SMC2846

glofitamab (Columvi®) concentrate for solution for infusion

Roche Products Ltd

05 June 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the end of life and orphan equivalent medicine process

glofitamab (Columvi®) is accepted for restricted use within NHSScotland.

Indication under review: in combination with gemcitabine and oxaliplatin for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS) who are ineligible for autologous stem cell transplant (ASCT).

SMC restriction: restricted to patients who have progressed during or after one systemic therapy only (that is, for patients in the second line setting).

In a phase III study of patients with relapsed or refractory DLBCL NOS who are ineligible for ASCT, glofitamab in combination with gemcitabine and oxaliplatin significantly improved overall survival compared with rituximab in combination with gemcitabine and oxaliplatin.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

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1. Clinical Context

1.1. Medicine background

Glofitamab is a bispecific antibody that binds bivalently to CD20 expressed on the surface of B cells and monovalently to CD3 in the T-cell receptor complex expressed on the surface of T cells. The simultaneous binding to CD20 and CD3 mediates glofitamab's formation of an immunological synapse with subsequent T-cell activation and proliferation, secretion of cytokines and release of cytolytic proteins that result in the lysis of CD20-expressing B cells. [1]

Glofitamab is administered by intravenous infusion in combination with gemcitabine and oxaliplatin at cycles one to eight, and as monotherapy from cycles nine to 12. Treatment is continued for a maximum of 12 cycles (each cycle is 21 days) or until disease progression or unmanageable toxicity, whichever occurs first. A dose step-up schedule is used to reach the recommended dose of 30 mg. For full information on administration of glofitamab, including pretreatment with obinutuzumab, doses of gemcitabine and oxaliplatin, premedication/prophylaxis treatments, and glofitamab dose step-up schedule, refer to the Summary of Product Characteristics (SPC). [1]

Glofitamab is accepted for use within NHSScotland as monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, after two or more lines of systemic therapy (SMC2614).

1.2. Disease background

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma, accounting for approximately 30% to 40% of all cases. The incidence increases with age with a median age at diagnosis of 64 years. Risk factors include a family history of lymphoma, autoimmune disease, human immunodeficiency virus infection, hepatitis C virus seropositivity, a high body mass as a young adult and some occupational exposures. Although approximately half of newly diagnosed patients with DLBCL receive curative treatment, the disease is aggressive and approximately 30% of cases relapse and 10% to 15% are refractory to first-line therapy. [2-5]

1.3. Company proposed position

The submitting company have requested that glofitamab in combination with gemcitabine and oxaliplatin is restricted to patients who have progressed during or after one systemic therapy only (that is, for patients in the second line setting).

1.4. Treatment pathway and relevant comparators

Treatment for relapsed or refractory DLBCL NOS should be individualised based on patient fitness, prior first-line therapy, suitability for chimeric antigen receptor (CAR) T-cell therapy or autologous stem cell transplant (ASCT), and suitability for anti-CD3xCD20 bispecific antibody therapy (glofitamab SMC2614 or epcoritamab SMC2632) in the third-line setting. [3]

Sufficiently fit patients with DLBCL relapsed within 12 months from completion of, or refractory to, first-line chemoimmunotherapy may receive CAR T-cell therapy, axicabtagene ciloleucel (SMC2695). Treatment options for patients with progression unfit for CAR T-cell therapy or ineligible for ASCT after first-line chemotherapy include rituximab in combination with

gemcitabine and oxaliplatin (R-GemOx) or polatuzumab vedotin in combination with bendamustine and rituximab (Pola-BR, SMC2524), where polatuzumab vedotin has not previously been used in the first-line. [3]

The Public Health Scotland Cancer Medicines Outcome Programme (PHS-CMOP) analysed a cohort of patients with relapsed or refractory DLBCL who were not eligible for ASCT and who had received either R-GemOx or Pola-BR between June 2023 and May 2025. Pola-BR was identified as the most commonly used treatment.[6] The submitting company considered that axicabtagene ciloleucel and R-GemOx were the relevant comparators.

