NCPE Assessment Summary

Glofitamab (Columvi®)

25037

31 July 2026

Applicant: Roche Products Ireland Ltd

Glofitamab 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).

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of glofitamab (Columvi®) in combination with gemcitabine and oxaliplatin for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma not otherwise specified who are ineligible for autologous stem cell transplant.

Following assessment of the Applicant's submission, the NCPE recommends that glofitamab (Columvi®), for the specified indication, be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Roche Products Ireland Ltd) Health Technology Assessment of glofitamab (Columvi®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In December 2025, Roche Products Ireland Ltd submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of glofitamab (Columvi®) in combination with gemcitabine and oxaliplatin (Glofitamab+GemOx) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS) who are ineligible for autologous stem cell transplant (ASCT). DLBCL NOS is managed according to the same treatment principles as DLBCL. Roche Products Ireland Ltd is seeking reimbursement of glofitamab on the Oncology Drugs Management System.

Glofitamab is a monoclonal antibody and a bispecific T-cell engager. For the indication under assessment, glofitamab is given in combination with gemcitabine and oxaliplatin for Cycles 1 to 8 and, subsequently, as monotherapy for Cycles 9 to 12. Each cycle is 21 days. Glofitamab is administered by intravenous infusion. It is dosed according to a step-up schedule in Cycle 1, leading to a recommended dose of 30mg which is administered once on Day 1 of each cycle from Cycle 2 onwards. Pre-treatment with a once-off dose of obinutuzumab is also required. Glofitamab should be continued until disease progression, unacceptable toxicity, or up to a maximum of 12 cycles.

Second-line treatment options for patients with relapsed or refractory DLBCL NOS, and who are ineligible for ASCT, depend on the timing of relapse. Patients who relapse within 12 months of first-line treatment, and who are clinically fit, may receive chimeric antigen receptor T-cell (CAR T-cell) therapy, specifically axicabtagene ciloleucel (axi-cel). Patients who are ineligible for axi-cel, or who relapse more than 12 months after first-line treatment, may receive Pola+BR (polatuzumab vedotin in combination with bendamustine and rituximab), tafa+ len (tafasitamab in combination with lenalidomide), or a different rituximab-containing regimen. In the third-line setting, treatment options include CAR T-cell therapy (either axi-cel or tisagenlecleucel (tisa-cel)), Pola+BR, tafa+len, epcoritamab monotherapy, or rituximab-containing regimens. Treatment selection is informed by patient fitness, prior treatment exposure, and disease characteristics.

The Applicant included the following comparators in the base case cost-effectiveness

analysis: R+GemOx (rituximab in combination with gemcitabine and oxaliplatin), Pola+BR and tafa+len in the second and subsequent-line settings; axi-cel in the second-line setting only.

A comparison of Glofitamab+GemOx versus epcoritamab in the third-line setting was presented by the Applicant. However, due to methodological limitations, the outcomes were considered to be too uncertain to present here. Axi-cel and tisa-cel were not included as comparators in the third line setting. The lack of comparative outcomes to epcoritamab, axi-cel or tisa-cel (all in the third-line setting) is a limitation of the assessment.

1. Comparative effectiveness of Glofitamab+GemOx

The efficacy and safety of Glofitamab+GemOx was informed by outcomes from STARGLO, which is an ongoing phase III, international, open-label, randomised controlled trial. Eligible participants were adults with relapsed or refractory DLBCL NOS who were ineligible for ASCT. Participants were randomised to receive either Glofitamab+GemOx (n=183) or R+GemOx (n=91). The primary endpoint was overall survival (OS). A key secondary endpoint was progression-free survival (PFS). Health-related quality of life (HRQoL) outcomes were also collected.

Baseline demographic and disease-related characteristics were generally balanced across both treatment arms; however, some differences were noted. A higher proportion of Asian participants were enrolled to the R+GemOx arm (56% versus 47%, in the R+GemOx and Glofitamab+GemOx arms, respectively). More participants in the R+GemOx arm had stage IV disease (68.1% compared to 54.6% in the Glofitamab+GemOx arm).

