Single Technology Appraisal

Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic treatments [ID3943]

Committee Papers

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic treatments [ID3943]

Contents:

The following documents are made available to stakeholders:

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Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic treatments [ID3943]

Draft guidance comments form

Consultation on the draft guidance document – deadline for comments 5pm on Tuesday 24 October 2023. Please submit via NICE Docs.

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	Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced.
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Swedish Orphan Biovitrum Ltd (Sobi)
Disclosure Please disclose any funding received from the company bringing the treatment to NICE for evaluation or from any of the comparator treatment companies in the last 12 months. [Relevant companies are listed in the appraisal stakeholder list.] Please state: • the name of the company • the amount • the purpose of funding including whether it related to a product mentioned in the stakeholder list • whether it is ongoing or has ceased.	Sobi is the manufacturer for loncastuximab tesirine, the intervention under appraisal.
Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	None
Name of commentator person completing form:	[redacted]

Comment number	Comments
1	**Benefits not captured in the quality-adjusted life year (QALY) evaluation** The draft guidance states that the committee did not identify additional benefits of loncastuximab tesirine not captured in the economic modelling. The company believes that there are additional benefits not captured in the economic analysis, which may not have been sufficiently considered by the committee in the context of the ICER threshold to be applied. Patients with relapsed and refractory (R/R) diffuse large B-cell lymphoma (DLBCL) have gone through multiple lines of therapy, face a poor prognosis, and urgently need additional treatment options that extend survival with tolerable side-effect profiles. Loncastuximab tesirine has the potential to fulfill this unmet need having been shown in the LOTIS-2 trial to be both well-tolerated and to provide durable responses. Loncastuximab tesirine is available off-the-shelf and ready for infusion unlike some alternative treatments available. This is a significant benefit not captured in the economic

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	analysis since many R/R DLBCL patients have fast progressing disease and require a treatment without delay. Loncastuximab tesirine is also a chemotherapy-free and less intensive treatment that clinicians noted to have a particularly favourable treatment profile for frailer patients compared with other treatments with similar efficacy, such as polatuzumab plus bendamustine plus rituximab (Pola+BR) (1). These patients may not tolerate any other treatment and, without access to loncastuximab tesirine, could require end of life care. There is also a significant caregiver burden associated with alternative treatments due to frequent hospital visits, especially those requiring overnight stays, creating both emotional and financial burden to both patients and their families (2, 3). Additionally, unlike some recently NICE approved treatments such as bispecific and CAR-T therapies that require access to inpatient and specialist care to manage potential side-effects (4) (e.g. a neurosciences intensive care unit for glofitamab treatment due to the risk of cytokine release syndrome and neurological adverse events), loncastuximab tesirine has a strong safety profile and is available in an outpatient setting (e.g. a general hospital without access to specialist care). Therefore, in terms of equity of access, it would be accessible to a larger range of clinical centres, helping to reduce regional, rural–urban, and sociodemographic inequity issues resulting from uneven geographical availability of specialist sites. Patients being able to receive treatment closer to home helps reduce the financial and lifestyle burden of treatment. This is significant as many patients often have to travel long distances or stay in specialised facilities when receiving certain treatments, incurring additional expenses and disruptions to their daily lives. When patients can receive treatment in a location that is more convenient and closer to their home, they may be more willing to accept a course of treatment. The accessibility and reduced disruption to their lives may increase overall satisfaction and may improve adherence to the treatment (5). Loncastuximab tesirine is simple to administer, with only a single 30-minute infusion required per cycle. This lessens the burden of administration on both healthcare practitioners and patients compared with other treatment options, with more frequent dosing or more and longer infusions required. This allows both the NHS to free up chair time and space in cancer units for treating more patients as well as minimising the financial burden of treatment for patients.
2	**Subsequent autologous stem cell transplantation** The draft guidance states that the committee “concluded the rate of autologous stem cell transplantation (SCT) after chemotherapy was uncertain and that it could be as low as 3%, but that changing it did not have a large impact on the cost-effectiveness results”. The Company strongly disagrees with the assertion that it has a limited impact and would like the committee to reconsider this point. The ICER with the EAG base-case assumptions (severity-modified and updated PAS) is £26,807, compared to an ICER of £22,290 using the company’s approach to this issue. The Company acknowledges the possibility that the rates of subsequent ASCT reported in the CORAL extension study may be higher than what is typically expected in clinical practice, and even as low as 3%, as suggested by the committee's conclusion. However, the study reports a rate of 22%, and the company's approach was designed to accurately and simultaneously represent both the costs and outcomes for patients within the CORAL cohort. The company emphasizes that since economic evaluation hinges on the estimation of costs and benefits (6, 7), it is imperative that assumptions regarding both costs and benefits are in alignment to ensure a comprehensive and credible analysis. Crude adjustments to the cost allocation figure for the chemotherapy arm, following the

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	EAG approach, without due consideration for the potential impact on outcomes, run contrary to this fundamental principle. Moreover, it's impossible to assert with any degree of certainty that the ICER was not sensitive to the changes made without also taking into account the potential QALY losses. The Company upholds the concerns it raised during technical engagement on this point. Our primary concern with the EAG approach is that it reduces the costs for chemotherapy to reflect lower rates of ASCT, without also propagating the impact of this on outcomes. Importantly, the 30% patients in the CORAL extension study who went on to subsequently receive an SCT (22% ASCT, 8% AlloSCT) had significantly better survival outcomes compared to patients that did not (see Figure 1). The EAG approach lowers the amount of subsequent ASCT from 22% to 3%, which lowers the overall cost in the chemotherapy arm of the model, however this arm still retains the identical efficacy as before. This is a flawed and biased approach for economic analysis. To demonstrate our point, we have analysed the different efficacy dependent on subsequent SCT status in the CORAL extension studies, both of which have reported outcomes separately for those that did and did not go on to receive an SCT. These curves have been digitised to generate pseudo-individual patient data (IPD) by eventual SCT status and are presented in Figure 1 SCT status is a driver of overall survival (OS), with the KM curves showing that patients who went on to receive SCT have better OS than those who did not go on to receive SCT, with a clear distinction in the survival curves between the two populations. The difference may be attributed to the additional efficacy of SCT, and the better baseline fitness of patients who eventually go on to receive SCT.