1.5. Category for decision-making process

Eligibility for a PACE meeting

Glofitamab in combination with gemcitabine and oxaliplatin meets SMC end of life and orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of glofitamab in combination with gemcitabine and oxaliplatin for this indication comes from STARGLO. Details are presented in Table 2.1.

Table 2.1. Overview of relevant study

Criteria	STARGLO [4, 5]
Study design	International, randomised, open-label, phase III study.
Eligible patients	• Adults ≥18 years • Life expectancy ≥12 weeks • Histologically confirmed relapsed or refractory DLBCL NOS • Failed at least one line of prior systemic therapy but not a candidate for high-dose chemotherapy followed by ASCT • ECOG Performance Status of 0, 1 or 2
Treatments	Patients were randomised to receive: - Pretreatment with obinutuzumab 1000 mg IV on cycle one day 1, glofitamab IV as step-up doses on day 8 (2.5 mg) and day 15 (10 mg) of cycle one (plus gemcitabine 1000 mg/m^2 BSA IV and oxaliplatin 100 mg/m^2 BSA IV on cycle one day 2), then glofitamab 30 mg IV plus gemcitabine 1000 mg/m^2 BSA IV and oxaliplatin 100 mg/m^2 BSA IV on day 1 (or day 2 for gemcitabine and oxaliplatin) of cycles two through eight, followed by glofitamab 30 mg IV on day 1 of cycles nine to 12 (each cycle was 21 days), - or rituximab IV in combination with gemcitabine IV and oxaliplatin IV on day 1 (or day 2 for gemcitabine and oxaliplatin) of cycles one to eight (each cycle was 21 days). Treatment was to continue for a maximum of 12 treatment cycles (or eight cycles in the rituximab, gemcitabine and oxaliplatin arm), disease progression per investigator according to the 2014 Lugano Response Criteria for Malignant Lymphoma or unacceptable toxicity.
Randomisation	Patients were randomised in a 2:1 ratio. Randomisation was stratified according to number of previous lines of therapy (1 versus ≥2) and the outcome of last systemic therapy (relapsed versus refractory).
Primary	OS, defined as the time between date of randomisation and death due to any cause.

outcome	
Key secondary outcomes	• PFS assessed by IRC. Defined as time from randomisation to the first occurrence of disease progression or death from any cause, whichever occurred first. • CR rate assessed by IRC per 2014 Lugano response criteria. Defined as the proportion of patients whose best overall response was a CR on PET-CT. • DOCR assessed by IRC. Defined as the time from the first occurrence of a documented CR to disease progression, or death from any cause, whichever occurred first.
Statistical analysis	Efficacy analyses were performed in the ITT population, which included all patients who underwent randomisation. A hierarchical statistical testing strategy was applied in the study for the primary and key secondary outcomes in the order above with no formal testing of outcomes after the first non-significant outcome in the hierarchy.

Abbreviations: ASCT = autologous stem cell transplant; BSA = body surface area; CR = complete response; DOCR = duration of complete response; DLBCL NOS = diffuse large B-cell lymphoma, not otherwise specified; ECOG = Eastern Cooperative Oncology Group; GCSF = granulocyte colony stimulating factor; ITT = intention-to-treat; IRC = independent review committee; IV = intravenous; OS = overall survival; PET-CT = positron emission tomography–computed tomography; PFS = progression free survival.

At the primary analysis (data cut-off 29 March 2023), glofitamab in combination with gemcitabine and oxaliplatin demonstrated statistically significant improvements in overall survival (OS) compared with rituximab in combination with gemcitabine and oxaliplatin. This was supported by data from updated analyses. See Table 2.2 for further details.

