National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Glofitamab with gemcitabine and oxaliplatin for treating relapsed or refractory diffuse large B-cell lymphoma [ID6202]

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE 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 submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Roche	Roche agrees that the STA route is appropriate for the current appraisal.	Thank you for your comment. No action required.
	AbbVie	N/A	Thank you for your comment. No action required.
Wording	Roche	The anticipated license is as follows: Glofitamab 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): • After first-line systemic therapy, who are not candidates for autologous stem cell transplantation (ASCT), or	Thank you for your comment. No action required.

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		• After two or more lines of systemic therapy	
	AbbVie	N/A	Thank you for your comment. No action required.
Timing Issues	Roche	For patients who are ineligible for autologous stem cell transplant (ASCT), the most widely used regimens for patients after first relapse of DLBCL are gemcitabine and/or platinum-based chemotherapy with or without rituximab (e.g. R-GemOx). Unfortunately, the majority of patients will be refractory or relapse after these second line combinations and will require further lines of treatment. The CAR-T cell therapy, axicabtagene ciloleucel, has recently been approved for funding via the CDF for patients who are refractory to, or who have relapsed within 12 months of first line chemoimmunotherapy and are suitable for ASCT (TA895). Combining glofitamab with gemcitabine plus oxaliplatin is anticipated to provide improved response rates, which may translate into improved OS, compared with the combination of rituximab and GemOx, while maintaining an acceptable safety profile in the second line treatment of patients who are not suitable for ASCT. There have been several recent approvals of treatments for third and subsequent line treatment of DLBCL, including the CD20xCD3 bispecific antibodies, glofitamab and epcoritamab, as monotherapy (TA927, TA954). The combination of glofitamab with GemOx may provide improved outcomes for these patients, especially those who have not been exposed to platinum-based chemotherapy previously.	Thank you for your comment. Comments noted. NICE has scheduled this topic into its work programme. No action required.

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	AbbVie	N/A	Thank you for your comment. No action required.
Additional comments on the draft remit	Roche	No comments	Thank you for your comment. No action required.
	AbbVie	N/A	Thank you for your comment. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Roche	Following the NICE guidance, TA872 (published March 2023), Pola-R-CHP (polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin and prednisolone) is recommended for first-line treatment of DLBCL in patients with international prognositic index (IPI) 2-5. This should be acknowledged in the third paragraph where R-CHOP is stated due to the potential impact on Pola-BR (polatuzumab vedotin, bendamustine, rituximab) as a comparator in this appraisal. The British Society of Haematology has recently published an update to its guideline on management of newly diagnosed large B-cell lymphoma and this should be included for completeness.	Thank you for your comment. The scope has been updated to reflect the suggested changes.
		Some of the comparators are chemoimmunotherapy combinations (e.g. R-GemOx) that are used at first relapse in patients who do not receive high dose chemotherapy and autologous stem cell transplantation, so 'or in combination'	Thank you for your comment. The scope has been updated to

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		should be added to the end of the statement 'If stem cell transplantation is not suitable, further chemotherapy or immunotherapy may be used alone'.	reflect the suggested changes.
	AbbVie	For first-line treatment in DLBCL, polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisolone (R CHP) is recommended for untreated diffuse large B-cell lymphoma (DLBCL) in adults (TA874). Therefore, AbbVie suggests including this first-line treatment into the background information to accurately represent the current treatment pathway. For treatments recommended by NICE in relapsed or refractory DLBCL, AbbVie would like to highlight that TA954 recommends epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma in adults after 2 or more systemic treatments if they have had polatuzumab vedotin, or if polatuzumab vedotin is contraindicated or not tolerated. Therefore, AbbVie suggests including this recommendation as one of the bullet points after "For those with relapsed or refractory DLBCL, the following treatments are recommended by NICE:".	Thank you for your comment. The scope has been updated to reflect the suggested changes. Thank you for your comment. The scope has been updated to reflect the suggested changes.
Population	Roche	The study population in the registration study is adult patients with relapsed or refractory diffuse large B-cell lymphoma as second line therapy in patients who are transplant ineligible and as third line and beyond therapy (regardless of eligibility for transplant).	Thank you for your comment. No action required.

