

Mosunetuzumab for treating relapsed or refractory follicular lymphoma

Technology appraisal guidance

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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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1 Recommendations

- 1.1 Mosunetuzumab is not recommended, within its marketing authorisation, for treating relapsed or refractory follicular lymphoma in adults who have had 2 or more systemic therapies.
- 1.2 This recommendation is not intended to affect treatment with mosunetuzumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Treatment options for relapsed or refractory follicular lymphoma are limited and there is no standard care. After 2 previous therapies, treatment may include rituximab plus lenalidomide or rituximab plus chemotherapy.

Clinical evidence suggests that follicular lymphoma responds to treatment with mosunetuzumab, so the cancer may not get worse as quickly. But these results are from a trial that did not compare mosunetuzumab with placebo or any other treatment options. Indirect comparisons of mosunetuzumab with other treatment options are very uncertain with inconsistent results.

The cost-effectiveness estimates for mosunetuzumab are highly uncertain and do not represent a cost-effective use of NHS resources. So, mosunetuzumab is not recommended for routine use in the NHS.

Mosunetuzumab cannot be recommended with managed access. This is because mosunetuzumab is not likely to be cost effective. Also, more data collected in the Cancer Drugs Fund would not resolve the high level of uncertainty.

2 Information about mosunetuzumab

Marketing authorisation indication

- 2.1 Mosunetuzumab (Lunsumio, Roche) is indicated for 'the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for mosunetuzumab](#).

Price

- 2.3 Mosunetuzumab costs £220 per 1 mg/1 ml concentrate for solution for infusion vial and £6,600 per 30 mg/30 ml concentrate for solution for infusion vial (excluding VAT; company submission). The cost per course of treatment is £66,660 for 8 cycles and £126,600 for 17 cycles.
- 2.4 The company has a commercial arrangement, which would have applied if mosunetuzumab had been recommended.

3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Roche, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The condition and current treatment

Unmet need

- 3.1 Follicular lymphoma is a type of indolent, low-grade non-Hodgkin lymphoma. The patient expert noted that it is an incurable cancer that will return and people with the condition will need subsequent treatment for life. They explained that there is always the fear of relapse when living with the disease. Clinical experts noted that survival and remission duration worsen with each successive relapse. They explained that there is no current standard care and a lack of treatment options. This creates difficult treatment choices from a mixed basket of options for relapsed or refractory follicular lymphoma. The clinical experts explained that when selecting treatment, factors such as a person's age, frailty and wishes are considered. The patient expert noted that people value alternatives to chemotherapy. Stakeholders commented on the draft guidance that mosunetuzumab could provide an extra line of treatment. The committee concluded that new treatment options would be welcomed by patients and clinicians.

Current treatment

- 3.2 Clinical experts noted that in previously treated follicular lymphoma, treatment options include:
- lenalidomide with rituximab (see [NICE technology appraisal guidance on lenalidomide with rituximab for previously treated follicular lymphoma](#))

- obinutuzumab with bendamustine (see [NICE technology appraisal guidance on obinutuzumab with bendamustine for treating follicular lymphoma after rituximab](#)) and
- rituximab plus chemotherapy followed by rituximab maintenance therapy.

They explained that for rituximab plus chemotherapy, people are likely to have rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP), rituximab plus cyclophosphamide, vincristine and prednisolone (R-CVP) or rituximab plus bendamustine. Clinical experts noted that after first-line treatment, R-CHOP and R-CVP may be favoured over rituximab plus bendamustine. This is because rituximab plus bendamustine can be associated with greater toxicity. They noted that people aged over 70 do not tolerate bendamustine well. The committee noted that older people in mutual carer relationships would benefit from a non-chemotherapy treatment. Clinical experts explained that because of the long natural history of follicular lymphoma, some people have had potentially less effective treatments such as rituximab plus chemotherapy at second line. Others have had newer options such as rituximab plus lenalidomide or obinutuzumab plus bendamustine. So, the treatment landscape is complicated and changing. The experts noted that at third line and beyond, treatment choice will be influenced by previous therapy. This means people will have either rituximab plus lenalidomide if they have not had it before, or rituximab plus chemotherapy if they previously had rituximab plus lenalidomide. Rituximab plus chemotherapy may include rituximab plus bendamustine if a person is well enough and has not already had it. The NHS England Cancer Drugs Fund clinical lead noted that across second- and third-line treatment, more people currently have rituximab plus bendamustine than rituximab plus lenalidomide in NHS practice. The committee noted that obinutuzumab plus bendamustine is rarely used third line, so it is not a relevant comparator for this appraisal. The committee concluded that treatments used at third line or later are rituximab plus lenalidomide and rituximab plus chemotherapy, which may include rituximab plus bendamustine.