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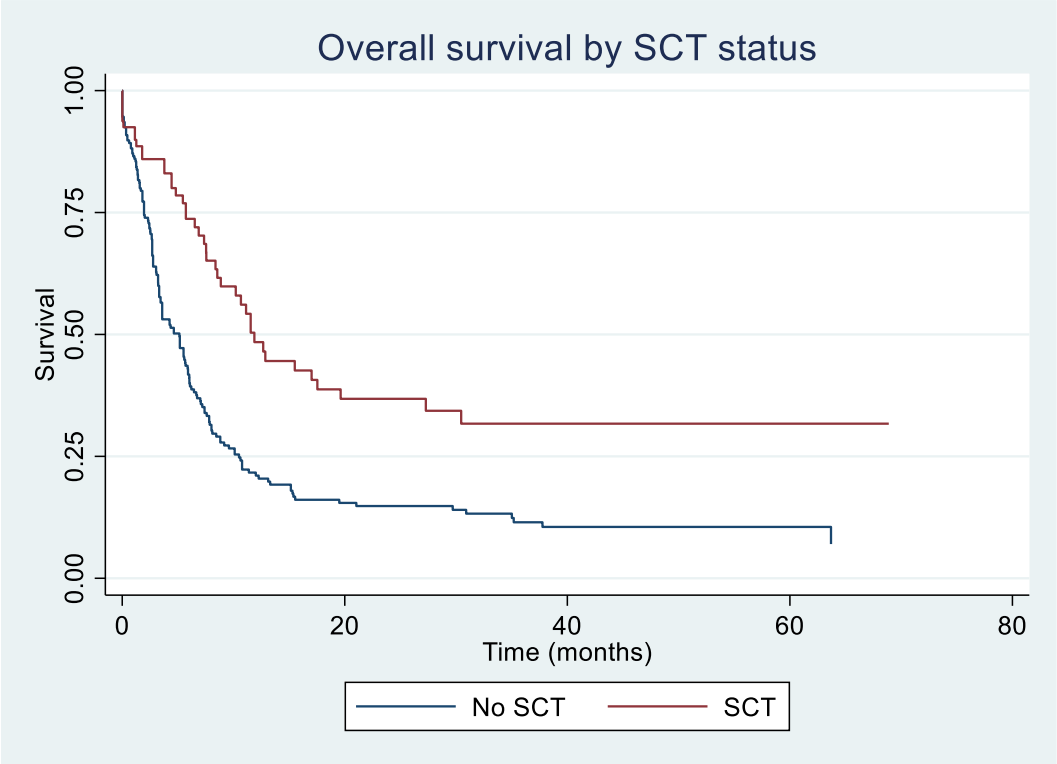
Figure 1: Overall survival curves for CORAL extension study split by eventual SCT status



Abbreviations: SCT, stem cell transplantation.

In order to assess the impact of alternative rates of SCT, an additional scenario analysis is presented for consideration by the committee. In the scenario, OS hazard ratios (HRs) have been generated for patients with and without an eventual SCT separately. The same counterfactual survival times for LOTIS-2 patients have been used, and as baseline characteristics are not reported by eventual SCT status, the same weights have been applied. The same proportion of patients have then been assumed to receive an SCT as was observed in LOTIS-2 (3% AutoSCT, 8% allogenic stem cell transplantation [AlloSCT]) and a weighted HR generated. The HR for patients with and without SCT and the weighted HRs are presented in Table 11.

Table 11: HRs for chemotherapy by eventual SCT status

	HR	SE	CI
No SCT	1.767	0.277	1.300–2.403
SCT	0.801	0.166	0.533–1.204
Weighted 11% SCT	1.659	–	–

Abbreviations: CI, confidence interval; HR, hazard ratio; SCT, stem cell transplantation; SE, standard error.

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	The scenario demonstrates that chemotherapy-treated patients who have received subsequent SCT accrue substantially greater health benefits than those who have not received it (a 0.801 vs 1.767 HR). Given the above points, the Company maintains that if 3% subsequent ASCT is applied in the economic analysis, the HR for chemotherapy should be adjusted to 1.659 to reflect the impact of deviating from the proportion seen in the CORAL extension studies. This figure is a weighted average of the HRs for patients that did and did not receive an SCT, assuming 11% of patients would go on to receive an SCT in clinical practice (3% ASCT, 8% AlloSCT). Alternatively, you could remove all patients entirely from the analysis that had subsequent SCT, producing a HR for chemotherapy of 1.767. Updated base-case results including an adjusted hazard ratio of 1.66 for chemotherapy to reflect 3% subsequent autologous stem cell transplant are provided in **Appendix A**.
3	**Cure/long-term remission assumptions** The Company believes that the choice of using a log-normal distribution for extrapolating overall survival (OS) in this context is overly pessimistic and inconsistent with the recent assumptions made by the EAG and the committee for a similar 3L R/R DLBCL treatment, namely the glofitamab appraisal (TA674) (8). As in the glofitamab appraisal (8), the Company employed standard parametric survival analysis, which involved fitting different parametric distribution models to the observed data. The selection of the most appropriate model was determined through a rigorous process that considered goodness-of-fit statistics, visual comparisons with Kaplan-Meier curves, and validation by clinical experts who assessed long-term extrapolations and the underlying hazard functions. This approach aligned with the guidance provided in the NICE Decision Support Unit (DSU) technical support document (9). Importantly, in this appraisal, the base-case model did not assume any cure for either treatment arm, as there was uncertainty regarding the proportion of patients achieving long-term remission. However, clinical experts did note that patients who remained progression-free after 2 years often ceased to require further treatment, and evidence indicated a plateau in survival for those treated with loncastuximab tesirine without the need for additional therapies (10). The Company's selection of the generalised gamma distribution was made to best reflect the clinicians' beliefs. Scenarios that considered the possibility of cure were explored in scenario analyses, assuming that patients remaining progression-free at 2, 5, and 10 years could be considered cured. These patients would return to general population utility values but might experience slightly elevated mortality. Following the committee's preference in TA649 (11), a standardized mortality ratio (SMR) of 1.41 was applied to the general population mortality for cured patients. The Company argues that the choice of a log-normal distribution for OS extrapolation is overly pessimistic. They propose that the generalised gamma distribution would better reflect the available data and clinical opinions regarding long-term remission and associated uncertainties in this patient population. This recommendation is further supported by the recent appraisal of glofitamab (TA674), in which clinical experts suggested that individuals could be considered cured if their cancer remained in complete remission at 2 years. While longer-term follow-up was deemed necessary to ascertain the proportion of glofitamab-treated patients for whom this applied, the committee concluded that assuming a cure point of 3 years was reasonable. Thus, the Company argues that the use of a log-normal distribution appears to be at odds with the committee's preferred assumptions in the glofitamab appraisal (TA674) (8).