Table 2.2: Primary and key secondary outcomes from STARGLO (ITT population). [4, 5, 7]

Data cut	**29 March 2023 (primary analysis)**		**16 February 2024 (updated analysis)** [a]		**1 May 2025 (updated analysis)** [a]	
	Glofit-GemOx (n=183)	**R-GemOx (n=91)**	**Glofit-GemOx (n=183)**	**R-GemOx (n=91)**	**Glofit-GemOx (n=183)**	**R-GemOx (n=91)**
Primary outcome: OS						
Median follow-up	11.3 months		20.7 months		35.1 months	
Deaths, n	61	40	80	52	NR	NR
Median OS, months	NE	9.0	25.5	12.9	25.5	12.5
KM estimate at 3 years	NR	NR	NR	NR	47%	27%
HR (95% CI), p-value	0.59 (0.40 to 0.89), p=0.01		0.62 (0.43 to 0.88)		0.60 (0.43 to 0.83)	
Key secondary outcome: PFS assessed by IRC						
Median follow-up	7.2 months		15.7 months		NR	
Events, n	68	44	90	54	NR	NR
Median PFS, months	12.1	3.3	13.8	3.6	14.4	3.3
HR (95% CI), p-value	0.37 (0.25 to 0.55), p<0.001		0.40 (0.28 to 0.57)		0.41 (0.29 to 0.57)	
Key secondary outcome: CR rate assessed by IRC (per 2014 Lugano response criteria)						
CR, %	50%	22%	58%	25%	58%	25%
Difference versus R-GemOx, % (95% CI), p-value	28% (16% to 40%), p<0.001		33% (21% to 46%)		NR	
Key secondary outcome: DOCR assessed by IRC						
Complete responders, n	92	20	107	23	107	23
Events, n	15	4	28	7	NR	NR
Median DOCR,	14.4	NE	NE	24.2	NE	24.2

months						
HR (95% CI), p-value	0.59 (0.19 to 1.83), p=0.36		0.59 (0.25 to 1.35)		NR	

Abbreviations: CI = confidence interval; CR = complete response; DOCR = duration of complete response; IRC = independent review committee; ITT = intention-to-treat; Glofit-GemOx = glofitamab, gemcitabine plus oxaliplatin; HR = hazard ratio; NE = not estimable; NR = not reported; OS = overall survival; PFS = progression free survival; R-GemOx = rituximab, gemcitabine plus oxaliplatin.

[a] Results of updated analyses are descriptive only.

2.2. Evidence to support the positioning proposed by the submitting company

The submitting company provided data from the second line subgroup of STARGLO (only one prior line of therapy, n=115 in the glofitamab, gemcitabine and oxaliplatin group and n=57 in the rituximab, gemcitabine and oxaliplatin group) to support the positioning.

At the second updated analysis (1 May 2025) median OS was not estimable in the glofitamab, gemcitabine and oxaliplatin group versus 14.4 months in the rituximab, gemcitabine and oxaliplatin group (HR: 0.58 [95% CI: 0.38 to 0.89]). Median PFS was 20.4 months versus 5.5 months (HR 0.49 [95% CI: 0.31 to 0.78]). [7]

2.3. Health related quality of life outcomes

Health Related Quality of Life (HRQoL) was assessed using three questionnaires: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLC-30), Functional Assessment of Cancer Therapy-Lymphoma subscale (FACT-LymS) and EQ-5D-5L. [8]

Time to deterioration was similar between treatment groups for fatigue, physical functioning and lymphoma symptoms. By cycle three, patients receiving glofitamab, gemcitabine and oxaliplatin appeared to show clinically meaningful improvements in pain and lymphoma symptoms and by cycle five, both groups demonstrated clinically meaningful improvements in these symptoms. At end of treatment, improvements in pain and lymphoma symptoms were maintained in both arms, with generally greater benefit observed in the glofitamab group. Across both treatment groups, median EQ-5D-5L scores remained unchanged from baseline during long-term follow-up. Overall, HRQoL results seemed comparable between treatment groups. [8, 9]

2.4. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing glofitamab in combination with gemcitabine and oxaliplatin with axicabtagene ciloleucel in patients with relapsed or refractory DLBCL in second line who were ineligible for ASCT, the submitting company presented an unanchored matching-adjusted indirect treatment comparison (MAIC). This has been used to inform the economic base case. Details are presented in Table 2.3.