Clinical evidence

Study population and generalisability

- 3.3 GO29781 was a phase 2, multicentre, single-arm, non-comparative study in people with relapsed or refractory haematologic malignancies expected to express the CD20 antigen. Clinical evidence for mosunetuzumab is from a pivotal cohort of 90 people with relapsed or refractory follicular lymphoma who have had at least 2 previous therapies that included both an anti-CD20 inhibitor and an alkylating agent. Patients had a median age of 60. The company noted that its clinical advisers considered the study population broadly representative of people who have had 2 or more previous treatments for follicular lymphoma in UK clinical practice, in terms of age (UK median age around 66), daily functioning, disease stage and prognosis. The EAG noted that only 2% of people in the study were from the UK and most were from the US (44%). Clinical experts confirmed that the study population broadly reflects UK clinical practice. They noted that the study population had a higher proportion of people with factors known to be associated with poorer outcomes for follicular lymphoma that is treated at third line or later. More than 50% of people in the study had cancer that was refractory to both an anti-CD20 inhibitor and an alkylating agent. Also, more than 50% had disease progression within 24 months after the first systemic therapy. The committee concluded that the study population included people with a poor prognosis and was broadly generalisable to UK clinical practice.

Outcomes and results

- 3.4 The primary efficacy endpoint in the GO29781 pivotal cohort was complete response as assessed by an independent review facility. In the primary analysis (March 2021), 58% of people who had mosunetuzumab had a complete response. This was statistically significantly higher than a historical control complete response rate of 14% in a similar patient population. After a median follow up of 18 months (August 2021), 60% of people who had mosunetuzumab had a complete tumour response. Median progression-free survival with mosunetuzumab was 17.9 months.

Median overall survival was not reached. Clinical experts stated that the complete response rate seen with mosunetuzumab was very encouraging. The committee noted that it would have liked to have seen results from a phase 3 trial of mosunetuzumab compared with standard care treatments. The lack of any comparative data makes it difficult to interpret the trial results. The company explained that a phase 3 trial was planned with idelalisib as the comparator, but this did not go ahead because of emerging safety findings for the comparator drug class. The committee noted that the most common adverse event in the single-arm study of mosunetuzumab was cytokine release syndrome, which was seen in more than 40% of people. However, more than 95% of people with cytokine release syndrome had less severe events (grade 1 or 2). The company noted that cytokine release syndrome usually happened in the first treatment cycle on day 15 when the dose level was being increased. They added that it could be effectively managed with good clinical awareness and preventative treatment when starting mosunetuzumab. Clinical experts noted that mosunetuzumab was well tolerated after 1 month. It was not associated with lingering effects that would be seen with chemotherapy, and the need for treatment every 3 weeks after the first cycle of mosunetuzumab was manageable. The experts explained that mosunetuzumab could be administered in non-specialist centres if staff are trained to identify and manage cytokine release syndrome. The committee concluded that mosunetuzumab was potentially a promising new treatment option in relapsed or refractory follicular lymphoma.

