National Institute for Health and Care Excellence

Health Technology Evaluation

Epcoritamab for treating relapsed or refractory follicular lymphoma after 2 or more systemic treatments [ID6338]
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	Company	AbbVie agrees that epcoritamab should be evaluated as a single technology appraisal for patients with relapsed or refractory lymphoma.	Thank you for your comment.
	Follicular Lymphoma Foundation	We are satisfied with the appropriateness of evaluation and proposed evaluation route.	Thank you for your comment.
Wording	Company	The wording of the remit reflects the issue of clinical and cost-effectiveness.	Thank you for your comment.
	Follicular Lymphoma Foundation	We feel the wording reflects the issues.	Thank you for your comment.
Timing issues	Company	As outlined by clinical experts in TA892 and TA894, patients with follicular lymphoma currently require active treatment for the remainder of their life.[1,2]	Thank you for your comment.

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		Clinicians additionally noted that existing treatment strategies for patients with relapsed/refractory follicular lymphoma after two or more lines of treatment include cycling through anti-CD20 therapies (e.g. rituximab as part of a chemotherapy regimen or obinutuzumab in combination with bendamustine); this highlights an urgent need for more treatment options for patients who relapse or become refractory to existing treatment regimens.[1,2] In addition, patients with relapsed/refractory follicular lymphoma in later lines of therapy (3L+) have a lower survival rate than patients in earlier lines of therapy, highlighting an area of unmet need in the target population.[3,4] The opinions from the clinical experts in TA892 and TA894 have been supported during AbbVie's engagement with clinicians in a UK advisory board and through individual consultations.	
	Follicular Lymphoma Foundation	There is an unmet need for patients with relapsed and refractory FL, to have access to effective treatments who otherwise have limited alternatives.	Thank you for your comment.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Company	AbbVie consider the background information to be factually accurate but does not fully reflect the symptom burden or the low survival rates experienced by patients with relapsed or refractory follicular lymphoma. As noted in the NICE Final Scope for TA627, follicular lymphoma is the most common type of indolent non-Hodgkin's lymphoma.[5] Owing to the indolent nature of the condition the majority of people (80%) therefore present with advanced disease (stage III to IV) at diagnosis.	Thank you for your comments. We were not aware of a reference that cited that follicular lymphoma is the most common type of non-Hodgkin's lymphoma or for the

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		As noted by patient experts in TA892 and TA894, living with follicular lymphoma can cause severe psychological distress and is associated with a substantial detriment to patients' health-related quality of life (HRQoL).[1,2] In addition, patients report significant and burdensome symptoms relating to extreme fatigue and unexplained fever.[6,7] AbbVie believe that the background information should be expanded to more completely reflect the patient burden of late-stage follicular lymphoma. AbbVie note that the background section states that the "The 5-year survival rate for those diagnosed with follicular lymphoma is around 90%." This statistic describes the intermediate risk group, as defined by the FLIPI scale, and does not specifically consider patients with disease that is relapsed/refractory to several lines of prior therapy, which is the target population for this appraisal.[8] AbbVie would prefer that this text be rewritten as "Patients in later lines of therapy have notably worse survival outcomes compared with patients in earlier lines of therapy.[3,4] Indeed, a systematic literature review and meta-analysis of 20 US/European studies found that median overall survival among patients with ≥2 prior treatments was less than five years (56.6 months) while median progression-free survival was less than one year (9.8 months), which worsens in patients with ≥3 prior treatments and each subsequent prior line of therapy.[4]" In addition, AbbVie believe that the worsening prognosis with each relapse should be outlined within the background section, e.g. "*Patients who have relapsed have worse survival outcomes at subsequent lines of treatment and a poorer HRQoL compared with patients who have not relapsed, as demonstrated in a systematic literature review followed by meta-analysis, and UK HRQoL data collection*.[4,9,10]"	80% figure of those who present with advanced disease. However, the scope has been changed to cite that it is the most common low-grade lymphoma (Cancer Research UK) and that it can present at a later stage of disease (Lymphoma Action UK). The sentence on survival has been amended to reflect that the survival may be less when additional risk factors are present or after more prior lines of therapy. This section is intended to be a brief summary. The company will be able to elaborate on the burden for this population in its submission.

