NICE National Institute for Health and Care Excellence

NICE guidance

Glofitamab with gemcitabine and oxaliplatin for treating relapsed or refractory diffuse large B-cell lymphoma

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Glofitamab plus gemcitabine and oxaliplatin can be used as an option to treat relapsed or refractory diffuse large B-cell lymphoma not otherwise specified in adults when:

- they have had 1 line of treatment only, and
- they are not eligible for an autologous stem cell transplant.

Glofitamab plus gemcitabine and oxaliplatin can only be used if the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with glofitamab plus gemcitabine and oxaliplatin that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

What this means in practice

Glofitamab plus gemcitabine and oxaliplatin must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. Glofitamab plus gemcitabine and oxaliplatin must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that glofitamab plus gemcitabine and oxaliplatin provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has produced tools and resources to support the implementation of this guidance.

Why the committee made these recommendations

Usual treatment for relapsed or refractory diffuse large B-cell lymphoma not otherwise specified in people who cannot have an autologous stem cell transplant is rituximab plus gemcitabine and oxaliplatin (R-GemOx) or polatuzumab vedotin plus rituximab and

bendamustine (Pola-BR).

For this evaluation, the company asked for glofitamab plus gemcitabine and oxaliplatin to be considered only for adults who have had 1 line of treatment. This is because it was only compared with treatments used after 1 line of treatment only. This does not include everyone who it is licensed for.

Clinical trial evidence shows that glofitamab plus gemcitabine and oxaliplatin increases how long people have before their cancer gets worse and how long people live compared with R-GemOx.

Glofitamab plus gemcitabine and oxaliplatin has not been directly compared in a clinical trial with Pola-BR. Indirect comparisons suggest it is likely to work as well. But this is uncertain because it is not clear if the evidence represents people who would have treatment in the NHS.

Although there are uncertainties in the evidence, the cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, glofitamab plus gemcitabine and oxaliplatin can be used.

2 Information about glofitamab with gemcitabine and oxaliplatin

Marketing authorisation indication

2.1 Glofitamab (Columvi, Roche) in combination with gemcitabine and oxaliplatin is indicated 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)'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for glofitamab.

Price

2.3 The list price for glofitamab is £687 per 2.5-mg vial and £2,748 per 10-mg vial (excluding VAT, BNF online, accessed July 2025).

2.4 The list price for gemcitabine is £14 per 200-mg vial of powder for solution for infusion and £25 per 1,000-mg vial of powder for solution for infusion (excluding VAT, BNF online, accessed July 2025).

2.5 The list price for oxaliplatin is £147.82 per 50 mg (10 ml) vial of concentrate for solution for infusion and £295.63 per 100 mg (20 ml) vial of concentrate for solution for infusion (excluding VAT, BNF online, accessed July 2025).

2.6 The company has a commercial arrangement. This makes glofitamab available to the NHS with a discount. The size of the discount is commercial in confidence.

Carbon Reduction Plan

2.7 For information, the Carbon Reduction Plan for UK carbon emissions for Roche guidance is published on Roche's 'about sustainability' webpage.

3 Committee discussion

The evaluation committee considered evidence submitted by Roche, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of the condition and patient perspective

3.1 Diffuse large B-cell lymphoma (DLBCL) is a type of fast-growing blood cancer that affects white blood cells called B lymphocytes (B cells). There are subtypes of DLBCL. But most people will not have a specific type, so have DLBCL not otherwise specified (DLBCL-NOS). Symptoms such as fever, night sweats, weight loss and local effects of lymph node enlargement can have a substantial impact on quality of life. Patient experts described the psychological impact of a diagnosis. People can have anxiety or insomnia, which can increase if their lymphoma has relapsed or treatment has not worked. Treatment aims to cure DLBCL-NOS but in many people it is refractory to treatment or relapses after a period of remission. Patient experts noted that having to wait for multiple relapses to access the newest treatments made a chance of cure smaller and could result in more side effects. Some people are not eligible for an autologous stem cell transplant (ASCT). These people are generally older and frailer than people who are eligible for an ASCT. So, having another treatment option available after the first relapse or treatment failure would be an advantage.