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	AbbVie	N/A	Thank you for your comment. No action required.
Subgroups	Roche	In accordance with the anticipated license wording, clinical and cost-effectiveness evidence will be presented for the following populations • Second line therapy in patients who are transplant ineligible and, • Third line and beyond (regardless of eligibility for transplant	Thank you for your comment. The committee will consider evidence in line with the marketing authorisation. No action required.
	AbbVie	N/A	Thank you for your comment. No action required.
Comparators	Roche	The listed comparators are reflective of treatments currently used in the NHS, with the exception of pixantrone, which has been excluded as a comparator in recent NICE technology appraisals in relapsed or refractory DLBCL (TA883, TA927, TA947, TA954) due to its lack of use in England. Given the proposed indication of glofitamab plus gemcitabine and oxaliplatin and its use as a second-line therapy in transplant ineligible patients only but all third-line and beyond relapsed/refractory DLBCL patients, the comparators should clearly stipulate which regimens are relevant for each setting; the comparators relevant to the second-line, transplant ineligible setting are rituximab in combination with chemotherapy (R-chemo, mainly R-GemOx) and polatuzumab vedotin in combination with bendamustine and rituximab (pola-BR). Pola-BR and R-GemOx are also relevant comparators for third and subsequent line therapy. The remaining suggested comparators (axicabtagene ciloleucel, glofitamab, epcoritamab and loncastuximab teserine [all	Thank you for your comment. The scope has been updated to reflect the suggested changes. Thank you for your comment. The committee will consider different positions that these comparators could be used in the

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		monotherapy]), are relevant to the third and subsequent line therapy comparisons (not second-line). NICE guidance on epcoritamab has been published now and '(only if previously treated with polatuzumab vedotin)' should be added to the indication.	treatment pathway during evaluation.
	AbbVie	TA954 recommends epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma in adults after 2 or more systemic treatments if they have had polatuzumab vedotin, or if polatuzumab vedotin is contraindicated or not tolerated. Therefore, AbbVie suggests removing "subject to NICE evaluation" and amending the last bullet point to "Epcoritamab for treating relapsed or refractory DLBCL after 2 or more systemic therapies (if previously treated with polatuzumab vedotin, or if polatuzumab vedotin is contraindicated or not tolerated)".	Thank you for your comment. The scope has been updated to reflect the suggested changes.
Outcomes	Roche	Yes, the listed outcomes capture the most important health-related benefits and harms.	Thank you for your comment. Comment noted. No action required.
	AbbVie	N/A	Thank you for your comment. No action required.
Equality	Roche	No equality issues have been identified.	Thank you for your comment. No action required.

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	AbbVie	N/A	Thank you for your comment. No action required.
Other considerations	Roche	**No other considerations**	Thank you for your comment. No action required.
	AbbVie	Under Related NICE recommendations, the epcoritamab appraisal is no longer in development. Therefore, AbbVie suggests moving the epcoritamab recommendation under "Related technology appraisals" and amending it as "Epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic treatments (2024). NICE technology appraisal guidance 954.".	Thank you for your comment. The scope has been updated to reflect the suggested changes.
Questions for consultation	Roche	**Where do you consider glofitamab with gemcitabine and oxaliplatin will fit into the existing care pathway for relapsed or refractory diffuse B-cell lymphoma?** As mentioned above, the indication population will be for adult patients with relapsed or refractory diffuse large B-cell lymphoma. As per the study population, patients will be eligible for glofitamab plus gemcitabine and oxaliplatin as a second line therapy for those patients who are transplant ineligible, and as third line and beyond therapy for all relapsed/refractory DLBCL patients, regardless of eligibility for transplant. **Would glofitamab with gemcitabine and oxaliplatin be a candidate for managed access?** Roche is committed to ensuring patient access to its innovative medicines and is therefore open to exploring all possible routes of funding. It should be noted however that the primary endpoint of the registration study is overall survival and data from the final analysis for this endpoint will be submitted, therefore	Thank you for your comment. Comments noted. No action required.

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		data collection during a managed access agreement is likely to only provide data from a UK clinical practice setting. **Do you consider that the use of glofitamab with gemcitabine, oxaliplatin can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Glofitamab in combination with gemcitabine and oxaliplatin offers a novel treatment option for patients with R/R DLBCL, and is the first indication to offer the combination of a CD20xCD3 bispecific antibody with chemotherapy. We expect glofitamab in combination with gemcitabine and oxaliplatin to be the first bispecific antibody to be available in the second-line setting for R/R DLBCL patients who are ineligible for transplant**.** In the context of the third-line plus setting, glofitamab plus gemcitabine and oxaliplatin is a readily available T-cell engaging therapy that does not require the lengthy manufacturing times involved with CAR-T cell therapy. It can be initiated very soon after the decision to treat, with no need for bridging treatments, which is important to patients with this aggressive disease. In addition, CAR-T cell therapy is currently delivered in 16 centres in England (https://www.england.nhs.uk/cancer/cdf/car-t-therapy/) or adults with large B-cell lymphoma. Bispecific antibodies, such as glofitamab, are expected to be deliverable to patients in any haematology/oncology units that have access to appropriate medical support to manage severe reactions associated with cytokine release syndrome. Unlike treatment with CAR-T cell therapy, most patients will not have to have lengthy periods away from home, with associated psychological impact, if they are treated with glofitamab.	
	AbbVie	N/A	Thank you for your comment. No action required.

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Additional comments on the draft scope	Roche	No comments	Thank you for your comment. No action required.
	AbbVie	N/A	Thank you for your comment. No action required.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Lymphoma action
Swedish Orphan Biovitrum