Table 2.3: Summary of indirect treatment comparison [5, 10]

Criteria	Overview
Design	Unanchored MAIC
Population	Patients with relapsed or refractory DLBCL ineligible for ASCT in the second line setting.
Comparators	Glofitamab in combination with gemcitabine and oxaliplatin (Glofit-GemOx) Axicabtagene ciloleucel
Studies included	STARGLO and ALYCANTE [5, 10]
Outcomes	Primary outcome: OS Key secondary efficacy outcome: PFS
Results	The point estimate favoured axicabtagene ciloleucel for OS while the point estimate

	favoured Glofit-GemOx for PFS; however, the 95% CIs for both the OS and PFS HRs included one, suggesting no evidence of a difference between treatments for OS and PFS.

Abbreviations: ASCT = autologous stem cell transplant; CI = confidence interval; DLBCL = diffuse large B-cell lymphoma; HR = hazard ratio; MAIC = matching adjusted indirect treatment comparison; OS = overall survival; PFS = progression free survival.

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

Evidence from the intention-to-treat (ITT) population of STARGLO supports the safety of glofitamab in combination with gemcitabine and oxaliplatin compared with rituximab in combination with gemcitabine and oxaliplatin for the indication under review. The submitting company's indirect treatment comparison did not compare safety outcomes with axicabtagene ciloleucel.

At the updated analysis (16 February 2024), the median number of treatment cycles in the glofitamab, gemcitabine and oxaliplatin group was 11 cycles of glofitamab and eight cycles of gemcitabine and oxaliplatin, and was four cycles in the rituximab, gemcitabine and oxaliplatin group. [5]

In the glofitamab, gemcitabine and oxaliplatin group versus rituximab, gemcitabine and oxaliplatin group respectively, grade ≥3 adverse events (AEs) were reported in 78% (140/180) versus 41% (36/88) and these were considered related to study treatment in 47% versus 23%. Patients that discontinued treatment due to an AE related to study treatment were 7% versus 3%. [5]

The most commonly reported AEs with an incidence of ≥30% patients in either group were: thrombocytopenia (48% in both groups), cytokine release syndrome (44% versus not applicable), neutropenia (42% versus 31%), anaemia (41% versus 22%), nausea (39% versus 40%) and peripheral neuropathy (36% versus 26%). [5]

Overall, the safety profile of glofitamab in combination with gemcitabine and oxaliplatin was consistent with the known safety of the individual medicines and no new safety concerns were identified. The safety profile in the second line subgroup was comparable to the ITT population. [11] There were generally a higher frequency of AEs in the glofitamab, gemcitabine and oxaliplatin group, however treatment exposure was longer in this group which may explain the unfavourable safety profile compared with rituximab, gemcitabine and oxaliplatin. [4] See the SPC recommendations for the management of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome (ICANS). [1]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- At the primary analysis of the phase III study STARGLO (29 March 2023) in the ITT population, with a median follow-up of 11.3 months, glofitamab in combination with gemcitabine and oxaliplatin was associated with a statistically significant and clinically relevant improvement in OS compared with rituximab in combination with gemcitabine and oxaliplatin. [5] This was supported by descriptive data from a later cut-off (1 May 2025), which showed continued OS benefit of glofitamab, with a median OS gain of 13 months. [7]

- Statistically significant improvements in the key secondary outcomes, PFS and complete response rate, further supported the treatment benefit of glofitamab. [5]
- The OS and PFS benefit were observed across the second line preplanned subgroup, and this was consistent with the primary analysis, thereby supporting the proposed positioning. [5, 7]

