Technology Guidance

Glofitamab

for relapsed or refractory diffuse large B-cell lymphoma not otherwise specified in patients who are not candidates for autologous stem cell transplant

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has recommended:

- ✓ Glofitamab 2.5 mg and 10 mg concentrate for solution for infusion, for use in combination with gemcitabine and oxaliplatin, for relapsed or refractory diffuse large B-cell lymphoma not otherwise specified in patients who are not candidates for autologous stem cell transplant.

Funding status

Glofitamab 2.5 mg and 10 mg concentrate for solution for infusion are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 September 2026.

Clinical indication, subsidy class and MediShield Life claims eligibility for glofitamab are provided in the Annex.

Published: 1 July 2026

Technology Evaluation

1.1. At the April 2026 meeting, the MOH Drug Advisory Committee ("the Committee") considered the technology evaluation of glofitamab, in combination with gemcitabine and oxaliplatin (glofitamab-GemOx), for relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS) in patients who are not candidates for autologous stem cell transplant (ASCT). The evaluation considered the company's evidence submission by Roche Singapore Pte Ltd for glofitamab (Columvi), and a review conducted by one of ACE's evidence review centres.

1.2. Expert opinion from clinicians at public healthcare institutions, the MOH Cancer Drug Subcommittee, and patient experts from local patient and voluntary organisations helped ACE ascertain the clinical value of glofitamab.

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. For patients with DLBCL NOS who are not candidates for ASCT, the current subsidised second-line treatment options are rituximab, gemcitabine, oxaliplatin (R-GemOx), and rituximab, gemcitabine, dexamethasone, cisplatin (R-GDP). The Committee acknowledged the clinical need for an additional subsidised treatment option in this setting and considered that funding of glofitamab-GemOx may improve access to care.

2.3. The Committee considered lived experiences included in the submission from a local patient and a carer, and from two patients who provided testimonials to ACE. The Committee heard that DLBCL had a significant negative impact on the daily lives of patients and carers. The patients had received chemotherapy, and one patient also had a stem cell transplant. They felt that the treatments were effective in controlling disease progression. However, they experienced side effects such as body weakness, breathlessness, weakened immunity, hair loss, diarrhoea and pancytopenia. Two patients included in the submission received glofitamab as a third-line or later treatment and found that it worked well with minimal side effects, improved their quality of life, and provided relief for carers. The Committee noted that the patients were concerned about the financial burden of treatments, consultations, investigations and hospital stays. Overall, they considered that any new treatment for DLBCL should extend survival, prevent relapse, be more affordable, enable them to return to work, and have manageable side effects.

Clinical effectiveness and safety

3.1. The Committee reviewed the clinical evidence for glofitamab-GemOx from an ongoing phase III randomised controlled trial (STARGLO), which compared glofitamab-GemOx with R-GemOx in patients with relapsed or refractory DLBCL NOS who failed at least one line of therapy and were not candidates for ASCT. The Committee considered that R-GemOx was a reasonable proxy for R-GDP, as neither regimen has been shown to be superior in this setting.

3.2. Results from two clinical cut-off dates (CCOD) were used in the submission. At the updated analysis (February 2024 data cut-off), with median follow-up of 19.7 to 22.5 months, glofitamab-GemOx improved overall survival (OS) and progression-free survival (PFS) compared with R-GemOx (Table 1). However, interpretation of the OS benefit was limited by immature data, violations of the proportional hazard assumption, and inconsistent subgroup results between Asian and non-Asian patients.

Table 1: Results for glofitamab-GemOx and R-GemOx of the STARGLO trial

Outcome	Glofitamab-GemOx (n=183)		R-GemOx (n=91)		Difference in median, months	HR (95% CI), p value
	n with event (%)	Median time to event, months (95% CI)	n with event (%)	Median time to event, months (95% CI)		
Primary analysis (CCOD: 29 March 2023)						
OS	61 (33.3)	NE (13.8, NE)	40 (44.0)	9.0 (7.3 to 14.4)	NE	0.59 (0.40, 0.89), 0.011
PFS by IRC	68 (37.2)	12.1 (6.8, 18.3)	44 (48.4)	3.3 (2.5 to 5.6)	8.8	0.37 (0.25, 0.55), <0.000001
Updated analysis (CCOD: 16 February 2024)						
OS	80 (43.7)	25.5 (18.3 to NE)	52 (57.1)	12.9 (7.9 to 18.5)	12.6	0.62 (0.43, 0.88)[a]
PFS by IRC	90 (49.2)	13.8 (8.7 to 20.5)	54 (59.3)	3.6 (2.5 to 7.1)	10.2	0.40 (0.28, 0.57)[a]

Abbreviations: CCOD, clinical cut-off date; CI, confidence interval; glofitamab-GemOx, glofitamab plus gemcitabine and oxaliplatin; R-GemOx, rituximab plus gemcitabine and oxaliplatin; HR, hazard ratio; IRC, independent review committee; NE, not estimable; PFS, progression-free survival; OS, overall survival.

