National Institute for Health and Care Excellence

Health Technology Evaluation

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

Response to stakeholder organisation comments on the draft remit and draft scope

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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	NCRI-ACP-RCP-RCR	The single technology clinical and cost effectiveness appraisal of Loncastuximab tesirine for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies is highly appropriate.	Thank you for your comment. No action needed.
	Sobi	Sobi agrees with the decision to evaluate loncastuximab tesirine via the single technology appraisal process.	Thank you for your comment. No action needed.

Section	Stakeholder	Comments [sic]	Action
Wording	NCRI-ACP-RCP-RCR	Yes	No action needed
	Sobi	The UK marketing authorisation indication is expected to be: Zynlonta as monotherapy is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy. Therefore, Sobi suggests that the draft remit is altered to: To appraise the clinical and cost effectiveness of loncastuximab tesirine as monotherapy for treating relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma after 2 or more systemic therapies.	Thank you, the remit has been amended.
Timing issues	NCRI-ACP-RCP-RCR	Relapsed or refractory diffuse large B-cell lymphoma is a difficult disease to treat as patients often need urgent treatment and having failed R-CHOP have already demonstrated some resistance to chemotherapy. There are a number of treatment options but these are not suitable for all patients and the failure rate with these treatments is also significant and often further lines of therapy are required. Loncastuximab tesirine would offer an alternative/additional treatment option so evaluation within 12 months would be ideal.	Thank you for your comment. No action needed.
	Sobi	There is a need to evaluate loncastuximab tesirine in a timely manner. The difficult-to-treat patient population with relapsed or refractory disease can	Thank you for your comment. No action

Section	Stakeholder	Comments [sic]	Action
		reach a therapeutic impasse. These patients tend to have poor quality of life and overall survival rates. Therefore, there is a need for an additional and effective treatment option for diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL). Sobi believes that loncastuximab tesirine addresses a critical unmet need, especially for treating patient populations that are not responding to current treatments, ineligible for chimeric antigen receptor (CAR) T-cell therapy, or older and frailer. Loncastuximab tesirine may be a suitable treatment option for these patients given that it is administered as a monotherapy (not in combination with chemotherapy), has a quick onset of action and a lower incidence of adverse events as demonstrated in the pivotal trial, LOTIS-2.	needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	NCRI-ACP-RCP-RCR	Information is correct and complete	Thank you for your comment.
	Sobi	Sobi agrees in general with the accuracy of the background information.	Thank you for your comment. The background section of

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		However, we would like to highlight that the recent NICE TA scope for ID3970 includes information on later line prevalence: “Although most patients are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.” NICE could consider also adding this information to the final scope of this appraisal. We would also like to request that additional information is provided on the clinical background and prevalence associated with high-grade B-cell lymphoma (HGBL).	the scope is intended to give a brief overview of the condition and treatment pathway. Additional prevalence information and information on high-grade lymphomas has been included..
Population	NCRI-ACP-RCP-RCR	Yes	No action needed.
	Sobi	As previously mentioned, Sobi expects the indication for loncastuximab tesirine to be broader than stated in the draft scope’s population. Therefore, we suggest that the population is altered to ‘adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) or high-grade B-cell lymphoma (HGBL) who have had two or more systemic therapies’.	Thank you for your comment. The population has been amended to account for this.

Section	Consultee/ Commentator	Comments [sic]	Action
Subgroups	NCRI-ACP-RCP-RCR	Significant research into the molecular understanding of DLBCL is ongoing but it is not possible to identify at this time, subgroups that would preferentially benefit from this treatment. Therefore this should be made available to all patients with relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies	Thank you for your comment. No action needed.
	Sobi	Sobi does not believe that there are definable subgroups that could be considered separately.	Thank you for your comment. No action needed.
Comparators	NCRI-ACP-RCP-RCR	Yes, the list is complete.	Thank you for your comment. No action needed.
	Gilead	The chemotherapy regimens should be in combination with rituximab	Thank you for your comment. “With or without rituximab” has been added to the