Indirect treatment comparisons

Comparators

- 3.5 Because of the lack of direct comparative evidence for mosunetuzumab, the company did indirect treatment comparisons for the outcomes of overall survival, progression-free survival, tumour response and stopping treatment because of adverse events. Stakeholders commented on the draft guidance that real-world datasets could potentially have been incorporated into the indirect treatment comparisons. The committee noted some of these included people in the UK. The company noted that

these datasets were not used because they included people who had treatment at an earlier line of therapy or included a mixed histology (not all follicular lymphoma). The company used rituximab plus lenalidomide and rituximab plus bendamustine in its indirect comparisons with mosunetuzumab. Rituximab plus lenalidomide and rituximab plus chemotherapy, which may include rituximab plus bendamustine, are used at third line or later in follicular lymphoma (see [section 3.2](#)). The company acknowledged that in practice, people may have other types of chemotherapy with rituximab (such as R-CHOP and R-CVP). It explained that an indirect comparison with R-CHOP was attempted but was not feasible because of several limitations. The EAG agreed that an indirect comparison with R-CHOP could not be done reliably. The committee noted that in the company's approach, the comparator rituximab plus bendamustine would also be used to represent other types of rituximab plus chemotherapy in the indirect comparison. Clinical experts suggested that it is not plausible for rituximab plus bendamustine to represent rituximab used in combination with other types of chemotherapy. However, there is limited data to challenge whether rituximab plus bendamustine is representative of rituximab plus chemotherapy had by people at third line or later. The clinical experts added that if rituximab plus bendamustine is representative, it sets the bar high for the indirect treatment comparison because people having treatment will be younger and fitter. They noted that differences seen between rituximab plus bendamustine and other rituximab plus chemotherapy combinations at first line may be less evident at third line, but it is not clear if this is the case. The committee concluded that rituximab plus lenalidomide is a suitable comparator for mosunetuzumab in an indirect treatment comparison. It also concluded that rituximab plus bendamustine is a reasonable comparator, but whether it is representative of other types of rituximab plus chemotherapy is highly uncertain.

Comparison with rituximab plus lenalidomide

- 3.6 For the comparison of mosunetuzumab with rituximab plus lenalidomide, the company used the AUGMENT study of rituximab plus lenalidomide, for which it did not have access to individual patient data. Therefore, a matching-adjusted indirect comparison (MAIC) was done. In this, the GO29781 study cohort was matched and statistically adjusted to

resemble that of the AUGMENT study population, to predict treatment effects as if mosunetuzumab had been evaluated in the AUGMENT study population. The EAG noted that some important prognostic factors and effect modifiers were not included in the MAIC. These were: number of previous therapies, refractory status to previous anti-CD20 inhibitor, previous stem cell transplant and size of the largest lymph node lesion. The company explained that it was not possible to match for these variables because data was not available from AUGMENT. The EAG also noted that the variable 'low haemoglobin' should have been excluded from the MAIC because it was taken from the full GO29781 study population, not the relevant study cohort. Clinical experts noted that 'number of previous therapies' was an important prognostic variable missing from the MAIC. They also stated that stem cell transplant is increasingly uncommon in this population so is less relevant. The EAG noted that having several unmatched variables in the MAIC leads to high uncertainty in the results and the potential for bias, with the amount and direction of bias unclear. It added that the selection of covariates in the analysis had failed to maximise the effective sample size available to represent the efficacy of mosunetuzumab. The committee concluded that the indirect comparison of mosunetuzumab with rituximab plus lenalidomide was not matched for some important variables, making it highly uncertain with a potential for bias.

Comparison with rituximab plus bendamustine

- 3.7 For the comparison of mosunetuzumab with rituximab plus bendamustine, the company used the CONTRALTO and GO29365 studies of rituximab plus bendamustine, which had individual patient data. Therefore, propensity score analyses were done. In these, an estimate of treatment effect is calculated after accounting for differences in covariates believed to be prognostic factors or treatment-effect modifiers across the treatment groups. The company explored several approaches and after technical engagement selected an inverse probability of treatment weighting method. In this, subjects are weighted by the inverse probability of treatment. This is done to balance the baseline characteristics between individuals in 2 separate studies and remove confounding. The company explained that the selection of variables in the analysis was based on improving the overall balance of

these. The EAG noted that generally the important prognostic factors and effect modifiers were included in the analysis. It suggested that it was unclear whether double-refractory status should have been included in the analysis because it had wide standard errors making it unreliable. It noted that when the interaction of double-refractory status with treatment arm was included, there was an impact in the mosunetuzumab arm but a neutral effect in the rituximab plus bendamustine arm. The clinical plausibility of this is unclear. The committee concluded that there was some uncertainty associated with the indirect comparison of mosunetuzumab with rituximab plus bendamustine.

