National Institute for Health and Care Excellence

Health Technology Evaluation

Tafasitamab with lenalidomide and rituximab for treating relapsed or refractory follicular lymphoma after 1 or more systemic treatments [ID6413]

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	Incyte (company)	We welcome the evaluation of this topic and agree the single technology appraisal route proposed is appropriate for this evaluation.	Thank you for your comment. No action needed.
	Follicular Lymphoma Foundation	We are satisfied with the appropriateness of evaluation and proposed evaluation route.	Thank you for your comment. No action needed.
Wording	Incyte (company)	Yes, the wording of the remit is appropriate. Please note, a later question for consultation asks “where do you consider tafasitamab will fit into the existing care pathway for follicular and marginal zone lymphoma” – this does not reflect the wording of the remit which correctly limits the decision problem to the follicular lymphoma (FL) pathway.	Thank you for your comments. The question has been removed from the final scope.

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	Follicular Lymphoma Foundation	Tafasitamab has been studied, and is being recommended to be given in combination with lenalidomide + rituximab. One of the comparators listed is lenalidomide, implying as a single agent, but in the clinic and in the NICE Technology Asessment referred to for lenalidomide it is given with rituximab. There are also caveats about lenalidomide drug supply, which may need to be updated as generics are or will be available. These considerations will affect cost and use of the tafa-R2 regimen as tested.	Thank you, we have updated the list of comparators to make it clear that lenalidomide is given in combination with rituximab.
Timing issues	Incyte (company)	There is an urgent need for new treatment options in relapsed or refractory follicular lymphoma (R/R FL). While FL is typically responsive to front-line treatment of anti-CD20 (rituximab or obinutuzumab) with chemotherapy, almost all patients eventually relapse. The disease becomes more difficult to treat with each subsequent recurrence and progression-free survival times shorten with each line of treatment.[1, 2] The combination of tafasitamab plus lenalidomide and rituximab addresses an unmet need in the second-line (2L) and third-line (3L) treatment of R/R FL by offering a novel regimen with a dual-target anti-CD19 and anti-CD20 mechanism of action.[3, 4] This innovative mechanism of action overcomes the limitations of current 2L and 3L treatment options that largely replicate front-line treatment and are only built around the anti-CD20 backbone, to which FL becomes increasingly resistant over time.[1, 2] The InMIND Phase III randomised controlled trial (RCT) provides data demonstrating statistically significant and clinically meaningful improvements in treatment response and progression-free survival outcomes with tafasitamab plus lenalidomide and rituximab versus current standard of care	Thank you for your comments. No action needed.

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		(lenalidomide and rituximab).[5] Such benefit was observed in all patient groups, regardless of patients' treatment history or baseline disease characteristics, and including those with early progression of disease within 24 months of initial treatment (POD24), for whom outcomes with existing treatment options remain poor.[6]	
	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. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Incyte (company)	Please add to the description of non-Hodgkin lymphomas (NHL) the following information: *"NHLs can be low grade, or indolent, meaning slow growing, or high-grade, meaning they grow faster and more aggressively."* Please update the first sentence of the second paragraph to more accurately state: *"Follicular lymphomas are commonly staged from I (localized and has best prognosis) to IV (spread to multiple organs and locations in the body and has worse prognosis)"* Please update the final sentence of the fourth paragraph to more accurately reflect CRUK data and Rivas-Delgado paper referenced:	This information is already supplied in the second paragraph. No action needed. Thank you, the sentence has been amended. We have amended the sentence.