4.2. Key uncertainties

- The submitting company did not consider polatuzumab vedotin in combination with bendamustine and rituximab (Pola-BR) to be a relevant comparator and therefore, no comparative evidence versus Pola-BR was submitted.
- In the absence of direct evidence versus axicabtagene ciloleucel, the submitting company conducted an unanchored MAIC. There were several limitations of the MAIC including generalisability issues with the ALYCANTE study; substantial differences in study eligibility criteria and follow-up periods; incomplete data availability in ALYCANTE; missing variables required for matching; and wide confidence intervals. Results were also inconsistent depending on the outcome assessed. The company concluded that, given these limitations, it remains uncertain whether one treatment offered a greater advantage for survival. However, in the economic model, the treatments were assumed to have equivalent efficacy. Given the limitations of the MAIC, the company's conclusions and assumption of equivalent efficacy are highly uncertain.
- The submitting company provided data from the second line subgroup of STARGLO to support the positioning. While the number of prior lines of therapy was a stratification factor in STARGLO, the study was not statistically powered to detect differences in OS within subgroups; therefore, these results should be considered exploratory only. [4]
- There remain some uncertainties regarding the generalisability of the STARGLO study to the Scottish population. However, a regulator requested further post hoc subgroup analyses by geographical region and concluded that, despite regional heterogeneity, the overall treatment effect observed in the ITT population is applicable to Europe. [4]

4.3. Clinical expert input

Clinical experts consulted by SMC considered that glofitamab in combination with gemcitabine and oxaliplatin is a therapeutic advancement and that it fills an unmet need, providing better outcomes compared with currently available treatments.

4.4. Service implications

Clinical experts considered that glofitamab in combination with gemcitabine and oxaliplatin may require at least one initial hospital admission compared with some comparators. The regimen also initially requires more frequent dosing than some comparators, however this lessens once on glofitamab monotherapy.

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of **glofitamab**, as an **end of life and orphan equivalent** medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) is a severe, rapidly progressive condition with poor prognosis, often leading to death within months without effective treatment. Patients experience debilitating symptoms such as extreme fatigue, pain, breathlessness, weight loss and psychological distress, substantially impairing quality of life and independence.
- There is a clear unmet need for more effective and tolerable second-line treatments in relapsed or refractory DLBCL, as current options have limited durability and survival benefit. Glofitamab in combination with gemcitabine and oxaliplatin (Glofit-GemOx) offers improved response rates and survival outcomes compared with currently available treatments, providing a valuable alternative for patients who are ineligible for intensive therapies such as autologous stem cell transplant (ASCT).
- Glofit-GemOx is expected to improve patients' quality of life by relieving symptoms, increasing energy and enabling greater independence, while being better tolerated than existing treatments. Improved outcomes may also reduce the burden on families and carers by allowing patients to maintain daily activities and a more normal family life.
- Glofit-GemOx is associated with risks such as cytokine release syndrome (CRS), particularly during initial doses, which may require monitoring or short hospital stays but is generally mild and manageable with established protocols. While treatment requires ongoing outpatient visits, existing haematology services have established services to safely deliver and manage these side effects.
- PACE participants consider that the most appropriate place in treatment for Glofit-GemOx is in the second line, aligning with the company's proposed positioning.