Results of indirect treatment comparisons

- 3.8 The company considers the results of the indirect treatment comparisons to be confidential so they cannot be described here. The EAG noted that there were inconsistent results within the 2 indirect comparisons, making them highly uncertain. That is, the results favoured mosunetuzumab for some endpoints but the comparator for others. Differences in the results across the 2 indirect comparisons also made them difficult to interpret. The company noted that in both indirect comparisons there were differences between the mosunetuzumab and comparator study populations that may lead to bias against mosunetuzumab. In the AUGMENT study used in the MAIC, less than 50% of people having rituximab plus lenalidomide had treatment at third line or later and none had follicular lymphoma that was refractory to rituximab. The committee noted that the mosunetuzumab study cohort had more relapses and greater treatment refractoriness than people in AUGMENT (see [section 3.3](#)). The company noted that in the propensity score analysis, there were also important differences between the study populations. This suggests that people who had treatment with mosunetuzumab had a poorer prognosis than those in the pooled studies of rituximab plus bendamustine. Clinical experts had said that people having treatment with rituximab plus bendamustine would typically be younger and fitter than people having other types of rituximab plus chemotherapy (see [section 3.5](#)). The committee concluded that the results of the indirect treatment comparisons were highly uncertain. It also concluded that the inconsistencies within them made them very unreliable.

Economic model

Company's modelling approach

- 3.9 The company used a partitioned survival model to represent progression-free and overall survival for mosunetuzumab compared with rituximab plus lenalidomide and rituximab plus bendamustine. It had 3 health states: progression-free, post-progression, and dead. The model had a lifetime time horizon (40 years). Each model cycle lasted 1 week. The company and EAG agreed that a half-cycle correction should be applied. The committee considered that a partitioned survival model is a standard approach to estimate the cost effectiveness of many cancer drugs. But it noted that a response-based modelling approach could be more suitable for comparing mosunetuzumab with rituximab plus lenalidomide. This may have avoided some of the problems seen with the survival modelling of mosunetuzumab compared with rituximab plus lenalidomide (see [section 3.8](#) and [section 3.12](#)) and more fully captured the benefits of complete response. However, a response-based model would have its own uncertainty because of the limitations in the data available to model outcomes in people having different response levels. The committee suggested that external data would also be needed for estimating overall survival. The committee concluded that the company's economic model used a standard approach, but this was not reliable for the comparison of mosunetuzumab with rituximab plus lenalidomide. It also concluded that an alternative approach could help inform decision making in the comparison of mosunetuzumab with rituximab plus lenalidomide.

Survival distributions selected

- 3.10 For the comparison of mosunetuzumab with rituximab plus lenalidomide, both the company and EAG selected a log normal distribution to model progression-free survival in the rituximab plus lenalidomide arm. The company used the Weibull distribution for the mosunetuzumab arm. The EAG preferred to use a log normal distribution for the mosunetuzumab arm using available data and switched to the log normal distribution used for rituximab plus lenalidomide when observed data was not available.

Both the company and EAG selected a Weibull function to model overall survival in the mosunetuzumab and rituximab plus lenalidomide arms. For the comparison of mosunetuzumab with rituximab plus bendamustine, the company and EAG took the same approach to model progression-free survival. In this comparison, the company considered rituximab plus bendamustine to also be representative of other types of rituximab plus chemotherapy (see [section 3.5](#)). The company and EAG selected a log normal distribution for both the mosunetuzumab and rituximab plus bendamustine arms. The company and EAG agreed on using an exponential distribution to model overall survival in the mosunetuzumab and rituximab plus bendamustine arms. The committee concluded that the company and EAG agreed on most survival distributions and all would be considered.