Comparators

Treatment options

3.2 Initial treatment for DLBCL-NOS is rituximab with cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) or polatuzumab vedotin, rituximab, doxorubicin, cyclophosphamide and prednisolone (Pola-R-CHP; see NICE's

technology appraisal guidance on polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma [TA874]). Treatment options if DLBCL-NOS relapses or is refractory to treatment depend on whether the person is eligible for an ASCT. When DLBCL-NOS is not cured after first-line treatment in people who are not eligible for an ASCT, the possible treatments are rituximab combined with 1 or more chemotherapy or polatuzumab vedotin plus rituximab and bendamustine (Pola-BR; see NICE's technology appraisal guidance on polatuzumab vedotin with rituximab and bendamustine for relapsed or refractory diffuse large B-cell lymphoma [TA649]). At the second committee meeting, the company and clinical experts stated that the current treatment options were unsatisfactory and there is an unmet need at second line for people who are not eligible for an ASCT. The committee acknowledged the input from the company and clinical experts.

Rituximab with gemcitabine plus oxaliplatin

3.3 The company stated rituximab plus gemcitabine and oxaliplatin (R-GemOx) represented the standard treatment in UK clinical practice for DLBCL-NOS in people who are not eligible for an ASCT. The clinical experts agreed that R-GemOx is the most appropriate rituximab chemotherapy option used as a second-line treatment for DLBCL-NOS in people who are not eligible for an ASCT. The clinical experts also agreed that R-GemOx is the most commonly used treatment at this point in the pathway. The committee accepted the positioning of glofitamab plus gemcitabine and oxaliplatin (Glofit-GemOx) as a second-line treatment option for relapsed or refractory DLBCL-NOS in people who are not eligible for an ASCT. It agreed that R-GemOx was a relevant comparator.

Pola-BR

3.4 Pola-BR is a treatment option for relapsed or refractory DLBCL-NOS in people who are not eligible for an ASCT. Based on advice from UK clinical experts, the company stated that Pola-BR is rarely used at second line because:

- Polatuzumab vedotin is recommended as a combination first-line treatment for DLBCL-NOS and commissioning criteria do not allow retreatment with

polatuzumab vedotin.

- Pola-BR should be avoided by people who may have chimeric antigen receptor (CAR) T-cell therapy in the future. The British Society of Haematology's guidance states that previous bendamustine treatment is associated with CAR T-cell therapy manufacturing failure and inferior outcomes. There is also concern that bendamustine can have a negative impact on the efficacy of subsequent bispecific antibodies (glofitamab and epcoritamab).

  The company stated that Pola-BR use at this point in the pathway would continue to decline. So, it did not consider it a relevant comparator. The NHS England (NHSE) clinical lead for the Cancer Drugs Fund advised that the number of new registrations of Pola-BR reduced from 34 per month in 2024 to 28 per month in the first 4 months of 2025, but the proportion of these registrations that were for second-line use remained high (about 59%). So, NHSE's opinion is that Pola-BR should be a comparator. The clinical experts noted that the use of Pola-BR has declined and will continue to do so. But they explained it would still be a treatment option for people who did not have Pola-R-CHP at first line because they were not eligible or were diagnosed before it was available. The committee concluded that although Pola-BR use is declining, there are still some people who would have it as second-line treatment. So, it is a relevant comparator. At the second committee meeting, the clinical experts said that use of Pola-BR at second line in people who were not eligible for an ASCT differed between individual clinics. But they believed it was becoming unfavourable because using bendamustine before CAR T-cell therapy at third line can affect how well CAR T-cell therapy works. They said that Pola-BR would only be offered to people who were expected to be ineligible for CAR T-cell therapy and other bispecific antibodies at third line, which is a small minority. The NHSE clinical lead for the Cancer Drugs Fund explained that use of Pola-BR across all treatment lines had decreased slightly but the number of people having Pola-BR at second line was stable. They maintained that Pola-BR is a relevant comparator for second-line treatment in people who are not eligible for an ASCT. The committee acknowledged that R-GemOx is used most often (see section 3.3) and that Pola-BR use would likely decrease over time. But it concluded that Pola-BR remained a relevant comparator for this appraisal.