[a] As the primary analysis of OS crossed the pre-specified stopping boundary, p-values for all updated analyses were considered descriptive.

3.3. The Committee further noted that the differing overseas regulatory decisions (European Medicines Agency [EMA] approval and US Food and Drug Administration [FDA] rejection) reflected concerns about the robustness and generalisability of the evidence to the local population.

3.4. In terms of safety, the Committee heard that compared with R-GemOx, glofitamab-GemOx had a higher incidence of grade 3 to 5 adverse events (AEs; 77.8% versus 40.9%), serious AEs (54.4% versus 17.0%), AEs leading to treatment discontinuation (26.7% versus 12.5%) and fatal AEs (8.3% versus 4.5%). The Committee noted that glofitamab was associated with a range of black box warnings regarding cytokine-release syndrome and immune effector cell-associated neurotoxicity syndrome.

3.5. The submission described glofitamab-GemOx as superior in terms of clinical effectiveness but with increased rates of AEs, compared to R-GemOx. The Committee considered that the claim of superior clinical effectiveness to be reasonable; however, the magnitude and durability of the benefit remained uncertain. In terms of safety, the Committee considered glofitamab-GemOx to be inferior to R-GemOx.

Cost effectiveness

4.1. The Committee considered the results of the submission's cost-utility analysis that compared glofitamab-GemOx with R-GemOx for relapsed or refractory DLBCL NOS in patients who are not candidates for ASCT, based on the STARGLO trial. Overall, the model was limited by its construction, complexity and lack of internal functional validity, which impacted the credibility of the results presented. Key components of the base-case economic evaluation provided in the submission are summarised in Table 2.

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

Component	Description
Type of analysis	Cost-utility analysis
Population	Patients with r/r DLBCL NOS who are not candidates for ASCT
Outcomes	Total and incremental costs; total and incremental LYs; total and incremental QALYs; ICER
Perspective	Singapore healthcare system
Type of model	Markov model
Time horizon	30 years in the model base case, based on a median follow-up of 19.7 to 22.5 months in the STARGLO trial
Health states	PFS 1 (2L), PFS 1 (3L), PFS 2 (R-Chemo), PFS 2 (CAR-T), post-progression, long-term survival, death
Cycle length	30 days
Extrapolation methods used to generate results	Extrapolation of the PFS and OS curves were informed by time-to-event data from STARGLO trial and fitted using standard parametric distributions in the base case: PFS1 • 2L and 3L glofitamab-GemOx = log normal • 2L and 3L R-GemOx = log normal OS1 • 2L and 3L glofitamab-GemOx = log normal • 2L and 3L R-GemOx = log normal PFS2 • CAR-T= log normal • R-Chemo (BR) = log-logistic OS2 • CAR-T= log normal • R-Chemo (BR) = log-logistic The submission did not assume treatment effect waning. The model included a cure assumption with the cohort remaining in the PFS health state for 5 years transitioning to the long-term survival health state.

Health-related quality of life	Utilities for PFS1 health state were based on EQ-5D questionnaires from the STARGLO trial. Utilities for PFS2, post-progression, and long-term survival were sourced from published literature. • PFS 1 on treatment: 0.758 • PFS 1 off treatment: 0.751 • PFS 2 treatment disutility: -0.15 (Wakase et al., 2021) • PFS 2 off treatment: 0.65 (Pola-BR NICE appraisal TA649) • Post-progression: 0.39 (Wakese et al., 2021) • Long-term survival: 0.88 (aged-based population normal for Singapore Abdin et al., 2015)
Types of healthcare resources included	• Drug and drug administration • Subsequent treatment costs • AE management costs • Terminal care costs Costs of disease management were not included.