Additional Patient and Carer Involvement

We received a patient group submission from Lymphoma Action, which is a registered charity. Lymphoma Action has received 7.2% pharmaceutical company funding in the past two years, including from the submitting company. A representative from Lymphoma Action participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An economic case was presented and is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis and cost-minimisation analysis
Time horizon	60-years
Population	Adults with RR DLBCL NOS who are ineligible for ASCT who have progressed during or after one systemic therapy only.
Comparators	Rituximab plus gemcitabine and oxaliplatin and axicabtagene ciloleucel.
Model description	A cohort-based partitioned survival model was used with three health states: progression-free (PF), progressed disease (PD) and death. The cycle length was 1-week.
Clinical data	Data for progression-free survival (PFS), overall survival (OS), time to off treatment (TTOT) and adverse events (AEs) for glofitamab plus gemcitabine and oxaliplatin, and rituximab plus gemcitabine and oxaliplatin, were from the respective treatment arms of the second line (2L) only subpopulation of the STARGLO study. The company conducted a matching-adjusted indirect comparison (MAIC) comparing OS and PFS with glofitamab plus gemcitabine and oxaliplatin to axicabtagene ciloleucel, assuming equal efficacy based on the non-statistically significant estimates of a difference.
Extrapolation	The company extrapolated long-term OS and PFS for glofitamab plus gemcitabine and oxaliplatin, and rituximab plus gemcitabine and oxaliplatin, using parametric survival modelling with distributions fitted to the respective treatment arm Kaplan-Meier data from the 2L-only subpopulation of STARGLO. [5] Curve selection was based on goodness of fit statistics, visual fit and clinical expert opinion. The company also provided longer term data from the literature for patients with RR DLBCL treated with rituximab plus gemcitabine and oxaliplatin to externally validate the model predictions in the rituximab arm. Independently fitted log-normal curves for both OS and PFS were selected for the base case analysis. A long-term remission assumption was included that assumed patients who remained progression-free at 3-years in the model were no longer at risk of disease progression. A standardised mortality rate of 1.09 was included for patients who achieved long-term remission in the model to account for a higher prevalence of comorbidities amongst patients with RR DLBCL in long-term remission based on the literature. [12] TTOT data from STARGLO for glofitamab plus gemcitabine and oxaliplatin, and rituximab plus gemcitabine and oxaliplatin, were complete and so were applied directly in the model.
Quality of life	EQ-5D-5L data from the STARGLO study were mapped to the EQ-5D-3L value set and were analysed to estimate health state utility values in the model. This resulted in health-state utility values of 0.756 for PF on treatment, 0.750 for PF off treatment and 0.690 for the PD health state. AE disutilities were not included as the company argued that the impact of AEs on health related quality of life was likely to be included in the EQ-5D data collected during STARGLO. Patients who achieved long-term remission were assumed to experience 90% general population utility.
Costs and resource use	Medicine costs were included for acquisition and administration, monitoring, subsequent treatments and management of treatment related AEs. Additional monitoring costs were included in the glofitamab arm to account for the increased frequency of cytokine release syndrome (CRS). The cost of obinutuzumab was also included in the glofitamab arm prior to the first dose of glofitamab, to mitigate CRS. Subsequent treatments were applied as a one-off cost upon disease progression. The distribution of subsequent treatments were based on those observed in STARGLO modified

	according to Scottish clinical expert opinion sought by the company and varied by 2L treatment arm. Administration costs for axicabtagene ciloleucel were assumed to be equal to those published in a health technology assessment of another CAR-T therapy. Healthcare resource use costs for professional and social services, healthcare and hospital resource use and treatment follow-up were included and varied by progression status and whether patients were on/off treatment. A one-off cost for various imaging modalities was included at disease progression. Patients who achieved long-term remission no longer attracted costs in the model.
PAS/contract price	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price for glofitamab. PAS discounts are in place for axicabtagene ciloleucel and obinutuzumab and a National Framework Contract Price was in place for rituximab, and these were included in the results used for decision-making by using estimates of the comparator and combination PAS prices, respectively.

Abbreviations: 2L = second line; AE = adverse event; CAR-T = chimeric antigen receptor T-cell; CRS = cytokine release syndrome; DLBCL = diffuse large B-cell lymphoma; OS = overall survival; PAS = Patient Access Scheme; PASAG = Patient Access Scheme Assessment Group; PD = progressed disease; PF = progression-free; PFS = progression-free survival; RR = relapsed or refractory; TTOT = time to off treatment

6.2. Results

SMC considered results for decision-making that took into account all relevant PAS and NHSScotland National Framework Contract prices. SMC is unable to present these results due to competition law issues.

6.3. Sensitivity analyses

A range of sensitivity analyses and scenario analyses were considered and a description of key scenarios are provided in Table 6.2 and Table 6.3 for the comparison to rituximab plus gemcitabine and oxaliplatin, and axicabtagene ciloleucel, respectively.