At the most recent data cut (May 2025), Glofitamab+GemOx demonstrated improvements in OS and PFS compared to R+GemOx. Median OS was 25.5 months (95% confidence interval (CI) 17.0 months to not estimable (NE)) versus 12.5 months (95% CI 7.9 to 16.5 months), respectively. Median PFS was 14.4 months (95% CI 8.8 to 27.4 months) versus 3.3 months (95% CI 2.3 to 5.6 months). The associated p-values were consistent with results observed from the primary analysis (March 2023), which indicated statistical significance. HRQoL remained stable, with no statistically significant differences observed across both arms in the trial.

There were several limitations to the clinical evidence from STARGLO, including immature OS data, a lack of direct comparative evidence for Glofitamab+GemOx versus other treatments for DLBCL NOS, and baseline imbalances in participant characteristics between study arms. In addition, the STARGLO protocol classified participants who refused ASCT as ASCT-ineligible. This potentially facilitated inclusion of fitter individuals than those meeting conventional ASCT-ineligibility criteria.

STARGLO provided direct comparative evidence for Glofitamab+GemOx versus R+GemOx. In the absence of direct comparative evidence for Glofitamab+GemOx versus the other comparators, unanchored indirect treatment comparisons (ITCs) were conducted by the Applicant. The efficacy of axi-cel, Pola+BR, and tafa+len were informed by the ALYCANTE, GO29365, and L-MIND trials, respectively. Although baseline characteristics between the trial populations were generally similar, some differences were identified. To control for confounding associated with this heterogeneity, the Applicant performed statistical adjustments to align the trial populations. For the comparison of Glofitamab+GemOx versus Pola+BR, an inverse probability of treatment weighting (IPTW) approach was used. For the comparisons of Glofitamab+GemOx versus tafa+len, and Glofitamab+GemOx versus axi-cel, the matching-adjusted indirect comparison (MIAC) method was used. Application of unanchored MAIC and IPTW methods are associated with a substantially higher risk of bias and corresponding lower certainty of evidence than randomised controlled trials. The validity of these approaches relies on the assumption that all prognostic and effect-modifying variables are included in the model, which is challenging to achieve in practice. Results of the ITC analyses suggested that Glofitamab+GemOx was associated with a numerical improvement in survival benefits (OS and PFS) compared to Pola+BR and tafa+len. Glofitamab+GemOx was also associated with a numerical improvement in PFS, but a numerical detriment in OS, when compared with axi-cel. However, none of these results demonstrated statistical significance.

2. Safety of Glofitamab+GemOx

Clinical safety of Glofitamab+GemOx was informed by data from the STARGLO trial. Treatment-related adverse events (TRAEs) occurred in 95.3% of participants in the Glofitamab+GemOx arm and 92.0% in the R+GemOx arm, with grade ≥3 TRAEs reported in

67.5% and 36.3%, respectively. The most common TRAEs (any grade) were decreased platelet count (38.4% versus 30.7%), nausea (36.0% versus 35.2%), increased aspartate aminotransferase (32.6% versus 18.2%), and anaemia (32.6% versus 15.9%). Serious adverse events occurred in 52.3% of the Glofitamab+GemOx arm and 17.0% in the R+GemOx arm. Cytokine release syndrome (CRS) was the most common serious adverse event in the Glofitamab+GemOx arm (20.3%). Adverse events of special interest were grade ≥ 2 CRS and immune effector cell-associated neurotoxicity syndrome (ICANS). Grade ≥ 2 CRS occurred in 12.8% of participants in the Glofitamab+GemOx arm and in no participants in the R+GemOx arm; grade ≥ 2 ICANS occurred in 34.3% and 15.9% of participants, respectively.

3. Cost effectiveness of Glofitamab+GemOx

Methods

Cost-effectiveness was assessed, from the perspective of the HSE, using a partitioned survival model developed in Microsoft Excel®. The population considered was patients with relapsed or refractory DLBCL NOS who are ineligible for ASCT; baseline characteristics were informed by the STARGLO trial population. The modelled intervention was Glofitamab+GemOx. The modelled comparators were R+GemOx, Pola+BR, and tafa+len; all prescribed in the second- or subsequent-line settings. Axi-cel, prescribed in the second-line setting only, was also included as a comparator.