Clinical effectiveness

Data sources

3.5 Clinical evidence came from an ongoing international, phase 3, open-label randomised study (STARGLO). This evaluated the efficacy and safety of Glofit-GemOx (n=183) compared with R-GemOx (n=91) in adults with relapsed or refractory DLBCL-NOS who had had at least 1 line of systemic therapy and were not eligible for an ASCT. People in the Glofit-GemOx arm had pre-treatment with a single dose of obinutuzumab before having stepped-up dosing of glofitamab. People who had had only 1 line of treatment were a post-hoc second-line subgroup (n=172) of the whole trial population (n=274). Evidence from this subgroup directly informed the company's economic model (see section 3.8). The second-line subgroup had a median follow-up of 20.2 months for overall survival. There was a 33% reduction in risk of death in people having Glofit-GemOx compared with people having R-GemOx (hazard ratio [HR] 0.67, 95% confidence interval [CI] 0.41 to 1.07; p=0.092). The median follow-up for progression-free survival in the second-line subgroup was 15.5 months. The risk of a progression-free survival event was 59% lower for people having Glofit-GemOx compared with R-GemOx (HR 0.41, 95% CI 0.25 to 0.67; p=0.0002). The committee noted that the confidence interval for the overall survival hazard ratio crossed 1, so was not statistically significant. The company explained that more recent data from STARGLO has become available that reduces the uncertainty in the estimates. The committee noted that the results of these further follow-up analyses in the second-line subgroup may help resolve some of the uncertainties. In its response to draft guidance consultation, the company provided the results from the latest data cut of STARGLO. In the latest data cut for the second-line subgroup, the median follow-up for overall survival was 34.9 months and showed a 42% reduction in risk of death for people having Glofit-GemOx compared with people having R-GemOx (HR 0.58, 95% CI 0.38 to 0.89; p=0.012). The median follow-up for progression-free survival was 26.3 months and showed a 59% reduction in progression-free survival events for people having Glofit-GemOx compared with people having R-GemOx (HR 0.41, 95% CI 0.25 to 0.65; p=0.0001). The committee noted that the results for overall survival now showed statistical significance, reducing the uncertainty in the results.

Generalisability of the STARGLO population to the NHS

Variability in regional subgroups

3.6 The committee noted at the first committee meeting that the data for the second-line subgroup in STARGLO initially showed non-significant results for overall survival but statistically significant results for progression-free survival. It also noted there had been more censoring for people in the Glofit-GemOx arm than in the R-GemOx arm. The EAG noted the analyses without censoring for people who had any new anti-lymphoma treatment, which were not permitted during the trial (including radiotherapy and systemic treatments). These analyses gave similar results to those with censoring for progression-free survival, which explained the consistent statistically significant outcomes for progression-free survival across the analyses. But the second-line subgroup of STARGLO was a post-hoc subgroup of the full trial population and had not been pre-specified in the trial protocol. So, the EAG suggested that statistical analyses of the second-line subgroup should be considered exploratory. The EAG noted that subgroup analyses of STARGLO showed differences in outcomes between geographical regions. Ethnicity was a pre-specified subgroup in STARGLO but the results were not reported for the second-line subgroup. The company had identified differences in the hazard ratio for overall survival in the subgroups from the full trial population by ethnicity (Asian HR 0.40, 95% CI 0.25 to 0.65; White HR 1.24, 95% CI 0.66 to 2.3) and by geographical region (Europe HR 1.09, 95% CI 0.54 to 2.18; North America HR 2.62, 95% CI 0.56 to 12.34; 'rest of world' HR 0.41, 95% CI 0.27 to 0.64). It stated this was because of the small patient numbers and the subgroups being underpowered resulting in wide confidence intervals. It also stated that geographical region was not a stratification factor so there are imbalances in populations. The clinical experts agreed that these results may have been influenced by small patient numbers and the differences may be because of different patient characteristics, which are imbalanced within subgroups. The committee noted that data presented to the European Medicines Agency (EMA) showed a higher rate of people deciding not to have an ASCT (rather than being ineligible for it) in Asia than in Europe. This might have contributed to regional differences between treatment arms. The committee noted this might have meant people in the Asian region may have been fitter than

those who would not be eligible for an ASCT or eligible for second-line treatment with Glofit-GemOx in UK clinical practice. The clinical experts explained that the open-label design and access to subsequent treatments might also contribute to uncertain outcomes. The committee noted that evidence presented to the US Food and Drug Administration showed variation in the baseline data by region for the whole population of STARGLO because in Asia:

- people were younger (median age 62 years) than in the non-Asian region (median age 71)
- 65% of people had refused an ASCT compared with 7% of people in the non-Asian region
- 2% of people had previously had CAR T-cell therapy compared with 13% of people in the non-Asian region
- 81% of people had relapse within 12 months of first-line treatment compared with 64% of people in the non-Asian region
- people had shorter duration of treatment with R-GemOx (1.1 months) compared with the non-Asian region (3.1 months).

At the first meeting, the committee agreed that the substantial variability contributed to uncertainty in interpreting the STARGLO data. It could not conclude if the trial was generalisable to the UK clinical population. So, it asked for further statistical analyses to help explore this variability and to inform conclusions about the applicability of the STARGLO second-line data to UK clinical practice.

Additional analyses to explore variability in regional subgroups

3.7 In response to draft guidance consultation, the company provided a submission it had given to the EMA including several analyses done after STARGLO to support the generalisability of the data in Europe. The submission included:

- a summary of baseline characteristics in the intention-to-treat population compared with the European population. The European population had a higher percentage of people with Ann Arbor stage 3 or 4 lymphoma and

higher use of previous CAR T-cell therapy. It had lower percentages of people with lymphoma that was refractory to last treatment, refractory within 12 months of last treatment or double refractory. The company said these differences may have confounded the results

- an event-free survival analysis across the different regional subgroups, which included starting a new treatment as an event. The company said that the difference in third-line and beyond treatment was a main confounding factor and this analysis adjusted for these differences. The event-free survival results were more favourable than the progression-free survival results for Glofit-GemOx, which the company said suggested that the progression-free survival results were biased in favour of R-GemOx because of informative censoring. The company also presented inverse probability of censoring weighting analysis in the submission to adjust for differences in subsequent treatments for overall survival and progression-free survival. This showed numerically lower HRs compared with the unadjusted results for the European subgroup (the company considers the exact results of the analysis to be confidential so they cannot be reported here)
- 3 different sensitivity analyses to adjust for COVID-19 related events that censored COVID-19 events differently. In the European population, the analyses showed more favourable results for progression-free survival and overall survival than the unadjusted analysis (the company considers the exact results of the analysis to be confidential so they cannot be reported here)
- a comparison of the results of the R-GemOx arm in the intention-to-treat population and the European population with the results from the R-GemOx arm of the NIVEAU trial, a phase 3 trial based in Europe that compared R-GemOx plus nivolumab with R-GemOx alone. The analysis showed similar results between the NIVEAU R-GemOx arm and the intention-to-treat population R-GemOx arm of STARGLO.

  The company also noted that the Medicines and Healthcare products Regulatory Agency, EMA and European Society for Medical Oncology were satisfied the results were generalisable to their regions. It also noted that the British Society for Haematology had included Glofit-GemOx as the preferred second-line treatment for people who are ineligible for an ASCT in their

recently published guidelines.

The EAG raised concerns about the company's analysis, including:

- it was unclear how the company concluded that differences in subsequent treatments and COVID-19 events were the main confounding factors
- much of the company's analysis was based on the European subgroup, and the company did not discuss whether European practice is similar to NHS practice
- it was unclear whether other studies, not only NIVEAU, could have been used as a comparison for the R-GemOx arm of STARGLO
- it was unclear whether the inverse probability of censoring weighting. approach to the analysis was suitable, because the assumption of no unmeasured confounders needed for the analysis was not demonstrated and the company did not explore other methods of adjustment for subsequent treatment differences
- the data for the analysis came from the whole population at the second data cut instead of the second-line population at the third data cut, which was the main population for this evaluation.