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	Updated base-case results including the log-normal distribution to extrapolate OS for loncastuximab tesirine are provided in **Appendix A**. Scenario analyses using the generalised gamma distribution to extrapolate OS and applying the assumption of a cure point at 3 years aligned with the assumption in the glofitamab appraisal are also presented in **Appendix A.**

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in turquoise and information that is 'academic in confidence' in yellow. If confidential information is submitted, please submit a second version of your comments form with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the NICE Health Technology Evaluation Manual (section 5.4) for more information.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations.
- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
- If you have received agreement from NICE to submit additional evidence with your comments on the draft guidance document, please submit these separately.

Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory committees.

References

1. Sobi. Data on File: Clinical Interviews, Summary Report. 2023.

2. Lenz G, Rutherford SC, Davies A, Zinzani PL, Salles G, Hasskarl J, et al. The Burden of Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): A Systematic Literature Review (SLR). Blood. 2018;132:2241.

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3. Lin V, Oak B, Snider J, Epstein J. Health-related quality of life burden in patients with relapsed/refractory diffuse large B-cell lymphoma and non-Hodgkin's lymphoma. Presented at: American Society of Clinical Oncology Annual Meeting 2020 [virtual meeting]. Abstract e20070. 2020.

4. Xie J, Wu A, Liao L, Nastoupil LJ, Du EX, Noman A, et al. Characteristics and treatment patterns of relapsed/refractory diffuse large B-cell lymphoma in patients receiving >/=3 therapy lines in post-CAR-T era. Curr Med Res Opin. 2021;37(10):1789-98.

5. Heckman BW, Mathew AR, Carpenter MJ. Treatment Burden and Treatment Fatigue as Barriers to Health. Curr Opin Psychol. 2015;5:31-6.

6. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes: Oxford university press; 2015.

7. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual 2022 [Available from: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation.

8. National Institute for Health and Care Excellence (NICE). Glofitamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic treatments. Final draft guidance. Available at: https://www.nice.org.uk/guidance/ta927/documents/674 (last accessed 17 October 2023).

9. Latimer NR. NICE DSU Technical Support Document 14: Undertaking survival analysis for economic evaluations alongside clinical trials - extrapolation with patient-level data. Available from http://www.nicedsu.org.uk Last accessed 9th November 2022. 2011.

10. Caimi PF, Ai W, Alderuccio JP, Ardeshna KM, Hamadani M, Hess B, et al. Data on file. Long-term responses with loncastuximab tesirine: Updated results from LOTIS-2, the pivotal Phase 2 study in patients with relapsed/refractory diffuse large B-cell lymphoma (EHA 2023). 2023.

11. National Institute for Health and Care Excellence. Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma: TA649. Available at: https://www.nice.org.uk/guidance/ta649 (last accessed 8th November 2022). 2020.

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Company ACD Response: Appendix A

24 October 2023

File name	Version	Contains confidential information	Date
ID3943- Loncastuximab tesirine-RR-DLBCL-ACDResponse_Appendix A_Redacted	1	Redacted	24 October 2023

1. Appendix A

1.1. Loncastuximab tesirine vs chemotherapy

The deterministic and probabilistic base case results for the comparison against chemotherapy are presented in Table 1 and Table 2, respectively. The base case is based on an updated patient access scheme (PAS) price of [redacted] for loncastuximab tesirine, which has been offered by the Company during the ACD process step, and an adjusted hazard ratio of 1.66 for chemotherapy to reflect 3% subsequent autologous stem cell transplant. In the Company base case, the CORAL extension study weights are applied to the data from LOTIS-2 in the loncastuximab tesirine arm and a log-normal distribution is used to extrapolate overall survival (OS), in line with the preferred assumptions of the external assessment group (EAG).

Table 1: Company deterministic base-case results, loncastuximab tesirine vs chemotherapy, loncastuximab tesirine PAS price

Technologies	Total costs (£)	Total LYG	Total QALYs	Inc. costs (£)	Inc. LYG	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£26,748	£22,290

Abbreviations: ICER, incremental cost-effectiveness ratio; Inc., incremental; LYG, life-years gained, PAS, patient access scheme; QALY, quality adjusted life-years.

Table 2: Company probabilistic base-case results, loncastuximab tesirine vs chemotherapy, loncastuximab tesirine PAS price

Technologies	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	£29,248	£24,374

Abbreviations: ICER, incremental cost-effectiveness ratio; Inc., incremental; LYG, life-years gained, PAS, patient access scheme; QALY, quality adjusted life-years.