The cost-effectiveness model (CEM) comprised three mutually exclusive health states: Progression-Free (PF), Post-progression (PPS) and Death. These health states captured PFS and OS, which were endpoints in the STARGLO trial. In each model cycle, patients accrued quality adjusted life years (QALYs) and incurred costs based on the health state occupied, treatment arm, and time on treatment. Model cycle length was one week; a half-cycle correction was applied. A 60-year time horizon was modelled.

In the CEM, OS and PFS were modelled independently. Outcomes from STARGLO were used to inform treatment effectiveness of Glofitamab+GemOx versus R+GemOx; outcomes from the ITCs were used to inform treatment effectiveness for Glofitamab+GemOx versus all other comparators. Mortality risk was adjusted to be no lower than age-related general population mortality. General population mortality was also adjusted by a standardised mortality ratio (SMR) to account for increased mortality risk due to excess comorbidities.

Parametric distributions were fitted to the data to estimate long-term projections of OS and PFS. The Review Group considered the Applicant's approach to extrapolation of OS and PFS to be appropriate in the main. However, for extrapolation of PFS for Pola+BR, the Applicant selected the lognormal distribution. In this case, the Review Group considered the generalised gamma distribution to be more appropriate as it offered the best statistical and visual model fit.

For the intervention and all comparator arms, it was assumed that patients who were progression-free at three years entered long-term remission. A plateau appears to be observed in the PFS outcomes for participants randomised to Glofitamab+GemOx in the STARGLO trial, which the Applicant considered justified this assumption. Clinical opinion obtained by both the Applicant and Review Group also indicated the assumption was plausible. Whilst it was retained for the NCPE adjusted base case on this basis, the Review Group still considered it to be uncertain. It is possible that some patients may experience disease relapse at a later timepoint, despite having remained progression-free for three years or more. Furthermore, OS data from STARGLO remains immature. Long term survival associated with Glofitamab+GemOx remains unknown. The Review Group also identified limitations in the methodology by which this assumption was modelled. From Year Three, it was assumed that absolutely no patients in the PF health state could experience death from any causes. The Review Group considered this implausible. It was also assumed that, from Year Three until the OS and PFS curves crossed, the mortality risk for all patients in the PPS health state was equal to that of the age- and SMR-adjusted general population. After crossing of the OS and PFS curves, the mortality risk of all patients in the PF state was also assumed to be equal to that of the age- and SMR-adjusted general population. The Review Group considered this lacked plausibility as patients with progressed DLBCL NOS disease would have a greater risk of death than that of the adjusted general population. Furthermore, these patients continued to accrue costs and HRQoL associated with the PPS health state. Health-state resource use costs for the PPS state were considerably greater than those for the PF state. The compounded effect was that patients in the PPS health state lived longer whilst accruing greater costs. This likely resulted in an overestimation of costs for the comparator treatments, potentially biasing in favour of Glofitamab+GemOx.

A systematic literature review (SLR) was conducted to identify HRQoL evidence in patients

with relapsed and refractory DLBCL NOS. There was a paucity of evidence available to inform HRQoL generalisable to the modelled population. Utility values used in the CEM were derived from STARGLO. Patient-reported outcomes collected in STARGLO may have been subject to bias due to the open-label design of the trial.

Costs and resources included were drug acquisition costs, drug administration costs, subsequent treatment costs, adverse event costs, and disease management costs. A once-off, end of life cost was also included.

Results

All cost-effectiveness analyses presented here are based on the publicly available price to wholesaler for each drug. However, established commercial arrangements are in place for polatuzumab vedotin, tafasitamab, axi-cel and tisa-cel, which are not reflected in these analyses. Results of the Applicant base case deterministic cost-effectiveness analysis are presented in Table 1.