Section	Consultee/ Commentator	Comments [sic]	Action
		"Survival is lower for people with high-risk disease and for those whose disease has relapsed or is refractory (does not respond to treatment) with survival decreasing with each subsequent relapse" Please update the first-line treatment description to more accurately state: *"First-line treatment for follicular lymphoma includes 'watch and wait' or rituximab monotherapy for people with stage IIA disease who are asymptomatic, radiotherapy for people with localised Stage IIA disease, or CD20-chemotherapy (rituximab-chemotherapy or obinutuzumab-chemotherapy) for people with symptomatic Stage IIA-IV disease"* Please update the treatment description for R/R FL to more accurately state: *"For follicular lymphoma that is refractory, or relapses after initial response to treatment, NICE recommended treatment options include:* • *obinutuzumab with bendamustine followed by obinutuzumab maintenance for follicular lymphoma that did not respond to or progressed up to 6 months after treatment with rituximab or a rituximab-containing regimen (NICE technology appraisal guidance 629)* • *lenalidomide with rituximab for previously treated follicular lymphoma (grade 1 to 3A); NICE technology appraisal guidance 627)*	The background section of the scope is intended to give a brief overview of the condition and treatment pathway. As first line treatment is not the focus of this appraisal, it's appropriate to give a broad overview. We have added 'watch and wait' to the list of treatment options Description updated.

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		• *rituximab alone or in combination with chemotherapy for stage 3 or 4 follicular lymphoma (NICE technology appraisal 137).* *People in remission for the second time (or later) who meet the eligibility criteria may also be offered stem cell transplantation."*	
	Follicular Lymphoma Foundation	See comments under wording. Also, note that the lymphoma guidelines published in 2016 need to be updated as the field has dramatically changed since then.	Thank you for your comment. Action noted in Wording section.
Population	Incyte (company)	Please note, a later question for consultation asks *"where do you consider tafasitamab will fit into the existing care pathway for follicular and marginal zone lymphoma"* The wording of the population to consider for this appraisal should be 'adults with relapsing or refractory follicular lymphoma after 1 or more systemic treatments'. This aligns with the anticipated marketing authorisation for tafasitamab which includes follicular lymphoma only.	Thank you for your comments. The question has been removed in the final scope.
	Follicular Lymphoma Foundation	Yes [the population is defined appropriately]	Thank your for your comment. No action needed.
Subgroups	Incyte (company)	Treatment options are guided by prior line(s) of treatment and response to prior treatment in clinical practice (see comparators comments below). Tafasitamab plus lenalidomide and rituximab offers a new treatment in the 2L or 3L setting. The proposed subgroup of 'adults with relapsing or refractory follicular lymphoma after 2 or more systemic treatments' is therefore appropriate to consider separately to the total population.	Thank you for your comments. NICE keeps the subgroups list inclusive. Subgroups may be discussed by the committee if it feels

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		Other subgroups proposed are less likely to impact treatment options in the relapsed or refractory setting and therefore do not need considering separately to the total population. There are other factors such as POD24 disease or intermediate to high Follicular Lymphoma International Prognostic Index (FLIPI) scores that more strongly indicate an aggressive disease course and thus poorer prognosis. Tafasitamab plus lenalidomide and rituximab is shown to be clinically effective across all patient types, irrespective of baseline disease characteristics.[5]	they are appropriate and evidence allows.
	Follicular Lymphoma Foundation	Nothing to add	No action needed.
Comparators	Incyte (company)	Recently published European Society for Medical Oncology (ESMO) guidelines recommend the use of tafasitamab plus lenalidomide and rituximab as a 2L or 3L treatment option.[7] Alternative 2L treatment options included in the guidelines are lenalidomide with rituximab or anti-CD20 with chemotherapy. Of the alternative 3L treatment options included in the guidelines, only lenalidomide with rituximab or rituximab monotherapy are available to patients in England and Wales, but rituximab monotherapy is only recommended for elderly or frail patients after prior long-term remissions – patients who are unlikely to be candidates for tafasitamab plus lenalidomide with rituximab. Please update the comparators list to more accurately reflect the current care pathway split by line of therapy:	Thank you for your comments. We have removed best supportive care as a comparator. NICE keeps the comparators list inclusive. The most appropriate comparators will be discussed by the committee. In its evidence submission, the company should