The deterministic base case results based on the EAG assumptions for the comparison against chemotherapy are presented in Table 3. The base case is based on a hazard ratio of 1.43 for chemotherapy.

Table 3: EAG deterministic base-case results, loncastuximab tesirine vs chemotherapy, loncastuximab tesirine PAS price

Technologies	Total costs (£)	Total LYG	Total QALYs	Inc. costs (£)	Inc. LYG	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£32,168	£26,807

Abbreviations: EAG, external assessment group; ICER, incremental cost-effectiveness ratio; Inc., incremental; LYG, life-years gained, PAS, patient access scheme; QALY, quality adjusted life-years.

Figure 1 presents the cost-effectiveness acceptability curve for the comparison with chemotherapy. This shows a 4% probability of being cost-effective at a willingness-to-pay (WTP) threshold of £20,000 per QALY and 61% at £30,000 per QALY. With the severity weights applied, this becomes 20% and 84% respectively.

Figure 1: Cost-effectiveness acceptability curve vs chemotherapy, no severity multiplier

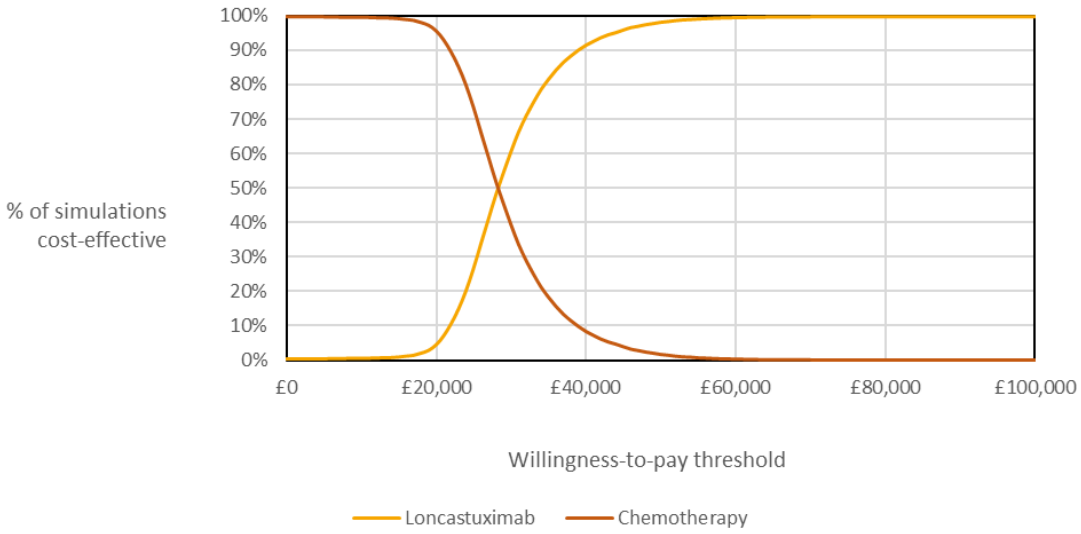

Table 4 presents the outcomes of the additional scenario analyses comparing to chemotherapy. Scenarios are presented in which a generalised gamma distribution is used to extrapolate OS for loncastuximab tesirine and assumptions of long-term remission are applied.

Table 4: Additional scenario analyses vs chemotherapy

Scenario	Incremental costs	Incremental QALYs	ICER	ICER with severity weighting
Base-case	[redacted]	[redacted]	£26,748	£22,290
EAG base-case	[redacted]	[redacted]	£32,168	£26,807
Generalised gamma distribution for OS – Company	[redacted]	[redacted]	£19,584	£16,320
Generalised gamma distribution for OS – EAG	[redacted]	[redacted]	£23,359	£19,466
Cure at 3 years – Company	[redacted]	[redacted]	£14,382	£11,985
Cure at 3 years – EAG	[redacted]	[redacted]	£17,928	£14,940

Abbreviations: EAG, external assessment group; ICER, incremental cost-effectiveness ratio; QALY, quality adjusted life-years.

1.2. Loncastuximab tesirine vs Pola+BR

The deterministic and probabilistic cost-effectiveness results for the base-case analysis comparing loncastuximab tesirine with Pola+BR are presented in Table 5 and Table 6, respectively. The base-case analysis is based on an updated PAS price of [redacted] for loncastuximab tesirine, which has been offered by the Company during the ACD process step, and assumes equal efficacy between loncastuximab tesirine and Pola+BR. The Company base case is aligned with the EAG's preferred assumptions for the comparison to Pola+BR.

Table 5: Company and EAG deterministic base-case results, loncastuximab tesirine vs Pola+BR, loncastuximab tesirine PAS price

Technologies	Total costs (£)	Total LYG	Total QALYs	Inc. costs (£)	Inc. LYG	Inc. QALYs	ICER (£/QALY)
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	Dominated

Abbreviations: EAG, external assessment group; ICER, incremental cost-effectiveness ratio; Inc., incremental; LYG, life-years gained, PAS, patient access scheme; Pola+BR, polatuzumab plus bendamustine plus rituximab; QALY, quality adjusted life-years.

Table 6: Company probabilistic base-case results, loncastuximab tesirine vs Pola+BR, loncastuximab tesirine PAS price

Technologies	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	-
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	Dominated

Abbreviations: ICER, incremental cost-effectiveness ratio; Inc., incremental; LYG, life-years gained, PAS, patient access scheme; Pola+BR, polatuzumab plus bendamustine plus rituximab; QALY, quality adjusted life-years.

Figure 2 presents the cost-effectiveness acceptability curve (CEAC) for the comparison with Pola+BR. Loncastuximab tesirine is cost-effective in 100% of scenarios at a WTP threshold of £20,000 per QALY and 100% of scenarios at £30,000 per QALY.