The clinical experts stated there was a difference in practice in the Asian region, but European practice was largely aligned with NHS practice. They noted that the duration of treatment for R-GemOx in Asia was lower than was usual practice and they would expect a duration of treatment in NHS practice more similar to the non-Asian region. The clinical experts agreed that the R-GemOx arm results from the intention-to-treat population were closely aligned to other studies. The committee considered that the generalisability of the STARGLO data to NHS practice was still uncertain. It noted that if the company had presented comparisons with other studies including R-GemOx, it would reduce the uncertainty and would have supported the committee's decision making. But it acknowledged that the analysis the company provided, alongside the clinical experts' advice that European practice was similar to NHS practice, mitigated some of this uncertainty. So, the committee concluded that the data from STARGLO was suitable for decision making.

Indirect comparison for Pola-BR

3.8 The company did an inverse probability of treatment weighting analyses. It compared people having second-line treatment with Glofit-GemOx from STARGLO with people having second-line treatment with Pola-BR in GO29365, a phase 1b and 2 study that was the main trial informing TA649. Subsets of the trial populations were used to remove differences in enrolment criteria and to limit the analyses to people who had previously had 1 line of treatment. But even after subsetting the populations, there were still imbalances between the covariates of interest and the effective sample size was reduced. The company did 4 analyses; unadjusted, inverse probability of treatment weighting adjusted without multiple imputation (the company's main analysis), inverse probability of treatment weighting adjusted with multiple imputation, and fully matched samples. But its main analysis did not adjust for 2 missing covariates (cell type or origin and bone marrow involvement) in the GO23965 study. Missing values of other covariates were set to be equal to the mean or mode of each covariate. The EAG was satisfied that the lack of adjustment for the missing covariates would not create any significant bias. But it was uncertain about the impact that other missing data might have on the results. So, it decided the most robust analysis was the analysis with multiple imputation for any missing values. It noted that the hazard ratios and 95% confidence intervals for overall survival and progression-free survival were similar across all analyses. But the proportional hazards assumption (that hazard ratios remain constant over time) did not hold, so uncertainty from the indirect comparison was not captured in the model. The company considers all results from the indirect comparison confidential so they cannot be reported here. The committee noted that the evidence used to inform the company's scenario analysis comparing the cost effectiveness of Glofit-GemOx with Pola-BR came from the second-line subgroup of STARGLO. It noted the uncertainty about generalising the STARGLO data to UK clinical practice (see section 3.6). So, at the first meeting, it concluded that it would like to see further evidence on the effectiveness and generalisability of the STARGLO data to inform its decision about the appropriateness of the company's indirect comparison. Also, the GO23965 study had substantially longer follow-up than STARGLO. So, the committee concluded that analyses updated with the latest data cut from STARGLO would help to reduce the uncertainty. In response to draft guidance consultation, the company updated its indirect comparison to include the latest data cut from STARGLO. It said that the results of the main analysis had improved

with the inclusion of the latest data cut. But the company also noted that several uncertainties remained in the evidence and the results should be used with caution. The company also provided more information about the analysis with multiple imputation. It used the multivariate imputation by chained equations technique to adjust for missing data in the cell-of-origin and bone-marrow-involvement covariates. The company noted that the multiple imputation analysis was only intended as a sensitivity analysis and it increased uncertainty in the results. It maintained that its main analysis was the most robust. The EAG agreed that the results of the indirect comparison should be used with caution. It noted that the company's multiple imputation analysis was poorly explained and implemented. The EAG would have preferred an analysis with multiple imputation, but agreed that the company's main analysis was more suitable than its multiple imputation approach. The committee decided that the inclusion of the latest data cut from STARGLO reduced the uncertainty, but agreed the results should be interpreted cautiously. It remained concerned about the generalisability of the STARGLO data to NHS practice (see section 3.6 and section 3.7). But it noted that much of the uncertainty was in the R-GemOx arm of STARGLO, which would not apply to the indirect comparison. So, the committee concluded that the indirect comparison was suitable for decision making.