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		"Established clinical management without tafasitamab. *Treatment choice will depend on previous treatments, and how effective those treatments were.* ***Second line treatment choices include:*** *1. Lenalidomide with rituximab* *2. Rituximab with chemotherapy (with or without rituximab maintenance)* Although NICE also recommend obinutuzumab with bendamustine followed by obinutuzumab maintenance, this is restricted to FL that did not respond to or progressed up to 6 months after treatment with rituximab or a rituximab-containing regimen, and <5% of patients are eligible for such treatment in clinical practice.[8, 9] Market share data show 0% use of obinutuzumab in the R/R FL setting year to date.[10] Therefore, to be removed as comparator for the 2L setting. Only lenalidomide with rituximab or rituximab with chemotherapy can therefore be considered established 2L treatment choices. Rituximab with chemotherapy will be used to treat relapsing or refractory patients whose FL responded well to frontline treatment of the same nature. This allows lenalidomide with rituximab to be reserved for 3L use as the only treatment regimen with a different mechanism of action to frontline therapy available to patients in England and Wales. For patients whose FL did not respond well to frontline treatment, lenalidomide with rituximab will be used in the 2L setting. Market share data support clinical expert estimates that 30-40% of R/R FL patients receiving 2L therapy are treated with lenalidomide with rituximab and 60-70% are treated with rituximab with chemotherapy.[8, 10]	provide a clear rationale for excluding any comparators listed in the final scope.

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		Third line and beyond treatment choices include: *3. Lenalidomide with rituximab* By the time patients reach the 3L setting, lenalidomide with rituximab is the only treatment choice available to patients in England and Wales. All patients who received rituximab with chemotherapy in the 2L setting and require further treatment will receive lenalidomide with rituximab (unless contraindicated). Patients who received lenalidomide with rituximab in the 2L setting have no treatment options remaining once their disease has progressed. Clinicians may resort to revisiting rituximab with chemotherapy treatment in these patients but only because there are no other options available; this is not a recommended regimen in the third-line and beyond setting in the recent ESMO guideline and as these patients will have already received lenalidomide with rituximab in the 2L setting, or are otherwise not suitable for lenalidomide with rituximab in the 3L+ setting (by virtue of the fact they are receiving rituximab with chemotherapy), they are not likely to be candidates for tafasitamab plus lenalidomide with rituximab in the 3L+ setting. Therefore, although market share data and clinical experts indicate that 60% of R/R FL patients receiving 3L therapy are treated with lenalidomide with rituximab and 30% are treated with rituximab with chemotherapy,[8, 10] rituximab with chemotherapy would not be a relevant comparator for tafasitamab plus lenalidomide with rituximab in the third line setting and beyond.	

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		None of the other comparators proposed in the draft scope are standard treatments currently used in the NHS with which tafasitamab should be compared: 4. Rituximab alone is only used to treat people with stage IIA disease who are asymptomatic (first-line) or as maintenance following R-chemotherapy 5. Epcoritamab is the subject of an ongoing evaluation and is targeting a later line positioning (relapsed or refractory follicular lymphoma after 2 or more systemic treatments). Even if it is accepted for routine commissioning as a third-line treatment choice in Q4 2025 it will not be established clinical management by the time of the tafasitamab evaluation (also Q4 2025) Best supportive care is only used to manage patients not fit enough to receive active treatment and therefore would not be displaced by tafasitamab	
	Follicular Lymphoma Foundation	Lenalidomide should note that it is given with rituximab	Thank you, this has been amended.
Outcomes	Incyte (company)	Please update the outcome measures to be considered to include time to next treatment. Alongside the outcomes listed, tafasitamab plus lenalidomide with rituximab also represents an important health related benefit, reflected in a proven treatment-free, progression-free period of living. [1]	We have updated the outcome measures
	Follicular Lymphoma Foundation	Yes [the outcomes listed are appropriate]	Thank you, no action needed.

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Equality	Incyte (company)	No equality issues are foreseen	Thank you, no action needed.
	Follicular Lymphoma Foundation	We are satisfied with the equality.	Thank you, no action needed.
Other considerations	Follicular Lymphoma Foundation	As noted above, this is a 3-drug regimen, and cost and availability of lenalidomide for this population may be changing which likely will affect cost-benefit analyses.	Thank you for your comment. The cost of concurrent treatments in the NHS at the time of the appraisal will be taken into account.
Questions for consultation	Incyte (company)	*Where do you consider tafasitamab will fit into the existing care pathway for follicular and marginal zone lymphoma?* Recently published European Society for Medical Oncology (ESMO) guidelines for Follicular lymphoma recommend the use of tafasitamab plus lenalidomide and rituximab as a 2L or 3L treatment option for R/R FL.[7] This is the proposed positioning for use in the existing care pathway in England and Wales. Please see previous comments confirming that tafasitamab is only being positioned in the existing care pathway for FL, aligning with the anticipated marketing authorisation for tafasitamab. Tafasitamab plus lenalidomide and rituximab will primarily displace current use of lenalidomide plus rituximab, but is also expected to displace some current use of rituximab with chemotherapy in the 2L setting [8, 9]	Thank you for your comments. References to marginal zone lymphoma have been removed.