Figure 2: Cost-effectiveness acceptability curve vs Pola+BR

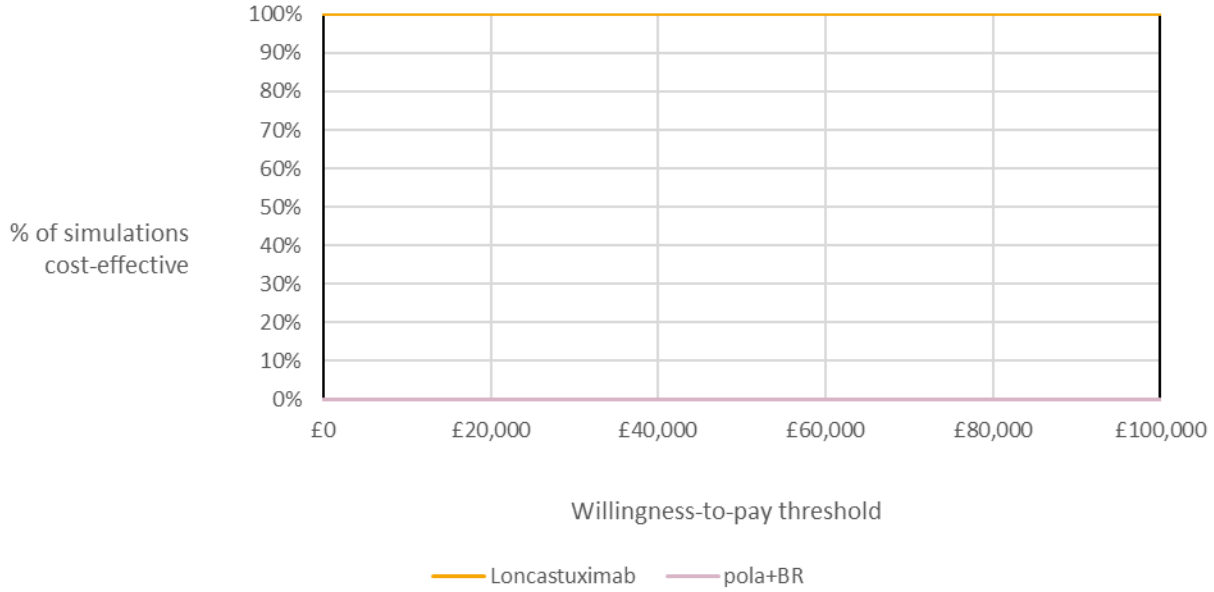

Table 7 presents the outcomes of the additional scenario analyses comparing to Pola+BR based on assumptions of long-term remission and using a generalised gamma distribution to extrapolate OS for loncastuximab tesirine.

Table 7: Additional scenario analyses vs Pola+BR

Scenario	Incremental costs	Incremental QALYs	ICER
Base-case	[redacted]	[redacted]	Dominant
EAG base-case	[redacted]	[redacted]	Dominant
Generalised gamma distribution for OS – Company	[redacted]	[redacted]	Dominant
Generalised gamma distribution for OS – EAG	[redacted]	[redacted]	Dominant
Cure at 3 years – Company	[redacted]	[redacted]	Dominant
Cure at 3 years – EAG	[redacted]	[redacted]	Dominant

Abbreviations: EAG, external assessment group; ICER, incremental cost-effectiveness ratio; Pola+BR, polatuzumab plus bendamustine plus rituximab; QALY, quality adjusted life-years.

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Swedish Orphan Biovitrum Ltd (Sobi)
Disclosure Please disclose any funding received from the company bringing the treatment to NICE for evaluation or from any of the comparator treatment companies in the last 12 months. [Relevant companies are listed in the appraisal stakeholder list.] Please state: • the name of the company • the amount • the purpose of funding including whether it related to a product mentioned in the stakeholder list • whether it is ongoing or has ceased.	Sobi is the manufacturer for loncastuximab tesirine, the intervention under appraisal.
Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	None
Name of commentator person completing form:	[redacted]

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Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic treatments [ID3943]

Draft guidance comments form

Consultation on the draft guidance document – deadline for comments 5pm on Tuesday 24 October 2023. Please submit via NICE Docs.

Comment number	Comments	EAG response
1	**Benefits not captured in the quality-adjusted life year (QALY) evaluation** The draft guidance states that the committee did not identify additional benefits of loncastuximab tesirine not captured in the economic modelling. The company believes that there are additional benefits not captured in the economic analysis, which may not have been sufficiently considered by the committee in the context of the ICER threshold to be applied. Patients with relapsed and refractory (R/R) diffuse large B-cell lymphoma (DLBCL) have gone through multiple lines of therapy, face a poor prognosis, and urgently need additional treatment options that extend survival with tolerable side-effect profiles. Loncastuximab tesirine has the potential to fulfill this unmet need having been shown in the LOTIS-2 trial to be both well-tolerated and to provide durable responses. Loncastuximab tesirine is available off-the-shelf and ready for infusion unlike some alternative treatments available. This is a significant benefit not captured in the economic analysis since many R/R DLBCL patients have fast progressing disease and require a treatment without delay. Loncastuximab tesirine is also a chemotherapy-free and less intensive treatment that clinicians noted to have a particularly favourable treatment profile for frailer patients compared with other treatments with similar efficacy, such as polatuzumab plus bendamustine plus rituximab (Pola+BR) (1). These patients may not tolerate any other treatment and, without access to loncastuximab tesirine, could require end of life care. There is also a significant caregiver burden associated with alternative treatments due to frequent hospital visits, especially those requiring overnight stays, creating both emotional and financial burden to both patients and their families (2, 3). Additionally, unlike some recently NICE approved treatments such as bispecific and CAR-T therapies that require access to inpatient and specialist care to manage potential side-effects (4) (e.g. a neurosciences intensive care unit for glofitamab treatment due to the risk of cytokine release syndrome and neurological adverse events), loncastuximab	The company's main point is that loncastuximab is available off-the-shelf and ready for infusion. This benefit was not described by the EAG's clinical expert, and the company do not quantify this potential benefit against the comparator treatments in any form, so the EAG is unable to validate this point in the timeframe available. The EAG suspect that any gain would be marginal. Other points described by the company included the fact loncastuximab tesirine is a chemotherapy-free regimen and has a reduced administration time which is already reasonably represented in the existing analyses. Comparisons to CAR-T therapies are not relevant as they are not a comparator in this appraisal.