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	Follicular Lymphoma Foundation	We are satisfied with the accuracy and completeness	Thank you for your comments.
Population	Company	The proposed population wording is broader than our anticipated licenced population: [redacted]	Thank you for your comments. While the proposed marketing authorisation wording is marked as confidential, we note that the line of therapy is included in public information about the NHL-1 trial, so have amended this section, and also changed the title.
	Follicular Lymphoma Foundation	Population is defined appropriately	Thank you for your comments.
Subgroups	Company	AbbVie does not believe that there are any subgroups that should be examined separately.	Thank you for your comments.
	Follicular Lymphoma Foundation	Patients whose disease recurs early after initial therapy (POD24) have unique challenges and may benefit more from this treatment	Thank you for your comments. The population addressed within this appraisal includes on people who

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			have had prior treatments.
Comparators	Company	Of the comparators listed in the draft scope, AbbVie consider rituximab with chemotherapy to be the primary comparator. Obinutuzumab with bendamustine (OB) and rituximab with lenalidomide (R^2) are most often used in earlier lines of relapsed or refractory follicular lymphoma, in line with clinical expert opinions presented in TA892, TA894 and a clinical advisory board organised by AbbVie. Further, rituximab monotherapy and best supportive care are used in later lines of treatment or reserved for patients who are not fit enough to receive an active intervention. Liso-cel is not considered a comparator as it is not currently recommended by NICE and is under evaluation for patients with large B-cell lymphomas (including high-grade follicular lymphoma), which is outside the scope of this appraisal.	Thank you for your comments. TA894 notes that lenolidomide with rituximab or obinutuzumab with bendamustine may be offered after first relapse, or after an additional rituximab-chemotherapy combinations followed by rituximab maintenance. As this would mean it could be offered after 2 or more systemic treatments in line with the company's proposed positioning, these have been retained as comparators. TA894 noted that whilst rituximab monotherapy is usually used as a first-line treatment, it

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			may be used after prior treatment in disease that is resistant or intolerant to chemotherapy. Also, TA894 note that the committee broadly accepted both best supportive care and rituximab monotherapy to be excluded as comparators. However, TA894 was in a population after 3 or more systemic treatments and it is not clear if this conclusion apples after 2 or more systemic treatments. So, best supportive care and rituximab monotherapy have been retained as comparators. Lisocabtagene maraleucel has been removed as a comparator. The company will be

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			able to provide more information at submission about the comparators which it considers relevant in NHS clinical practice, including providing more detail from the company's clinical advisory board following guidance from sections 3.3.21 – 3.3.23 of the NICE's health technology evaluations manual.
	Follicular Lymphoma Foundation	Should Zanubrutinib (+ CD20) be considered, recently approved in US.	Zanubrutinib with obinutuzumab has not yet been assessed by NICE (see TA978) and so cannot be considered a comparator.
Outcomes	Company	AbbVie considers the outcomes listed to be appropriate and believe these measures will capture the most important health benefits in patients treated with epcoritamab.	Thank you for your comments.

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	Follicular Lymphoma Foundation	Treatment-free interval will impact HRQOL; monitoring for late infections/need for prophylactic IVIG may affect HRQOL and cost/QALY	Thank you. The administration of treatments including use of any monitoring or prophylaxis required in the NHS should be captured within the economic model.
Equality	Company	No further inequalities have been identified.	Thank you for your comments.
	Follicular Lymphoma Foundation	We are satisfied with the equality.	Thank you for your comments.
Other considerations	Company	None	N/A
	Follicular Lymphoma Foundation	None	N/A
Questions for consultation	Company	**Where do you consider epcoritamab will fit into the existing care pathway for relapsed or refractory follicular lymphoma?** We envisage that epcoritamab will be used in line with the UK market authorisation: [redacted]	Thank you for your comments. Please see the response regarding the listed comparators above.