Table 1: Applicant base case incremental cost-effectiveness results [a,b,c,d]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
R+GemOx	122,409	2.82	-	-	-
Glofitamab+GemOx[e]	169,715	4.62	47,306	1.80	26,331
Pola+BR	161,237	3.85	-	-	-
Glofitamab +GemOx[f]	165,952	4.26	4,715	0.41	11,574
Tafa+len	256,945	4.99	-	-	-
Glofitamab +GemOx[g]	164,141	5.25	-92,804	0.26	Glofitamab+GemOx Dominant
Axi-cel	414,295	5.25	-	-	-
Glofitamab +GemOx[h]	177,935	5.02	-236,360	- 0.22	Glofitamab+GemOx less costly and less effective

Axi-cel: axicabtagene ciloleucel; **Glofitamab+GemOx:** glofitamab in combination with gemcitabine and oxaliplatin; **ICER:** incremental cost effectiveness ratio; **Pola+BR:** polatuzumab vedotin in combination with bendamustine and rituximab; **QALY:** Quality adjusted life year; **R+GemOx:** rituximab in combination with gemcitabine and oxaliplatin; **Tafa+len:** tafasitamab in combination with lenalidomide; **tisa-cel:** tisagenlecleucel.

[a] Corresponding probabilistic ICER using 2,000 simulations:
- Glofitamab+GemOx versus R+GemOx: €25,858/QALY
- Glofitamab+GemOx versus Pola+BR €10,228/QALY
- Glofitamab+GemOx versus tafa+len: Glofitamab+GemOx was dominant
- Glofitamab+GemOx versus axi-cel: Glofitamab+GemOx was dominant. (The incremental QALY difference observed for the comparison of Glofitamab+GemOx versus axi-cel was very small and could vary between QALY gain and QALY decrement in the PSA. This highlights the uncertainty. Results should be interpreted with caution.)

[b] Figures in the table are rounded, and so calculations may not be directly replicable.

[c] Total costs and QALYs presented are discounted (4%).

[d] Established commercial in confidence patient access schemes are in place for polatuzumab vedotin, tafasitamab, axi-cel and tisa-cel which are not reflected in this table.

[e] Glofitamab+GemOx was unweighted.

[f] Glofitamab+GemOx was adjusted to the Pola+BR (GO29365) population applying the IPTW ATE approach.

[g] Glofitamab+GemOx was adjusted to the tafa+len (L-MIND) population applying the MAIC approach.

[h] Glofitamab+GemOx was adjusted to the axi-cel (ALYCANTE) population applying the MAIC approach.

The Review Group made several changes to inform the NCPE-adjusted base case. The generalised gamma distribution was chosen to extrapolate PFS for Pola+BR. The PFS event risks were adjusted such that, after Year Three, they could not be lower than age- and SMR-adjusted general population mortality. This change was made to account for all-cause deaths among patients in the PF state, who were assumed to be in long-term disease remission, after Year Three. No meaningful change could be made for the NCPE adjusted base case to account for overestimation of survival of patients in the PPS state after Year Three. This was a limitation of the assessment. Results of the NCPE adjusted base case are presented in Table 2.

Due to observed data immaturity in the axi-cel treatment arm, the choice of parametric distributions to extrapolate survival parameters for the comparison of Glofitamab+GemOx versus axi-cel could not be assessed. Therefore, other than the adjustment to PFS event risk, no additional change was made to inform the NCPE adjusted base for Glofitamab+GemOx versus axi-cel. Results for the comparison of Glofitamab+GemOx versus axi-cel should be interpreted with caution.

Table 2: NCPE adjusted base case incremental cost-effectiveness results [a,b,c,d]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
R+GemOx	136,364	2.80	-	-	-
Glofitamab+GemOx[e]	188,383	4.60	52,018	1.80	28,951
Pola+BR	167,091	3.84	-	-	-
Glofitamab+GemOx[f]	180,307	4.24	13,216	0.40	33,107
Tafa+len	275,074	4.97	-	-	-
Glofitamab+GemOx[g]	182,972	5.23	-92,101	0.26	Glofitamab+GemOx dominant
Axi-cel	441,481	5.22	-	-	-
Glofitamab+GemOx[h]	201,449	5.00	-239,982	-0.22	Glofitamab+GemOx less costly and less effective

Axi-cel: axicabtagene ciloleucel; **Glofitamab+GemOx:** glofitamab in combination with gemcitabine and oxaliplatin; **ICER:** incremental cost effectiveness ratio; **Pola+BR:** polatuzumab vedotin in combination with bendamustine and rituximab; **QALY:** Quality adjusted life year; **R+GemOx:** rituximab in combination with gemcitabine and oxaliplatin; **Tafa+len:** tafasitamab in combination with lenalidomide; **tisa-cel:** tisagenlecleucel.