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	tesirine has a strong safety profile and is available in an outpatient setting (e.g. a general hospital without access to specialist care). Therefore, in terms of equity of access, it would be accessible to a larger range of clinical centres, helping to reduce regional, rural–urban, and sociodemographic inequity issues resulting from uneven geographical availability of specialist sites. Patients being able to receive treatment closer to home helps reduce the financial and lifestyle burden of treatment. This is significant as many patients often have to travel long distances or stay in specialised facilities when receiving certain treatments, incurring additional expenses and disruptions to their daily lives. When patients can receive treatment in a location that is more convenient and closer to their home, they may be more willing to accept a course of treatment. The accessibility and reduced disruption to their lives may increase overall satisfaction and may improve adherence to the treatment (5). Loncastuximab tesirine is simple to administer, with only a single 30-minute infusion required per cycle. This lessens the burden of administration on both healthcare practitioners and patients compared with other treatment options, with more frequent dosing or more and longer infusions required. This allows both the NHS to free up chair time and space in cancer units for treating more patients as well as minimising the financial burden of treatment for patients.	
2	**Subsequent autologous stem cell transplantation** The draft guidance states that the committee "concluded the rate of autologous stem cell transplantation (SCT) after chemotherapy was uncertain and that it could be as low as 3%, but that changing it did not have a large impact on the cost-effectiveness results". The Company strongly disagrees with the assertion that it has a limited impact and would like the committee to reconsider this point. The ICER with the EAG base-case assumptions (severity-modified and updated PAS) is £26,807, compared to an ICER of £22,290 using the company's approach to this issue. The Company acknowledges the possibility that the rates of subsequent ASCT reported in the CORAL extension study may be higher than what is typically expected in clinical practice, and even as low as 3%, as suggested by the committee's conclusion. However, the study reports a rate of 22%, and the company's approach was designed to accurately	The company originally modelled a rate of subsequent ASCT from CORAL of 22%. The EAG preferred to use the rate of 3% which was consistent with the other arm. The company outline concerns that this is removing the cost of ASCT whilst maintaining the benefit and present a new analysis of data from CORAL study. Whilst there does appear to be a difference between the outcomes for these patients based on ASCT status, this difference may not be attributable to the receipt of ASCT but could also be explained by baseline differences which is acknowledged by the company.

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	and simultaneously represent both the costs and outcomes for patients within the CORAL cohort. The company emphasizes that since economic evaluation hinges on the estimation of costs and benefits (6, 7), it is imperative that assumptions regarding both costs and benefits are in alignment to ensure a comprehensive and credible analysis. Crude adjustments to the cost allocation figure for the chemotherapy arm, following the EAG approach, without due consideration for the potential impact on outcomes, run contrary to this fundamental principle. Moreover, it's impossible to assert with any degree of certainty that the ICER was not sensitive to the changes made without also taking into account the potential QALY losses. The Company upholds the concerns it raised during technical engagement on this point. Our primary concern with the EAG approach is that it reduces the costs for chemotherapy to reflect lower rates of ASCT, without also propagating the impact of this on outcomes. Importantly, the 30% patients in the CORAL extension study who went on to subsequently receive an SCT (22% ASCT, 8% AlloSCT) had significantly better survival outcomes compared to patients that did not (see Figure 1). The EAG approach lowers the amount of subsequent ASCT from 22% to 3%, which lowers the overall cost in the chemotherapy arm of the model, however this arm still retains the identical efficacy as before. This is a flawed and biased approach for economic analysis. To demonstrate our point, we have analysed the different efficacy dependent on subsequent SCT status in the CORAL extension studies, both of which have reported outcomes separately for those that did and did not go on to receive an SCT. These curves have been digitised to generate pseudo-individual patient data (IPD) by eventual SCT status and are presented in Figure 1 SCT status is a driver of overall survival (OS), with the KM curves showing that patients who went on to receive SCT have better OS than those who did not go on to receive SCT, with a clear distinction in the survival curves between the two populations. The difference may be attributed to the additional efficacy of SCT, and the better baseline fitness of patients who eventually go on to receive SCT.	The company performs an additional analysis comparing LOTIS-2 data to CORAL. The analysis is not described clearly, however the EAG guesses that the LOTIS-2 data has been weighted as before to match the characteristics of the CORAL data for a limited set of three baseline covariates. Separate hazard ratios were estimated to compare the efficacy of loncastuximab tesirine to the two SCT-based subgroups from CORAL. The resulting two hazard ratios have been combined to match the combined Auto- and Allo-SCT rates observed in LOTIS-2. This analysis suggests a difference in relative efficacy of loncastuximab tesirine across the two subgroups, however this could be attributable to baseline characteristics rather than SCT. As so few variables were able to be matched to begin with, large amounts of uncertainty remain regardless. The analysis was not able to weight the LOTIS-2 data to each SCT subgroup individually as baseline characteristics were not reported. Hence this analysis is at risk of bias in excess of the original analyses with which the EAG has already outlined concerns. Furthermore, it is not clear whether a hazard ratio, which assumes proportionality, is an appropriate measure of benefit in either subgroup. The EAG maintains its preference to extrapolate OS for chemotherapy directly from the CORAL data rather than apply a hazard ratio as preferred by the company.