Section	Consultee/ Commentator	Comments [sic]	Action
			scope to cover instances in which non-rituximab regimens may be used.
	Sobi	We agree that polatuzumab vedotin with rituximab and bendamustine is a standard treatment for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies. It does not have specific market authorisation or NICE recommendation for high-grade B-cell lymphoma. We agree that salvage chemotherapy is established practice in the NHS, particularly second line in the treatment pathway. Use in third line, as per the remit of this appraisal, is far less common. There are a range of chemotherapy regimens used in the NHS. Therefore, we agree with the language used that emphasises a non-exclusive list of chemotherapy options. However, we would like to highlight that the scope could detail that some regimens include the addition of the anti–CD20 monoclonal antibody rituximab. Further, we understand that R-GEMOX (rituximab + gemcitabine + oxaliplatin) and BR (bendamustine and rituximab) are common third line treatment options. Sobi does not agree that pixantrone should be a relevant comparator in the appraisal and ask for it to be removed in the final scope. We note that within the same therapeutic area, the appraisals TA559, TA567, TA649 and TA10645 removed pixantrone as a comparator through the committee process. The respective committees were informed by clinical experts that	The comparator of polatuzumab vedotin with rituximab and bendamustine has been amended to specify that this only be used in DLBCL. With or without rituximab" has been added to the scope. R-GEMOX and BR Have been added to the scope. Pixantrone is used for some patients so it is considered a relevant comparator. The appraisal committee will discuss the most appropriate comparator during the development of this appraisal. This will depend on the final

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		pixantrone is rarely used in the UK; therefore, they concluded in each case that it was not a relevant comparator. Axicabtagene ciloleucel has not received a positive NICE recommendation within this indication at the time of writing. We do not believe it is an appropriate comparator given this reason, but also because we do not believe clinicians would use loncastuximab tesirine as an alternative to axicabtagene ciloleucel (if available), a chimeric antigen receptor (CAR) T-cell therapy. Axicabtagene ciloleucel is a treatment that has been shown to be clinically effective and 'cure' a proportion of patients. We therefore understand that clinicians would consider treating patients with this CAR-T (if available) ahead of loncastuximab tesirine in the treatment pathway. In these patients, should they be ineligible or refractory to axicabtagene ciloleucel, loncastuximab tesirine would be a considered treatment option.	marketing authorisation, the current treatment pathway, the clinical and cost-effectiveness evidence and current clinical practice Axicabtagene ciloleucel is included a comparator subject to NICE evaluation. This will not be considered a relevant comparator if axicabtagene is not recommended in routine practice. If it is recommended, the committee will consider the company's rationale for why it is not a relevant comparator.
Outcomes	NCRI-ACP-RCP-RCR	Yes, the five listed outcome measures will capture the benefit and harm of the intervention	No action needed.

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	Sobi	Sobi view the outcomes listed as appropriate	No action needed.
Equality	NCRI-ACP-RCP-RCR	Equality of opportunity demonstrated. No evidence of discrimination	No action needed.
	Sobi	Sobi supports the promotion of equality of opportunity. We are unaware of any facets of this appraisal that might impact equality.	No action needed.
Other considerations	NCRI-ACP-RCP-RCR	None	No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
Questions for consultation	NCRI-ACP-RCP-RCR	Please see below	No action needed.
	Sobi	The main data source used by the company will be from LOTIS-2, a Phase 2, multi-centre open-label, single-arm study of the efficacy and safety of loncastuximab tesirine. As LOTIS-2 is a single arm trial, outcomes data for comparators will be taken from the company's systematic literature reviews and matching-adjusted indirect comparisons. The company does not expect that loncastuximab tesirine will require managed access. 145 patients were enrolled in LOTIS-2, which represents a significant number for a patient population (third line) that is small. Therefore, further evidence via managed access may not be required to resolve any uncertainty. However, the company will remain open to options proposed by NICE.	No action needed.
Additional comments on the	NCRI-ACP-RCP-RCR	Would loncastuximab tesirine be a candidate for managed access? Yes Do you consider that the use of loncastuximab tesirine can result in any	No action needed.

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draft scope		potential substantial health-related benefits that are unlikely to be included in the QALY calculation? No	
	Sobi	Under the heading 'technology', we can provide additional information: Loncastuximab tesirine (Zynlonta, Swedish Orphan Biovitrum) is a humanized IgGk CD19-monoclonal antibody+ tesirine/SG3249 (a PBD dimer). It is administered intravenously.	Thank you for your comment. NICE scopes no longer contain information on mechanism of action.

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

Lymphoma action