National Institute for Health and Care Excellence

Health Technology Evaluation

Lisocabtagene maraleucel for treating relapsed or refractory large B-cell lymphoma after 2 or more systemic treatments (review of TA987) [ID6619]

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	AbbVie Ltd.	AbbVie agrees that lisocabtagene maraleucel (liso-cel) should be evaluated as a single technology appraisal for patients with relapsed or refractory large B-cell lymphoma after 2 or more systemic treatments (3L+ LBCL). The NICE manual states that "Cost-comparison analyses in a technology appraisal should be used for technologies likely to provide similar health benefits at similar or lower cost than comparator(s) that are recommended in published NICE guidance for the same population". A decision on whether to use the cost-comparison methodology should therefore consider the clinical effectiveness evidence relative to all comparators in the draft scope and the mode of administration for each comparator.	Thank you for your comment. No action required.
Wording	AbbVie Ltd.	The wording of the remit reflects the issue of clinical and cost-effectiveness.	Thank you for your comment.

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	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	Yes	Thank you for your comment.
Timing Issues	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	There is a similar treatment licenced in 3rd line treatment of DLBC in the form of Axicel. However, Lisocel is clearly less toxic and likely equally efficacious (in terms of response/CR rates)– with less morbidity and shorter inpatient stays. This mean this is an important treatment option, especially for older patients for which the longer T cell manufacturing process is not an issue (ie not very high cadence disease). There is a definite niche and the need is relatively urgent.	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AbbVie Ltd.	AbbVie considers the background information to be factually accurate. For completeness, it is worth noting that in the first-line setting for DLBCL, polatuzumab vedotin in combination with rituximab, cyclophosphamide, doxorubicin and prednisolone (Pola + R-CHP) has also been positively recommended by NICE in 2023 (TA874).	Thank you for your comment. The background section has been updated to include details of TA874.
	Bristol Myers Squibb	The description of the disease seems too broad by referring to non-Hodgkin lymphoma (NHL). There are approximately 60 different subtypes of NHL and, therefore, large B-cell lymphoma (LBCL) should be the main focus of the	Thank you for your comment. The background section has been updated to

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		discussion. As such, we suggest amending the wording of the second paragraph as follows: "The most common high-grade NHL is diffuse large B-cell lymphoma (DLBCL). **DLBCL is a subtype of Large B-cell Lymphoma (LBCL)**. There are other forms of **LBCL**. These include primary mediastinal large B-cell lymphoma (PMBCL) and FL grade 3B (FL3B). **PMBCL and FL3B are subtypes of LBCL that are** clinically and biologically distinct from DLBCL.[1] The symptoms of NHL depend on what organ or tissue the lymphoma is affecting. **LBCL** often presents as painless lumps (enlarged lymph nodes) in the neck, armpit or groin but sometimes may start in other parts of the body such as the stomach or bowel (extranodal disease). People may also have loss of appetite, tiredness or night sweats." The draft scope refers NICE TA895 but does not explicitly specify its position in the pathway. Therefore, we suggest amending the wording as follows: "Currently, axicabtagene ciloleucel is available within the Cancer Drugs Fund **for treating relapsed or refractory diffuse large b-cell lymphoma after first-line chemoimmunotherapy**, recommended through NICE technology appraisal 895." In the paragraph under the subheading "The Technology", there is a typo and a comma should be added after "FL3B", for clarity. Therefore, we suggest amending the wording as follows:	incorporate changes suggested to shift focus to LBCL. The technology section has been updated to include a comma after "FL3B".

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		"Lisocabtagene maraleucel (Breyanzi, Bristol Myers Squibb) has a marketing authorisation in the ~~the~~ UK for the treatment of treating relapsed or refractory DLBCL, PMBCL and FL3B**,** after 2 or more systemic treatments."	
	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	1st line treatment – RPCHP is now the SOC IPI 1 if fit with DLBC L Very little use for etoposide HG BCL. Differences in treatment of PMBCL – frontline – RCHOP 14 or DAEPOCHR given to reduce need for consolidatory RT NICE NG52 did recommend – now standard practice to give CAR T if refractory disease or progression in <12m from end of first line treatment. NICE 649 – PBR available for those who did not get R P CHP first line. Otherwise outside of clinical trails treatment is limited to chemoimmunotherapy – though this might change with potential availability to Glofit GemOx pending approval at second line.	Thank you for your comment. The scope background section is intended to give a brief overview of the condition, including potentially relevant comparators. It is anticipated that what represents current clinical practice in the NHS will be explored in the evaluation. No action needed.
Population	AbbVie Ltd.	AbbVie considers that the population is appropriately defined.	Thank you for your comment.
	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	Yes - Fits in to 2nd line for auto fit and 3rd line plus for CAR T fit patients (available to frailer patients than considered auto fit)	Thank you for your comment.