Table 6.2 Description of key scenario analyses versus rituximab plus gemcitabine and oxaliplatin

#	Parameter	Base case	Scenario
1a	Time horizon	60	40
1b			10
2a	PFS extrapolation	Log-normal	Generalised gamma
2b			Log-logistic
3a	OS extrapolation	Log-normal	Generalised gamma
3b			Log-logistic
4a	Cure point	3-years	2-years
4b			6-years

4c			No cure assumption
5	SMR in long-term remission	SMR 1.09 from Marauer 2014 [12]	SMR 1.41 Howlader 2017 [13]
6a	Health-state utility values	STARGLO ITT pooled treatment arms PF on treatment = 0.756 PF off treatment = 0.750 PD = 0.690	STARGLO 2L pooled treatment arms PFS on treatment = 0.757 PF off treatment = 0.757 PD = 0.691
6b			STARGLO 2L by treatment arm PF on treatment Glofit-GemOx = 0.758 PF on treatment R-GemOx = 0.751 PF off treatment Glofit-GemOx = 0.756 PF off treatment Glofit-GemOx = 0.750 PD Glofit-GemOx = 0.700 PD R-GemOx = 0.694
6c			NICE TA306 PF = 0.81 PD = 0.60
7	AE disutilities	Excluded	Included (analysis uses health state utility values from NICE TA649
8	Subsequent treatment costs	100% of patients eligible for subsequent treatment at PD	20% ineligible for subsequent treatment (-20% subsequent treatment costs, both arms)
9	Timepoint at which mortality reverts to general population adjusted by SMR	3-years	6-years
C1	Combined scenarios	Cure point = 3-years + 100% of patients eligible for subsequent treatment at PD + 60-year time horizon	Scenarios 1b + 4b 10-year time horizon + 6-year cure point
C2			Scenarios 1b + 4b 10-year time horizon + 6-year cure point
C3			Scenario 9 + 1b Timepoint at which mortality reverts to general population adjusted by SMR = 6-years + 10-year time horizon

Abbreviations: 2L = second line; AE = adverse event; C = combined scenario; GemOx = gemcitabine and oxaliplatin; Glofit = glofitamab; ICER= incremental cost effectiveness ratio; ITT = intention to treat; NICE = National Institute for Health and Care Excellence; OS = overall survival; PD = progressed disease; PF = progression-free; PFS =progression-free survival; QALY = quality adjusted life year; R = rituximab; SMR = standardised mortality rate; TA = technology appraisal.

Table 6.3 Description of key scenario analyses versus axicabtagene ciloleucel

#	Parameter	Base case	Scenario
1a	Axi-cel administration costs	Axi-cel administration costs included from NICE TA1048 (lisocabtagene maraleucel)	Axi-cel administration costs excluded
1b			Axi-cel administration costs from SMC2695
2	Analysis type	CMA	CUA
2a		PFS HR = OS HR = 1	Point estimate HR from the MAIC
2b			Upper bound of 95% CrI from the MAIC
2c			Lower bound of 95% CrI from the MAIC

Abbreviations: CMA = cost-minimisation analysis; CrI = credible interval; CUA = cost utility analysis; HR = hazard ratio; OS = overall survival; PFS = progression-free survival

*Other data were also assessed but remain confidential.**

6.4. Key strengths

- A partitioned survival model was an appropriate choice for the economic model.
- Unit costs for health care resource use were from appropriate sources.
- TTOT data from STARGLO were complete and were used to directly inform medicine acquisition costs for glofitamab plus gemcitabine and oxaliplatin and rituximab plus gemcitabine and rituximab.