[a] Corresponding probabilistic ICER using 2,000 simulations:
- Glofitamab+GemOx versus R+GemOx: €29,070/QALY
- Glofitamab+GemOx versus Pola+BR €31,054/QALY
- Glofitamab+GemOx versus tafa+len: Glofitamab+GemOx was dominant
- Glofitamab+GemOx versus axi-cel: Glofitamab+GemOx was dominant. (The incremental QALY difference observed for the comparison of Glofitamab+GemOx versus axi-cel was very small and could vary between QALY gain and QALY decrement in the PSA. This highlights the uncertainty. Results should be interpreted with caution.)

[b] Figures in the table are rounded, and so calculations may not be directly replicable.

[c] Total costs and QALYs presented are discounted (4%).
[d] Established commercial in confidence patient access schemes are in place for polatuzumab vedotin, tafasitamab, axi-cel and tisa-cel which are not reflected in this table.
[e] Glofitamab+GemOx was unweighted.
[f] Glofitamab+GemOx was adjusted to the Pola+BR (GO29365) population applying the IPTW ATE approach.
[g] Glofitamab+GemOx was adjusted to the tafa+len (L-MIND) population applying the MAIC approach.
[h] Glofitamab+GemOx was adjusted to the axi-cel (ALYCANTE) population applying the MAIC approach.

Sensitivity analysis

Cost effectiveness results were sensitive to discount rates on costs and outcomes, glofitamab treatment costs, the assumption about disease remission after Year Three, and subsequent therapy costs.

A price-ICER analysis, using NCPE adjusted base case assumptions, indicated that reductions of 31.5% and 16.9% on the price to wholesaler of glofitamab would be required for Glofitamab+GemOx to demonstrate cost-effectiveness versus R+GemOx and Pola+BR, respectively, at the €20,000 per QALY cost-effectiveness threshold.

4. Budget impact of Glofitamab+GemOx

The price to wholesaler for glofitamab concentrate for solution for infusion is €818.35 per 2.5mg vial and €3,269.88 per 10mg vial. The estimated cost, per patient, per treatment course of Glofitamab+GemOx, informed by data from STARGLO, is €93,040 (including VAT).

The eligible population was patients with relapsed or refractory DLBCL NOS who are ineligible for ASCT in the second- and third-line treatment settings. The eligible patient numbers were estimated to be 193 in Year One, increasing to 207 in Year Five. However, both the eligible population estimates and the assumed market shares for Glofitamab+GemOx and comparators were subject to considerable uncertainty. Epcoritamab monotherapy, axi-cel and tisa-cel, prescribed in the third-line setting, were all included in the budget impact analysis; these were not included as comparators in the cost-effectiveness analyses. The Applicant estimated a five-year cumulative gross drug budget impact of €37.1 million (including VAT) for Glofitamab+GemOx. The corresponding five-year cumulative net drug budget impact was estimated to result in cost savings of €993,471 (including VAT). The budget impact analyses presented here do not capture the commercial pricing arrangements negotiated for polatuzumab vedotin, epcoritamab, tafasitamab, axi-cel and tisa-cel. When these are considered, the net drug budget impact for Glofitamab+GemOx is cost-incurring.

5. Patient Organisation Submission

No patient organisation submissions were received during the course of the assessment.

6. Conclusion

The NCPE recommends that glofitamab (Columvi®) in combination with gemcitabine and oxaliplatin be considered for reimbursement, for the indication under assessment, if cost-effectiveness can be improved relative to existing treatments*.

This recommendation takes into account the confidential pricing arrangements negotiated for polatuzumab vedotin, epcoritamab, tafasitamab, axi-cel and tisa-cel, which are not reflected in the cost-effectiveness and budget impact estimates shown in this summary report.

*Next steps: The NCPE Assessment Report and recommendation will be considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found here.