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Subgroups	AbbVie Ltd.	AbbVie considers that patients unsuitable for polatuzumab vedotin represent a key subgroup of interest to the 3L+ LBCL clinical pathway in the UK.	Thank you for your comment. The subgroups in the scope are intended to be comprehensive and will be explored further in the evaluation. No action needed.
	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	Nil obvious	Thank you for your comment.
Comparators	AbbVie Ltd.	AbbVie agrees with the list of comparators outlined in the draft scope. I.e., all of the comparators listed in the draft scope are relevant and should be considered in the decision problem. We note a factual inaccuracy that should be amended ahead of the final scope. Glofitamab is incorrectly restricted to patients who are not suitable for polatuzumab vedotin. Further, the following restriction should be applied for loncastuximab tesirine and epcoritamab: “if previously had polatuzumab vedotin or if polatuzumab vedotin is contraindicated or not tolerated”.	Thank you for your comment. The comparator section has been updated to include the correct restrictions for the relevant treatments.
	Bristol Myers Squibb	The indication under scope has already been granted marketing authorisation by the MHRA for patients with relapsed or refractory DLBCL, PMBCL and FL3B**,** after 2 or more systemic therapies. As such, the scope of comparators should focus on treatment options available at the same point (3L+) in the treatment pathway. For this reason, BMS consider that the comparators that	Thank you for your comment. Thank you for your comment. The scope keeps the

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		are recommended or under evaluation for earlier lines of therapy should be removed from the scope. Furthermore, BMS consider lisocabtagene maraleucel is a suitable candidate for a cost comparison appraisal versus axicabtagene ciloleucel and, therefore, consider that only axicabtagene ciloleucel should be listed as a relevant comparator. Further details on the rationale for assessing lisocabtagene maraleucel through a cost comparison approach are included in the Comment on the draft scope section below.	potential comparators broad. No action needed.
	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	At 3rd line relapse: Axi-cel: post autograft in fit or post progression (if not auto fit)/refractory to salvage chemotherapy Glofit and epcor, Pola BR, Lonca, Chemoimmunotherapy, Clinical trial.	Thank you for your comment. No action needed.
Outcomes	AbbVie Ltd.	AbbVie considers the outcomes listed to be appropriate.	Thank you for your comment.
	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	Yes. Plus - Extra healthcare benefits not captures on QLAY assessment. Given the lower toxicity profile compared to stem cell transplant and axi-cel more of the care post infusion could be done in the ambulatory setting. There might be a potential for more of the follow up care to be given at the referring centres (rather than the CAR T centre) which will ease the financial and travel on patients and their carers	Thank you for your comment. The outcomes in the scope are intended to be comprehensive and additional benefits will be explored further in the evaluation. No action needed.

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Equality	The Royal College of Pathologists and Clatterbridge Cancer Centre, Liverpool	Ethnic minorities and patients from more deprived areas are less likely to be in enrolled in clinical trials. In the case of liso-cel the TRANSFORM study is likely to underrepresent these groups. Real world data collection may shed more light on the efficacy and safety in these patient groups. If granted licence Liso-cel will be given predominantly in the inpatient setting in tertiary care centres. The frequent face-to face follow up will also likely occur tertiary centres for at least 3months. This will mean that patients living further away from the tertiary centres (referred from Spoke hospitals) with have an associated greater travel burden. Given the reduced associated toxicity with liso-cel compared to stem cell transplant and axi-cel more of the care post infusion could be done in the ambulatory setting. There might be a potential for more of the follow up care to be given at the referring centres (rather than the CAR T centre) which will ease the financial and travel on patients and their carers. CAR T is a complex and confusing process for patients to understand – it must be remembered that a significant proportion of patients will not be able to understand written information (due to language barriers and illiteracy) – efforts must be made through translation and using various media types for patient information.	Thank you for your comment. The equalities points have been reflected in the equality impact assessment (EIA) document.

Questions for consultation	AbbVie Ltd.	**Where do you consider lisocabtagene maraleucel will fit into the existing care pathway for relapsed or refractory DLBCL, PMBCL and FL3B?** We expect that liso-cel will be used in line with the population for which it is expected to be appraised; i.e. for patients with DLBCL, PMBCL, or FL3B and with two prior systemic therapies. **Please select from the following, will lisocabtagene maraleucel be:** **A. Prescribed in primary care with routine follow-up in primary care** **B. Prescribed in secondary care with routine follow-up in primary care** **C. Prescribed in secondary care with routine follow-up in secondary care** **D. Other (please give details):** **For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** D. Other. Liso-cel will likely only be available in level 4 tertiary centres due to the intensive and highly complex mode of administration (i.e. similar to axicabtagene ciloleucel [axi-cel]. Other comparators differ to the CAR-T therapies. **Are there any considerations for the treatment of PMBCL and FL3B and how this differs to DLBCL?** AbbVie considers PMBCL, FL3B, and DLBCL to be similar in how they are treated after two prior therapies. **Would lisocabtagene maraleucel be a candidate for managed access?** No comments.	Thank you for your comment.

		Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. No comments. **Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?** The health resource costs of liso-cel are expected to be similar to currently reimbursed CAR-T therapy. However, comparators that are not CAR-T therapies (i.e. all comparators excluding axi-cel) are expected to have significantly lower health resource costs. **Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.** No comments. **Will the intervention be used to treat the same population as the comparator(s)?** No, liso-cel will not be used to treat the same population as all the comparators. The population for each comparator is different and is based on factors such as suitability for HSCT and/ or CAR-T therapy, and suitability for polatuzumab vedotin. **Is axicabtagene ciloleucel used for people with FL3B? FL3B is not included within the marketing authorisation.** No comments.	

		Overall is the technology likely to offer similar or improved health benefits compared with the comparators? No comments. **Would it be appropriate to use the cost-comparison methodology for this topic?** The NICE manual states that “Cost-comparison analyses in a technology appraisal should be used for technologies likely to provide similar health benefits at similar or lower cost than comparator(s) that are recommended in published NICE guidance for the same population”. A decision on whether to use the cost-comparison methodology should therefore consider the clinical effectiveness evidence relative to all comparators in the draft scope and the mode of administration for each comparator.	

Additional comments on the draft scope	Bristol Myers Squibb	Cost comparison questions - **Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?** Lisocabtagene maraleucel is anticipated to provide improved health benefit compared with axicabtagene ciloleucel, given the favourable safety profile of lisocabtagene maraleucel. A matching-adjusted indirect comparison (MAIC) of lisocabtagene maraleucel versus axicabtagene ciloleucel has demonstrated that lisocabtagene maraleucel has comparable efficacy to axicabtagene ciloleucel in the targeted population, that is, patients that are eligible for CAR-T therapy at 3L+. Full details of the MAIC have been published in a paper from Maloney et al. 2021, estimating the comparative efficacy and safety of lisocabtagene maraleucel from the TRANSCEND NHL 001 study (TRANSCEND NHL 001; data cut of August 2019) relative to axicabtagene ciloleucel using data from the ZUMA-1 study (data cut of August 2018) for patients with LBCL at 3L+.[2] The efficacy outcomes considered are PFS, OS, ORR and CR. Updated data cuts from the TRANSCEND NHL 001 study are available and the MAIC is being updated to incorporate these. In addition to the comparable efficacy demonstrated for lisocabtagene maraleucel and axicabtagene ciloleucel, lisocabtagene maraleucel has demonstrated a more favourable safety profile compared with axicabtagene ciloleucel. As such, lisocabtagene maraleucel is expected to be associated with reduced healthcare resource use compared with axicabtagene ciloleucel, which is expected to translate into additional cost-savings in UK clinical practice. This is partly attributed to the lower proportion of patients requiring intensive care unit admissions, associated with cytokine release syndrome and neurotoxicity.	Thank you for your comment.

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		- **Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.** Lisocabtagene maraleucel is anticipated to be used for patients with relapsed or refractory LBCL at 3L+, aligned with the current use of axicabtagene ciloleucel. - **Will the intervention be used to treat the same population as the comparator(s)?** Lisocabtagene maraleucel is licensed for a broader population than axicabtagene ciloleucel, inclusive of the subtype of FL3B. This additional subtype represents a small subgroup of all NHL cases, accounting for approximately 1% of NHL cases.[3] Given patients with FL3B tend to have comparable disease characteristics and clinical presentation as patients with DLBCL and PMBCL, these patients are expected to have similar outcomes in UK clinical practice. As such, similar clinical outcomes are anticipated for FL3B at 3L+. A similar issue was previously discussed as part of TA1048 (lisocabtagene maraleucel for treating relapsed or refractory large B-cell lymphoma after first-line chemoimmunotherapy when a stem cell transplant is suitable), where UK clinical experts indicated that DLBCL is generalisable to PMBCL and FL3B due to similar disease characteristics, treatment pathway and clinical outcomes at the second-line treatment setting. - **Is axicabtagene ciloleucel used for people with FL3B? FL3B is not included within the marketing authorisation.**	

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		Given patients with FL3B tend to have comparable disease characteristics and clinical presentation as patients with DLBCL and PMBCL, these patients are expected to have similar outcomes in UK clinical practice. Patients with FL3B make up a very small proportion of patients with LBCL. - **Overall is the technology likely to offer similar or improved health benefits compared with the comparators?** Lisocabtagene maraleucel is anticipated to provide improved health benefit compared to axicabtagene ciloleucel, as explained above. - **Would it be appropriate to use the cost-comparison methodology for this topic?** [redacted]	

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

Anthony Nolan