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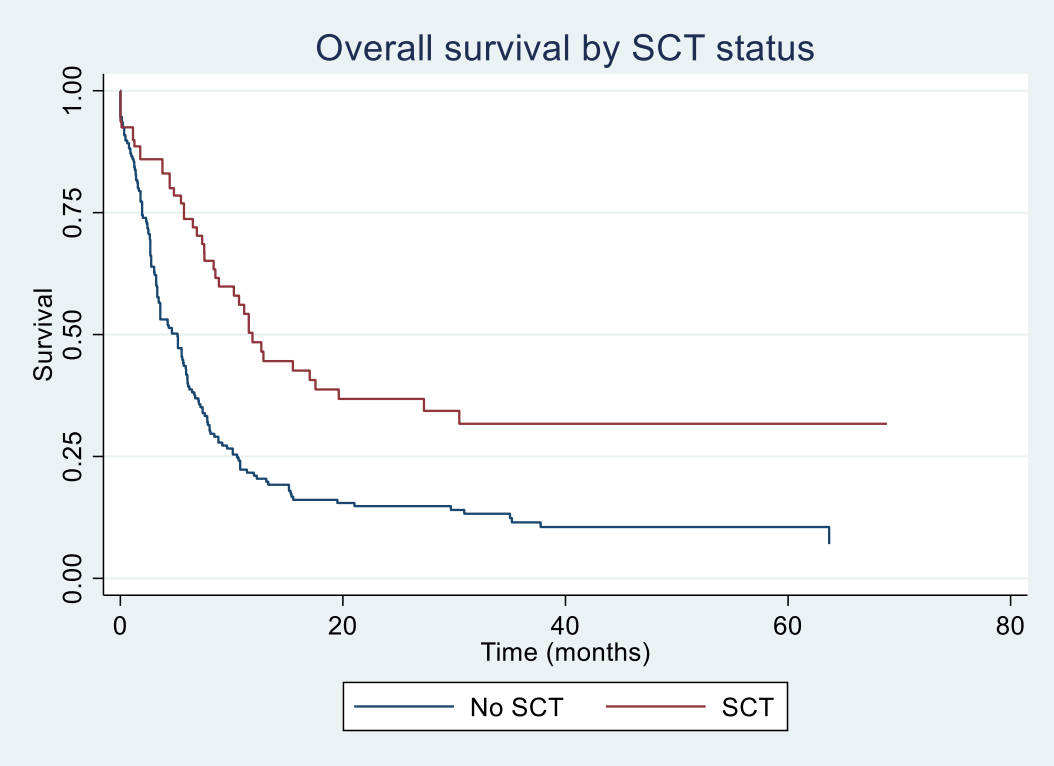
Figure 1: Overall survival curves for CORAL extension study split by eventual SCT status



Abbreviations: SCT, stem cell transplantation.

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In order to assess the impact of alternative rates of SCT, an additional scenario analysis is presented for consideration by the committee. In the scenario, OS hazard ratios (HRs) have been generated for patients with and without an eventual SCT separately. The same counterfactual survival times for LOTIS-2 patients have been used, and as baseline characteristics are not reported by eventual SCT status, the same weights have been applied. The same proportion of patients have then been assumed to receive an SCT as was observed in LOTIS-2 (3% AutoSCT, 8% allogenic stem cell transplantation [AlloSCT]) and a weighted HR generated. The HR for patients with and without SCT and the weighted HRs are presented in Table 11.

Table 11: HRs for chemotherapy by eventual SCT status

	HR	SE	CI
No SCT	1.767	0.277	1.300–2.403
SCT	0.801	0.166	0.533–1.204
Weighted 11% SCT	1.659	–	–

Abbreviations: CI, confidence interval; HR, hazard ratio; SCT, stem cell transplantation; SE, standard error.

The scenario demonstrates that chemotherapy-treated patients who have received subsequent SCT accrue substantially greater health benefits than those who have not received it (a 0.801 vs 1.767 HR).

Given the above points, the Company maintains that if 3% subsequent ASCT is applied in the economic analysis, the HR for chemotherapy should be adjusted to 1.659 to reflect the impact of deviating from the proportion seen in the CORAL extension studies. This figure is a weighted average of the HRs for patients that did and did not receive an SCT, assuming 11% of patients would go on to receive an SCT in clinical practice (3% ASCT, 8% AlloSCT). Alternatively, you could remove all patients entirely from the analysis that had subsequent SCT, producing a HR for chemotherapy of 1.767.

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	Updated base-case results including an adjusted hazard ratio of 1.66 for chemotherapy to reflect 3% subsequent autologous stem cell transplant are provided in **Appendix A**.	
3	**Cure/long-term remission assumptions** The Company believes that the choice of using a log-normal distribution for extrapolating overall survival (OS) in this context is overly pessimistic and inconsistent with the recent assumptions made by the EAG and the committee for a similar 3L R/R DLBCL treatment, namely the glofitamab appraisal (TA674) (8). As in the glofitamab appraisal (8), the Company employed standard parametric survival analysis, which involved fitting different parametric distribution models to the observed data. The selection of the most appropriate model was determined through a rigorous process that considered goodness-of-fit statistics, visual comparisons with Kaplan-Meier curves, and validation by clinical experts who assessed long-term extrapolations and the underlying hazard functions. This approach aligned with the guidance provided in the NICE Decision Support Unit (DSU) technical support document (9). Importantly, in this appraisal, the base-case model did not assume any cure for either treatment arm, as there was uncertainty regarding the proportion of patients achieving long-term remission. However, clinical experts did note that patients who remained progression-free after 2 years often ceased to require further treatment, and evidence indicated a plateau in survival for those treated with loncastuximab tesirine without the need for additional therapies (10). The Company's selection of the generalised gamma distribution was made to best reflect the clinicians' beliefs. Scenarios that considered the possibility of cure were explored in scenario analyses, assuming that patients remaining progression-free at 2, 5, and 10 years could be considered cured. These patients would return to general population utility values but might experience slightly elevated mortality. Following the committee's preference in TA649 (11), a standardized mortality ratio (SMR) of 1.41 was applied to the general population mortality for cured patients. The Company argues that the choice of a log-normal distribution for OS extrapolation is overly pessimistic. They propose that the generalised gamma distribution would better reflect the available data and clinical opinions regarding long-term remission and	No new data relevant to loncastuximab tesirine has been provided and so the EAG maintains its preference to use the log-normal extrapolation.