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		Please select from the following, will tafasitamab 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.* Tafasitamab is expected to be prescribed in secondary care with routine follow-up in secondary care (Option C). Comparators and subsequent treatments are also prescribed and followed up in this setting.	Thank you for confirming.
		Would tafasitamab be a candidate for managed access? Based on currently available evidence, we believe tafasitamab offers a clinically effective and cost effective treatment option to the NHS and therefore is a candidate for routine commissioning. However, if the evaluation concludes there are uncertainties, we are open to a managed access routing to address these. The inMIND trial is ongoing with final overall survival analysis planned after the last participant has completed a minimum of 5 years of post-treatment follow-up. This is anticipated in 2029.	Thank you for your comments.
		Do you consider that the use of tafasitamab 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.*	Thank you for your comments. Any potential uncaptured benefits will be considered by the

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		Tafasitamab is the first CD19-targeting treatment to be introduced to the FL care pathway. The combination of tafasitamab plus lenalidomide and rituximab results in dual targeting of CD19 and CD20 – this represents a step-change in FL disease management. Although the main health-related benefits of this novel treatment approach will be captured in the QALY calculation, it is difficult to fully quantify the value of such a step-change in FL disease management, which has been underserved for several years, and the hope this extension to treatment options can bring to patients and their families. *Please let us know if you think that the proposed remit and scope may need changing in order to promote equality* No equality issues are foreseen	committee during the appraisal process.

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

Lymphoma Action

References

1. Batlevi CL, Sha F, Alperovich A, et al. Follicular lymphoma in the modern era: survival, treatment outcomes, and identification of high-risk subgroups. *Blood Cancer J*. 2020; 10(7):74.
2. Casulo C, Larson MC, Lunde JJ, et al. Treatment patterns and outcomes of patients with relapsed or refractory follicular lymphoma receiving three or more lines of systemic therapy (LEO CReWE): a multicentre cohort study. *Lancet Haematol*. 2022; 9(4):e289–e300.
3. Wang L, Fang C, Kang Q, et al. Bispecific CAR-T cells targeting CD19/20 in patients with relapsed or refractory B cell non-Hodgkin lymphoma: a phase I/II trial. *Blood Cancer J*. 2024; 14(1):130.
4. Patra-Kneuer M, Chang G, Xu W, et al. Activity of tafasitamab in combination with rituximab in subtypes of aggressive lymphoma. *Frontiers in immunology*. 2023; 14:1220558.
5. Sehn L, Hubel K, Luminari S, et al. Outcomes From the Pahse 3 inMIND Study of Tafasitamab Plus Lenalidomide and Rituximab for Patients With Relapsed/Refractory Follicular Lymphoma. International Conference on Malignant Lymphoma (18th ICML). Lugano, Switzerland. 17–21 June 2025. 028.
6. Casulo C, Dixon JG, Le-Rademacher J, et al. Validation of POD24 as a robust early clinical end point of poor survival in FL from 5225 patients on 13 clinical trials. *Blood*. 2022; 139(11):1684–93.
7. Eyre TA, Cwynarski K, d'Amore F, et al. Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2025.
8. Incyte Corporation. Advisory Board Meeting: UK Follicular Lymphoma. 14 February 2025. Data on file.
9. Incyte Corporation. Clinical Validation Meetings: UK Follicular Lymphoma. August 2025 2025. Data on file.
10. Incyte Corporation. Market Share Data: UK Follicular Lymphoma. August 2025 2025. Data on file.