Economic model

Company's model

3.9 The company used a partitioned survival model to estimate the cost effectiveness of Glofit-GemOx. The model included 3 health states: progression-free survival, post-progression survival, and death. The proportion in each health state at different time points was calculated using progression-free survival and overall survival curves from STARGLO. The committee concluded that the model structure was acceptable for decision making.

Assumptions

Overestimation of survival estimates

3.10 The company extrapolated time-to-event outcomes using parametric curves over the time horizon of the cost-effectiveness analysis. It chose to use the log-normal distribution for both Glofit-GemOx and R-GemOx for overall survival in its base case. It assumed that people who are alive and progression-free at 3 years enter long-term remission. At this point, people do not continue to progress, and revert to near general-population utility values and do not accrue further costs. The company also assumed that people who were alive at 3 years had a similar mortality to the general population (with a 9% excess applied). It stated this was in line with what had been accepted in NICE's technology appraisal of glofitamab for treating relapsed or refractory DLBCL after 2 or more systemic treatments (TA927). The company's clinical expert had agreed that at 3 years it is clinically plausible that people with DLBCL-NOS who are not eligible for an ASCT would enter long-term remission if they were progression-free after second-line treatment. But the committee noted that the current evaluation is in an earlier treatment line than that in TA927, which assumed that mortality risk reverts to near the general population after 3 years. This was based on almost everyone in the cohort still alive being progression-free. But the EAG noted that at 3 years in this model there was still a substantial proportion of people alive with progressed disease (about 14% in the Glofit-GemOx arm and 18% in the R-GemOx arm). So, the EAG preferred to set mortality near to the general population from 6 years, because this was the point in the model when almost everyone in the cohort still alive was progression-free. The EAG also stated that the company's assumptions resulted in optimistic overall survival estimates compared with the literature. Overall survival in the company's model was 39% at 2 years and 26% at 5 years for people having R-GemOx. The EAG did a literature search of long-term survival in people with refractory or relapsed DLBCL-NOS having R-GemOx. It identified 2 studies: Cazelles et al. (2021) reported a 2-year overall survival rate of 32% and Mounier et al. (2013) reported a 5-year overall survival rate of 14%. Setting the time point at which mortality reverts to near general-population mortality to 6 years gave a 5-year overall survival estimate for R-GemOx of 17%, which was more aligned to the estimates reported in the literature. The committee noted that it was counterintuitive to consider someone 'cured' at 3 years if they have progressed disease. It concluded that it was most plausible to set the time point

at which people are considered cured and mortality reverts to near general-population mortality to when most people still alive are progression-free, and very few people have progressed disease. So, it agreed that the cure point should be set at 6 years and that doing so gave more plausible survival extrapolations. In its response to draft guidance consultation, the company updated the cure point to be 6 years. The committee was satisfied that the overall survival extrapolations were suitable.

Costs

Proportion having palliative care

3.11 In the company's model, the proportion of people having different subsequent treatments after progression was informed by data from STARGLO and UK clinical expert opinion. The company explained that this included a proportion of people who would go on to either a clinical trial or have palliative care. Based on clinical opinion, the company estimated that the proportion of people having palliative care or taking part in a clinical trial would be 15% after Glofit-GemOx and less than 5% after R-GemOx. This was because the company's clinical experts advised that most people would go on to have third-line treatments. But the clinical advice to the EAG was that about 20% to 50% of people would not have subsequent treatment and would have palliative care instead. So, the EAG had assumed that costs of palliative care should be applied for 30% of people. The company noted that the proportion of people having palliative care had already been factored into its model calculations within the subsequent treatment costs. So, the company stated that applying the EAG's additional proportion to the subsequent treatment costs was not appropriate. The clinical experts explained that the proportion of people going on to have palliative care was about 10% and closer to the company's estimate. The committee agreed that fewer people would now have palliative care since more subsequent treatments have become available. So, it accepted the costs for subsequent palliative care aligned with that in the company's base case.