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	associated uncertainties in this patient population. This recommendation is further supported by the recent appraisal of glofitamab (TA674), in which clinical experts suggested that individuals could be considered cured if their cancer remained in complete remission at 2 years. While longer-term follow-up was deemed necessary to ascertain the proportion of glofitamab-treated patients for whom this applied, the committee concluded that assuming a cure point of 3 years was reasonable. Thus, the Company argues that the use of a log-normal distribution appears to be at odds with the committee's preferred assumptions in the glofitamab appraisal (TA674) (8). Updated base-case results including the log-normal distribution to extrapolate OS for loncastuximab tesirine are provided in **Appendix A**. Scenario analyses using the generalised gamma distribution to extrapolate OS and applying the assumption of a cure point at 3 years aligned with the assumption in the glofitamab appraisal are also presented in **Appendix A.**	

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in turquoise and information that is 'academic in confidence' in yellow. If confidential information is submitted, please submit a second version of your comments form with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the NICE Health Technology Evaluation Manual (section 5.4) for more information.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations.

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- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
- If you have received agreement from NICE to submit additional evidence with your comments on the draft guidance document, please submit these separately.

Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory committees.

References

1. Sobi. Data on File: Clinical Interviews, Summary Report. 2023.

2. Lenz G, Rutherford SC, Davies A, Zinzani PL, Salles G, Hasskarl J, et al. The Burden of Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): A Systematic Literature Review (SLR). Blood. 2018;132:2241.

3. Lin V, Oak B, Snider J, Epstein J. Health-related quality of life burden in patients with relapsed/refractory diffuse large B-cell lymphoma and non-Hodgkin's lymphoma. Presented at: American Society of Clinical Oncology Annual Meeting 2020 [virtual meeting]. Abstract e20070. 2020.

4. Xie J, Wu A, Liao L, Nastoupil LJ, Du EX, Noman A, et al. Characteristics and treatment patterns of relapsed/refractory diffuse large B-cell lymphoma in patients receiving >/=3 therapy lines in post-CAR-T era. Curr Med Res Opin. 2021;37(10):1789-98.

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5. Heckman BW, Mathew AR, Carpenter MJ. Treatment Burden and Treatment Fatigue as Barriers to Health. Curr Opin Psychol. 2015;5:31-6.

6. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes: Oxford university press; 2015.

7. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual 2022 [Available from: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation.

8. National Institute for Health and Care Excellence (NICE). Glofitamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic treatments. Final draft guidance. Available at: https://www.nice.org.uk/guidance/ta927/documents/674 (last accessed 17 October 2023).

9. Latimer NR. NICE DSU Technical Support Document 14: Undertaking survival analysis for economic evaluations alongside clinical trials - extrapolation with patient-level data. Available from http://www.nicedsu.org.uk Last accessed 9th November 2022. 2011.

10. Caimi PF, Ai W, Alderuccio JP, Ardeshna KM, Hamadani M, Hess B, et al. Data on file. Long-term responses with loncastuximab tesirine: Updated results from LOTIS-2, the pivotal Phase 2 study in patients with relapsed/refractory diffuse large B-cell lymphoma (EHA 2023). 2023.

11. National Institute for Health and Care Excellence. Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma: TA649. Available at: https://www.nice.org.uk/guidance/ta649 (last accessed 8th November 2022). 2020.

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Revised cost-effectiveness results based on updated drug price.

Comparison with chemotherapy

For overall survival (OS), the EAG prefers weighted direct extrapolation of the CORAL study using generalised gamma distribution rather than the hazard ratio preferred by the company. This approach fits separate parametric models to the OS data of the SCT and non-SCT populations of the CORAL extension study. The weighted average of the models is then combined to match the proportion of SCT received in the relevant LOTIS-2 population. The loncastuximab extrapolation comes from the population weighted to match the original CORAL extension population and not the SCT-weighted CORAL population. In the cPAS appendix, the EAG presents a scenario where the CORAL data is extrapolated without weighting, which has a small effect on the ICER. The EAG maintains the use of a hazard ratio of 1.43 for modelling progression free survival (PFS) rather than the hazard ratio of 1.66 preferred by the company.

Table *1* and Table *2* presents company deterministic and probabilistic base case cost-effectiveness results. *Table 3* and *Table 4* presents the EAG deterministic and probabilistic base case cost-effectiveness results.

Table 1 Comparison with chemotherapy: company deterministic base case results

Technologies	Total costs (£)	Total LYG	Total QALYs	Inc. costs (£)	Inc. LYG	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£26,748	£22,290

Table 2 Comparison with chemotherapy: company probabilistic base case results

Technologies	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	£29,248	£24,374

Table 3 Comparison with chemotherapy: EAG deterministic base-case results

Technologies	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	£36,608	£30,507

Table 4 Comparison with chemotherapy: EAG probabilistic base-case results

Technologies	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	ICER with severity multiplier
Chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]	-	-
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	£39,052	£32,543

Comparison with POLA + BR

Both the EAG and company base case assumptions are the same in the pola + BR comparison. Table *5* and Table *6* report the company deterministic and probabilistic base case assumptions.

Table 5 Comparison with pola + BR: Company deterministic base case cost-effectiveness results

Technologies	Total costs (£)	Total LYG	Total QALYs	Inc. costs (£)	Inc. LYG	Inc. QALYs	ICER (£/QALY)
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	Dominated

Table 6 Comparison with pola + BR: Company probabilistic base case cost-effectiveness results

Technologies	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)
Loncastuximab tesirine	[redacted]	[redacted]	[redacted]	[redacted]	-
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	Dominated