients had received chemotherapy and one also had a stem cell transplant. The patients considered their treatments effective in controlling disease progression, but they experienced side effects such as body weakness, breathlessness and vomiting. The Committee noted that patients were concerned about the high cost of treatment. While the patients were not familiar with epcoritamab, they considered that any new treatment for lymphoma should extend survival, prevent relapse or cancer worsening, be more affordable, enable them to return to work, and have manageable side effects.

Clinical effectiveness and safety

3.1. The Committee heard that the clinical evidence of epcoritamab came from a single arm study (EPCORE NHL-1) in a DLBCL population (N=139). At a median follow-up of 25.5 months, the independent review committee (IRC)-assessed overall response rate (ORR) was 61.9% (95% confidence interval [CI] 53.3 to 70.0), with median progression survival of 4.4 months (95% CI 3.0 to 8.8) and median overall survival (OS) of 19.4 months (95% CI 11.7 to 27.7).

3.2. In the absence of direct comparative evidence, the Committee reviewed a matching-adjusted indirect comparison (MAIC) informed by EPCORE NHL-1 (epcoritamab) and a pooled observational study, SCHOLAR-1 (chemotherapy). Patients in EPCORE NHL-1 who had received prior CAR-T therapy (38.1%) were excluded from the MAIC as patients in the SCHOLAR-1 had not received prior CAR-T therapy.

3.3. The MAIC results favoured epcoritamab compared to chemotherapy in ORR, complete response (CR) and OS outcomes (Table 1). Results in the MAIC-adjusted analysis (N=29 in epcoritamab arm) were more favourable compared to the unadjusted analysis (N=86). However, the Committee considered results from the comparison were uncertain, given (i) the small effective sample size in the adjusted epcoritamab arm, (ii) lower survival rates in the SCHOLAR-1 subset used compared to its overall population, (iii) residual imbalances in prognostic factors between arms after adjustment, (iv) inclusion of patients receiving CAR-T therapy after epcoritamab in the EPCORE NHL-1, (v) residual bias caused by unobserved effect modifiers and prognostic factors, and (vi) that the adjusted EPCORE NHL-1 cohort were younger and had less severe disease which may not be generalisable to the local setting.

Table 1: Results of MAIC comparing ORR, CR and OS of epcoritamab to chemotherapy

	Epcoritamab (EPCORE NHL1)	Chemotherapy (SCHOLAR-1)
ORR		
Unadjusted population	67.4%	34.1%
Difference in percentage (95% CI), p value	33.3% (22.2% to 44.5%), p<0.001	
Adjusted population	70.1%	34.1%
Difference in percentage (95% CI), p value	36.0% (17.9% to 54.0%), p<0.001	
CR		
Unadjusted population	43.0%	12.1%
Difference in percentage (95% CI, p value)	31.0% (19.9% to 42.0%), p<0.001	
Adjusted population	49.5%	12.1%
Difference in percentage (95% CI), p value	37.4% (18.7% to 56.2%), p<0.001	
OS		
Unadjusted HR (95% CI), p-value	0.512 (0.378 to 0.693), p<0.001	
Adjusted HR (95% CI), p-value	0.344 (0.203 to 0.582), p<0.001	

Abbreviations: CI, confidence interval; CR, complete response; HR, hazard ratio; MAIC, matching-adjusted indirect comparison; ORR, overall response rate, OS, overall survival.

3.4. In terms of safety, the Committee heard that compared with chemotherapy, epcoritamab was associated with a range of black box warnings regarding cytokine-release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). However, the impact of these adverse events (AEs) was not assessed in the safety comparison.

3.5. For the treatment of DLBCL in the 3L+ setting, the submission described epcoritamab as superior in terms of clinical effectiveness compared with chemotherapy. Based on the evidence submitted, the Committee concluded that epcoritamab may be considered to have superior efficacy to R-GemOx and R-GDP in some CAR-T naïve patients, but the magnitude of such improvements was uncertain. For patients with prior CAR-T therapy, a superiority claim in clinical effectiveness could not be supported as no MAIC analyses for these patients were submitted. In terms of safety, the Committee considered that based on the limited safety data reported, the relative safety between epcoritamab and chemotherapy remained uncertain.

3.6. In the absence of direct comparative evidence, the Committee reviewed an MAIC that compared EPCORE NHL-1 (epcoritamab) and a single-arm NP30179 study (glofitamab). There was no significant difference between the two treatments in PFS (hazard ratio [HR] 1.05; 95% CI 0.78 to 1.41) and OS (HR 0.80; 95% CI 0.57 to 1.12). The Committee considered there were uncertainties in the MAIC due to differences in study designs, eligibility criteria, and an inability to match participants across relevant factors.

3.7. In terms of safety, the Committee heard that compared with glofitamab, epcoritamab was associated with higher rates of grade ≥3 AEs and discontinuations due to AEs, but lower rates of CRS and ICANS of any grade. The U.S. Food and Drug Administration and European Medicine Agency require additional safety monitoring for both epcoritamab and glofitamab.

3.8. The Committee noted that the submission did not present clinical claims between epcoritamab and glofitamab. Given the uncertainties associated with the evidence base, at best epcoritamab may be considered to be non-inferior to glofitamab in terms of clinical effectiveness and safety.

Cost effectiveness

4.1. The Committee considered the results of the submission's cost-utility analysis (CUA) that compared epcoritamab with chemotherapy, based on the MAIC-adjusted results for 3L+ DLBCL. Key components of the base-case economic evaluation are summarised in Table .