Abbreviations: 2L: second-line; 3L: third-line; AE, adverse event; ASCT, autologous stem cell transplant; BR, bendamustine, rituximab; CAR-T, chimeric antigen receptor T-Cell; ICER, incremental cost-effectiveness ratio; LY, life year; NICE, National Institute for Health and Care Excellence; OS, overall survival; PFS, progression free survival; QALY, quality-adjusted life year; r-chemo: rituximab-chemotherapy; r/r DLBCL NOS, relapsed or refractory diffuse large B-cell lymphoma not otherwise specified,

4.2. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG$15,000 and SG$45,000 per quality-adjusted life year (QALY) gained. However, the Committee considered the ICER to be highly uncertain and likely underestimated, in view of the following:

- The model was informed by subgroup data (2L and 3L+ populations) that had not been fully evaluated in clinical section of the submission. In addition, data used to model for subsequent treatment were sourced from external studies with different patient populations and disease characteristics to STARGLO, increasing uncertainty in modelled results.

- The submission included inaccurate implementation of parametric functions. The selection of base-case parametric function relied solely on Akaike Information Criterion (AIC) without considering visual fit or external validation of long-term survival estimates. This resulted in overly optimistic extrapolation of survival benefits over the time horizon.

- Some key utility values applied were inconsistent with previous glofitamab evaluation. In addition, the model failed to appropriately capture disutilities associated with AEs in the glofitamab-GemOx arm, biasing results towards glofitamab-GemOx.

4.3. The Committee considered the revised base case, which accounted for several uncertainties in the company's model. Key changes to the economic model included applying more plausible parametric extrapolations, removing cure assumptions and reducing the time horizon, and correcting technical syntax errors. These changes increased the ICER to between SG$45,000 and SG$75,000 per QALY gained. However, the uncertainty in the cost-effectiveness results cannot be fully addressed given the underlying deficiencies in the model structure.

4.4. Overall, the Committee considered that glofitamab-GemOx did not represent a cost-effective use of healthcare resources for treating relapsed or refractory DLBCL NOS in patients who are not candidates for ASCT 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 between SG$1 million and SG$3 million in the first year, and to between SG$5 million and SG$10 million in fifth year of listing glofitamab-GemOx on the MOH List of Subsidised Drugs for relapsed or refractory DLBCL NOS in patients who are not candidates for ASCT.

5.2. The Committee considered that the submission estimates were high due to an overestimation of the incidence rate of lymphoid neoplasm, and uncertain uptake rates of glofitamab. Based on the revised budget impact model, the annual cost impact to the public healthcare system was estimated to be between SG$1 million and SG$3 million over the first five years of listing. The Committee also noted that the price-volume agreement caps proposed by the company were unacceptably high and deviated from the company's budget impact analysis.

Recommendations

6.1. Based on available evidence and the company's pricing proposal, the Committee indicated that glofitamab-GemOx could be considered for listing on the MOH List of Subsidised Drugs, subject to an improved pricing proposal to address uncertainty in the ICER and provide greater budget certainty. The company subsequently submitted a revised pricing proposal to address the Committee's concerns.

6.2. Accordingly, the Committee recommended glofitamab 2.5 mg and 10 mg vials be listed on the Medication Assistance Fund (MAF) for the use in combination with gemcitabine and oxaliplatin for treating relapsed or refractory DLBCL NOS in patients who are not candidates for ASCT.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Approved clinical indication	Subsidy class (implementation date)	Eligible for MediShield Life claims (implementation date)
Glofitamab 2.5 mg and 10 mg concentrate for solution for infusion Obinutuzumab 1000 mg concentrate for solution for infusion	Glofitamab in combination with gemcitabine and oxaliplatin for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified who are not candidates for autologous stem cell transplant and have received at least one prior therapy. Maximum treatment duration of glofitamab is 12 cycles. Obinutuzumab may be used as pre-treatment in line with HSA-recommended dosing regimens.	MAF (1 Sep 2026)	Yes (1 Sep 2026)

Abbreviation: MAF, Medication Assistance Fund.
[1] Please refer to MOH's website for the MediShield Life claim limit starting from the implementation date.

Agency for Care Effectiveness - ACE Agency for Care Effectiveness (ACE)

About the Agency
The Agency for Care Effectiveness (ACE) was established by the Ministry of Health (Singapore) to drive better decision-making in healthcare through health technology assessment (HTA), clinical guidance, and education.

As the national HTA agency, ACE conducts evaluations to inform government funding decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

The guidance is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

Find out more about ACE at https://www.ace-hta.gov.sg/about-us/

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