6.5. Key uncertainties

- There was no analysis available for assessment that compared the cost-effectiveness of glofitamab plus gemcitabine and oxaliplatin to polatuzumab plus bendamustine and rituximab (Pola-BR). Pola-BR was also a relevant comparator in NHSScotland according to PHS-CMOP data and SMC clinical experts. However, the company did present an exploratory analysis comparing glofitamab to Pola-BR which provided some reassurance on the relative cost-effectiveness of these treatments.
- The company's assumption of equivalent efficacy for glofitamab plus gemcitabine and oxaliplatin compared to axicabtagene ciloleucel based on the results of the MAIC was uncertain. Cost-utility analysis scenarios were explored using the point estimate hazard ratios from the MAIC (Table 6.3, Scenario 2a), in addition to exploring the bounds of the credible intervals (Table 6.3, Scenarios 2b and 2c).
- There was some uncertainty around the long-term PFS and OS benefit with glofitamab plus gemcitabine and oxaliplatin compared to rituximab plus gemcitabine and oxaliplatin and the results of the economic analysis depended on extensive extrapolation of STARGLO data. The company selected independently fitted log-normal parametric curves fitted to the respective treatment arm's KM data for PFS and OS. This resulted in long-term PFS in the rituximab arm that was lower than the 5-year PFS reported in the literature for patients with RR DLBCL treated with rituximab plus gemcitabine and oxaliplatin. [14] However, the base case PFS curve selection was the closest available extrapolation to the literature estimates using the standard parametric curves explored. However, long-term OS in the rituximab arm was much higher than the 5-year OS reported in the literature for patients with RR DLBCL treated with rituximab plus gemcitabine and oxaliplatin. The company presented an additional scenario that extended the timepoint at which patients who achieved long-term remission in the model revert to general population mortality from 3-years to 6-years. This resulted in OS at 5-years in the rituximab arm of the model that more closely matched that observed in the literature but resulted in a higher estimate of cost-effectiveness (Table 6.2, Scenario 9).
- The lifetime time horizon selected for the base case presented a face validity concern because of the poor prognosis for patients with RR DLBCL. Therefore, a time horizon of 10-years (Table 6.2, Scenario 1b) was considered relevant to sufficiently explore the uncertainty around long-term outcomes projected by the model.

- Axicabtagene ciloleucel administration costs used in the analysis were based on those for a different CAR-T therapy and based on the administration costs of CAR-T therapy in NHS England and so there was some uncertainty whether these represented the costs faced by NHS Scotland for the administration of axicabtagene ciloleucel. Scenarios were explored where these costs were varied (Table 6.3, Scenarios 1a and 1b) and administration costs for CAR-T therapy were not found to be a key driver of the economic results in the comparison to axicabtagene ciloleucel.

7. Conclusion

The Committee considered the benefits of glofitamab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for a substantial improvement in life expectancy in the patient population targeted in the submission was satisfied. In addition, as glofitamab is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee accepted glofitamab for restricted use in NHSScotland.

8. Guidelines and Protocols

The British Society of Haematology published the guideline 'Management of relapsed or refractory large B-cell lymphoma' in May 2025. [3]

The European Society of Medical Oncology (ESMO) published the guideline 'Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up' in August 2025. [2]

ESMO published the ESMO Living Guideline for Relapsed/Refractory DLBCL v1.1 in February 2026. [15]

9. Additional Information

9.1. Product availability date

16 July 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per cycle (£)
glofitamab (in combination with gemcitabine and oxaliplatin)	**Cycle 1: glofitamab IV on day 8 (2.5 mg) and day 15 (10 mg) of cycle one (plus gemcitabine 1000 mg/m^2 BSA IV and oxaliplatin 100 mg/m^2 BSA IV on cycle one day 1)** **Cycle 2 to 8: glofitamab 30 mg IV on day 1 plus gemcitabine 1000 mg/m^2 BSA IV and oxaliplatin 100 mg/m^2 BSA IV on day 1 or 2 of cycles 2 through 8** **Cycle 9 to 12: glofitamab 30 mg IV on day one of cycles nine to 12 (each cycle is 21 days).**	**Cycle 1: 4,064** **Cycles 2 to 8: 8,873** **Cycles 9 to 12: 8,244**

Costs from BNF online on 04 March 2026. Costs calculated using the full cost of vials assuming wastage. Costs calculated assuming 1.8 m^2 body surface area (BSA) for an adult. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 17 April 2026.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.