End-of-life treatment costs

3.12 The company assumed that end-of-life treatment costs are included in the weekly resource-use costs used in the model. It had taken these from TA649. The EAG noted that many inpatient bed days are used in the last year of life. The cost of inpatient bed days was not accounted for in the weekly resource-use costs. So, the EAG preferred to model the end-of-life costs separately using the one-off end-of-life care costs specifically for cancer patients (based on the Nuffield Trust's report on exploring the cost of care at the end of life and adjusting for inflation). The committee accepted the approach using a one-off cost. In its response to draft guidance consultation, the company included a one-off end-of-life care cost. The committee was satisfied that the end-of-life treatment costs were suitable.

Incremental analysis

3.13 In response to draft guidance consultation, the company provided a fully incremental analysis including Glofit-GemOx, R-GemOx and Pola-BR. But it noted that Pola-BR dominated R-GemOx, so the analysis became a pairwise comparison between Glofit-GemOx and Pola-BR. It said that the pairwise comparison between Glofit-GemOx and R-GemOx should still be considered because R-GemOx was the comparator with the highest amount of use. The EAG agreed that, in this case, considering both pairwise comparisons was appropriate. The committee considered the clinical expert advice about the use of R-GemOx and Pola-BR (see section 3.3 and section 3.4). It concluded that considering the 2 pairwise comparisons alongside the incremental analysis was appropriate in this case.

Cost-effectiveness estimates

Acceptable ICER

3.14 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-

adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the level of uncertainty, specifically the issues of generalisability of STARGLO to NHS practice and the impact on the clinical- and cost-effectiveness results, including:

- uncertainty in interpreting the trial results for the second-line subgroup for the comparison with R-GemOx (see section 3.6)
- uncertainty about the indirect treatment comparison with Pola-BR (see section 3.8)
- variability in trial outcomes by region contributing to uncertainty in interpreting the subgroup analyses (see section 3.6 and section 3.7).

At the second committee meeting, the committee agreed that the inclusion of the latest data cut from STARGLO in the analysis provided by the company and the analysis of the generalisability of the STARGLO data helped to reduce the uncertainty in the comparison with R-GemOx (see section 3.7) and the indirect comparison with Pola-BR (see section 3.8). But it decided that a substantial amount of uncertainty remained. The committee concluded that, because of the uncertainties, an acceptable ICER would be towards the lower end of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

Committee's preferred assumptions

3.15 The committee's preferred assumptions for the cost-effectiveness analysis were:

- mortality should revert to near the general population (standardised mortality ratio of 1.09) after 6 years (see section 3.9)
- 15% of people in the Glofit-GemOx arm should go on to have subsequent palliative care (see section 3.10)

- one-off end-of-life healthcare costs should be applied, rather than being included in weekly healthcare resource-use costs (see section 3.11).

The committee considered both the fully incremental analysis and the 2 pairwise analyses in its decision making (see section 3.13). Because of the substantial uncertainty in both comparisons, the committee decided that the probabilistic analysis, rather than the deterministic analysis, was most suitable for decision making. For the comparison with R-GemOx, the company's and EAG's base-case ICERs were below the lower end of the range normally considered an acceptable use of NHS resources. For the comparison with Pola-BR, the results were above the lower end of the range normally considered a cost-effective use of NHS resources. But the results were below what the committee concluded would be an acceptable ICER in this evaluation. The exact ICERs cannot be reported here because they include confidential discounts for treatments included in the analysis.

Other factors

Equality

3.16 The committee did not identify any equality issues.

Conclusion

Recommendation

3.17 The cost-effectiveness estimates for both the comparison with R-GemOx and the comparison with Pola-BR were within what the committee considered a cost-effective use of NHS resources (see section 3.15). So, Glofit-GemOx can be used as an option for treating DLBCL-NOS in adults who have had 1 line of treatment only and who are not eligible for an ASCT.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient who is not eligible for autologous stem cell transplant has diffuse large B-cell lymphoma not otherwise specified and the healthcare professional responsible for their care thinks that glofitamab plus gemcitabine and oxaliplatin is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

Members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Richard Nicholas
Chair, technology appraisal committee C

Steve O'Brien
Former chair, technology appraisal committee C

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

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Technical leads

Alexandra Filby

Technical adviser

Louise Jafferally, Leena Issa
Project managers

Ross Dent, Lorna Dunning
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