Table 2: Key components of the company-submitted base-case economic evaluation

Component	Description
Type of analysis	Cost-utility analysis
Population	Adult patients with relapsed or refractory DLBCL after two or more lines of systemic therapy
Outcomes	Total and incremental direct medical costs; total and incremental LY gained; total and incremental QALYs; ICER
Perspective	Singapore healthcare system
Type of model	Partitioned survival model
Time horizon	45 years in the model base case, based on a median follow-up of 25.5 months in EPCORE NHL-1
Health states	Pre-progression; post-progression; death
Cycle length	28 days
Extrapolation methods used to generate results	Extrapolation of the OS, PFS, and TTD curves were informed by time-to-event data from MAIC subgroup of EPCORE NHL-1, and fitted using standard parametric distributions in the base case: • Epcoritamab ▪ OS, PFS, and TTD: log normal distribution • Chemotherapy (R-GemOx, R-GDP) ▪ OS: log normal distribution ▪ PFS: HR from chemotherapy vs. epcoritamab OS applied to the PFS of epcoritamab ▪ TTD: assumed equal to chemotherapy PFS The model assumed patients remaining in the pre-progression survival state after three years would be considered as being in long-term remission.
Health-related quality of life	Trial based utilities from EPCORE NHL-1 (EQ-5D-3L, UK preference weights). • Pre-progression utility = 0.772 • Post-progression utility = 0.700
Types of healthcare resources included	• Drug and drug administration • Disease management cost • Subsequent treatment costs • AE management costs

Abbreviations: AE, adverse events; DLBCL, diffuse large B-cell lymphoma; EQ-5D-3L, EuroQoL-5 dimensions-3 levels; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LYs, life years; MAIC, matching-adjusted indirect comparison; OS, overall survival; PFS, progression-free survival; QALYs, quality-adjusted life years; R-GDP, rituximab, gemcitabine, dexamethasone, cisplatin; R-GemOx, rituximab, gemcitabine, oxaliplatin; TTD, time to treatment discontinuation.

4.2. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG$45,000 and SG$75,000 per quality-adjusted life year (QALY) gained, compared with chemotherapy. However, the Committee considered the ICER to be uncertain and likely underestimated, given the following:

- The submitted model was limited by the uncertainties in the indirect comparison between epcoritamab and chemotherapy. The Committee noted the modelled population was limited to CAR-T naïve patients, whereas there was a potential place in therapy for epcoritamab in patients with prior CAR-T therapy.

- The modelled long-term benefit of epcoritamab was likely overestimated and appeared clinically implausible. This was coupled with an underestimation of OS for chemotherapy, which lacked face validity and favoured epcoritamab.

- The cure assumption was overly optimistic, particularly when used with an extended time horizon of 45 years, given the short median follow-up duration (25.5 months) in EPCORE NHL-1. This introduced substantial uncertainties in the extrapolation of survival estimates.

4.3. The Committee considered the revised base case, which accounted for several uncertainties in the submitted model. Key changes included applying results from unadjusted MAIC of epcoritamab versus chemotherapy, revising the choice of parametric distributions, reducing the time horizon, and removing the cure assumption. These changes substantially increased the ICER to between SG$165,000 and SG$205,000 per QALY gained versus chemotherapy.

4.4. The Committee noted that one-way sensitivity analysis and scenario analyses of the revised base case resulted in ICERs that remained unfavourably high. The key model drivers were the OS HR of epcoritamab versus chemotherapy, cure assumptions, and time horizon.

4.5. Given that epcoritamab may be considered non-inferior to glofitamab, the Committee agreed that a cost-minimisation analysis (CMA) would be appropriate to assess the cost-effectiveness of epcoritamab versus glofitamab. The Committee heard that a CMA was conducted based on drug and administration costs over the mean treatment cycles administered in the respective trials. However, the analysis was limited by the uncertainties in indirect comparison between epcoritamab and glofitamab.

4.6. Overall, the Committee considered that epcoritamab did not represent a cost-effective use of healthcare resources for relapsed or refractory DLBCL after two or more lines of systemic therapy, at the price proposed by the company.

Estimated annual technology cost

5.1. Using an epidemiological approach, the submission estimated that the annual cost impact to the public healthcare system would increase from less than SG$1 million in the first year, to between SG$3 and SG$5 million in the fifth year of listing epcoritamab on the MOH List of Subsidised Drugs for relapsed or refractory DLBCL after two or more lines of systemic therapy.

5.2. The Committee considered that the submission financial estimates were high due to an overestimation of annual growth rate of DLBCL cases, an overestimation of treatment costs, and an optimistic uptake rate for epcoritamab. Based on the revised budget impact model, the annual cost impact to the public healthcare system was estimated to be less than SG$1 million in the first year, increasing to between SG$1 million and SG$3 million in the fifth year of listing.

Recommendations

6.1. Based on the evidence submitted, the Committee recommended not listing epcoritamab on the MOH List of Subsidised Drugs for treating relapsed or refractory DLBCL after two or more lines of systemic therapy. The decision for epcoritamab was based on uncertainties surrounding its magnitude of clinical benefit, unfavourable cost effectiveness compared with chemotherapy, and the unacceptable price-volume agreement proposed by the company.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Approved clinical indication	Subsidy class	MediShield Life claim limit per month (implementation date)
Epcoritamab 4 mg/ 0.8 mL concentrate for solution for injection and 48 mg/ 0.8 mL solution for injection	For the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy	Not recommended for subsidy	$2,400 (1 November 2025)

VERSION HISTORY

Guidance on epcoritamab for relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic therapy

This Version History is provided to track any updates or changes to the guidance following the first publication date. It is not part of the guidance.

1. **Publication of guidance**

Date of Publication	4 Jun 2025

2. **Guidance updated to include epcoritamab on the Cancer Drug List**

Date of Publication	16 Sep 2025