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		Please select from the following, will epcoritamab 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)** Options C and D – Epcoritamab monotherapy will be prescribed in secondary care with routine follow-up also being performed in secondary care. Additionally, epcoritamab will be prescribed in tertiary care via specialist cancer centres with follow-up in tertiary or secondary care. **For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** AbbVie do not anticipate the prescribing and routine follow-up to differ for epcoritamab monotherapy compared with the comparators outlined previously or for subsequent treatments. Current standard of care requires significant inpatient time due to regular infusions whereas epcoritamab is administered subcutaneously and is expected to incur a smaller healthcare resource burden. **Are all the listed comparators appropriate comparators, such as obinutuzumab with bendamustine followed by obinutuzumab maintenance and rituximab monotherapy?** As outlined above, AbbVie consider rituximab with chemotherapy to be the primary comparator. Obinutuzumab with bendamustine (OB) and rituximab with lenalidomide (R^2) are most often used in earlier lines of relapsed or refractory follicular lymphoma, in line with clinical expert opinions presented in	

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		TA892, TA894 and a clinical advisory board organised by AbbVie. Further, rituximab monotherapy and best supportive care are used in later lines of treatment or reserved for patients who are not fit enough to receive an active intervention. Liso-cel is not considered a comparator as it is not currently recommended by NICE and is under evaluation for patients with large B-cell lymphomas (including high-grade follicular lymphoma), which is outside the scope of this appraisal. **Should any subgroups be considered?** AbbVie do not believe that there are any subgroups that should be examined separately. **Would epcoritamab be a candidate for managed access?** Based on currently available data from the EPCORE NHL-1 trial, AbbVie expect epcoritamab monotherapy to be a cost-effective use of resources for treating patients with relapsed or refractory follicular lymphoma and therefore suitable for routine commissioning. However, a managed access agreement may be considered if there is any need to address residual uncertainty. **Do you consider that the use of epcoritamab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** As outlined previously, a positive recommendation for epcoritamab in this patient population would offer a valuable new treatment regimen in people with relapsed or refractory follicular lymphoma.	

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		Currently, patients with relapsed or refractory follicular lymphoma receive chemo-immunotherapy regimens which can be associated with intense mental and physical side effects.[2] Introducing epcoritamab monotherapy as a treatment option in this setting provides a novel treatment option and may offer increased hope and improved treatment tolerability in patients with relapsed or refractory follicular lymphoma.	
	Follicular Lymphoma Foundation	None	N/A
Additional comments on the draft scope	Company	None	N/A
	Follicular Lymphoma Foundation	None	N/A

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

Lymphoma Action

References from company comments:

1. National Institute for Health and Care Excellence. Mosunetuzumab for treating relapsed or refractory follicular lymphoma [TA892]. 2023. Available at: https://www.nice.org.uk/guidance/ta892 [Accessed 19 November 2024].
2. National Institute for Health and Care Excellence. Axicabtagene ciloleucel for treating relapsed or refractory follicular lymphoma [TA894]. 2023. Available at: https://www.nice.org.uk/guidance/ta894 [Accessed 19 November 2024].
3. Wästerlid T, Dietrich CE, Oksanen A, et al. Treatment sequencing and impact of number of treatment lines on survival in follicular lymphoma: A national population-based study. eJHaem. 2024;5(3):516-26.

4. Kanters S, Ball G, Kahl B, et al. Clinical outcomes in patients relapsed/refractory after ≥2 prior lines of therapy for follicular lymphoma: a systematic literature review and meta-analysis. BMC Cancer. 2023;23(1):74.
5. National Institute for Health and Care Excellence. Lenalidomide with rituximab for previously treated follicular lymphoma and marginal zone lymphoma - Final Scope. 2019. Available at: https://www.nice.org.uk/guidance/ta627/documents/final-scope [Accessed 20 November 2024].
6. Lymphoma Action. Follicular lymphoma. 2023. Available at: https://lymphoma-action.org.uk/types-lymphoma-non-hodgkin-lymphoma/follicular-lymphoma [Accessed
7. Cancer Research UK. Follicular Lymphoma. 2024. Available at: https://www.cancerresearchuk.org/about-cancer/non-hodgkin-lymphoma/types/follicular-lymphoma [Accessed 19 November 2024].
8. Cancer Research UK. Survival for non-Hodgkin lymphoma. 2024. Available at: https://www.cancerresearchuk.org/about-cancer/non-hodgkin-lymphoma/survival [Accessed 19 November 2024].
9. Pettengell R, Donatti C, Hoskin P, et al. The impact of follicular lymphoma on health-related quality of life. Annals of Oncology. 2008;19(3):570-6.
10. Lee YP, Lee MS, Yoon SE, et al. Survival Outcomes of Patients with Follicular Lymphoma after Relapse or Progression: A Single-Center Real-World Data Analysis. J Oncol. 2022;2022:2263217.