Overall survival modelling

- 3.11 For both comparisons, the company modelled the mosunetuzumab and comparator arms separately. The EAG preferred to pool the mosunetuzumab and comparator arms, which removed the treatment difference for overall survival from both comparisons. The EAG noted that the overall survival data from the single-arm mosunetuzumab study was very immature. It preferred to pool the intervention and comparator arms because there was no clear overall survival benefit. The committee noted that the EAG's pooling of overall survival data for the 2 arms changed the cost-effectiveness estimate from that of the company's base case for mosunetuzumab compared with rituximab plus lenalidomide. It also noted that pooling overall survival data had a substantial impact on the cost-effectiveness estimate for mosunetuzumab compared with rituximab plus bendamustine. The committee noted that the EAG's approach assumed that both treatments have the same overall survival, whereas the clinical experts expected people to live longer with mosunetuzumab. The company and EAG took different approaches to model survival for the 2 comparisons, and the EAG preferred to pool overall survival. The committee concluded that it would consider both approaches.

Plausibility of the company's survival modelling

- 3.12 The company acknowledged that because of data sparsity and immaturity, there was some uncertainty in the efficacy estimates included in the model. It added that data from further follow up of people in the clinical study could reduce some of this uncertainty. Clinical experts suggested that the company's modelled progression-free survival curves appeared reasonable. The committee noted that the lower life-years gained by people in the company's model with mosunetuzumab compared with rituximab plus lenalidomide did not reflect the potential benefit of mosunetuzumab on tumour response suggested by the single-arm study data. The findings of the indirect treatment comparison cannot be reported. The committee recalled that the EAG preferred to use pooled overall survival data for the extrapolations (see [section 3.11](#)). It noted that this preference to pool overall survival data meant that life-years gained were the same for mosunetuzumab and its comparator in the EAG's model, for both comparisons. The company suggested that its own modelling may underestimate any survival benefit of mosunetuzumab because of limitations of the indirect treatment comparison (see [section 3.8](#)). It considered the EAG's preference to pool overall survival data to be overly conservative. The company noted that pooling overall survival data is inconsistent with the complete response rate seen in the mosunetuzumab study (see [section 3.4](#)). The findings of the indirect treatment comparison cannot be reported. Clinical experts noted that in follicular lymphoma, if you can achieve a durable complete response then you tend to see good progression-free survival. They added that in this cancer type, progression-free survival may not impact overall survival. But, it is unlikely that improved progression-free survival leads to a loss of overall survival. Stakeholders commented on the draft guidance that the model may place too much emphasis on overall survival. They explained that a progression-free survival benefit may not translate into improved overall survival in follicular lymphoma because of the long natural history of the condition and a heterogenous population having a range of treatments (see [section 3.2](#)). The committee concluded that the survival modelling was highly uncertain for both comparisons. It concluded that in the comparison with rituximab plus lenalidomide, the company's modelling of mosunetuzumab overall survival was unlikely to

be plausible. It also concluded that the EAG scenarios could be plausible even though they are conservative.

Utility values

- 3.13 In its original base case presented at the first committee meeting, the company's utility values for the health states of progression-free survival and post-progression survival were based on the GO29781 study cohort. The company noted that this data was collected beyond the end of treatment during study follow up. In total, 63 observations in post-progression survival were included. Of these, 19 were made after 1 year. The EAG noted that because the company used study data as the source of utility values, for anyone in the study in early post-progression the corresponding utility value is then extrapolated forwards for many years in the model. At the first meeting, the committee agreed that the company's approach was acceptable even though it was associated with some uncertainty. During the consultation the company changed its source of utility values, preferring to use those from the literature (Wild et al. 2006) in its updated base case. The company stated that this addressed the uncertainties because the values were elicited from 222 UK patients and were previously used in [NICE's technology appraisal guidance on idelalisib for treating refractory follicular lymphoma](#). In the present evaluation, the EAG noted that Wild et al. was published as an abstract only and the utility values cannot be validated. The committee noted that in the GO29781 study cohort, the utility value for post-progression represented people on subsequent treatment. It also noted that it was not known whether the utility value for post-progression from the Wild et al. abstract represented people on subsequent treatment or not. The EAG noted that Wild et al. data has a much larger difference in utility value between the progression-free and post-progression states than the GO29781 study cohort. It noted that both potential sources have limitations. So, the EAG preferred not to change the utility values in its base case, which are from the GO29781 study cohort. The committee considered that the company and EAG took different approaches and both were associated with some uncertainty. It concluded that it preferred the GO29781 study cohort values because they were from a clinical study of people having mosunetuzumab, while Wild et al. may not be a robust source and could not be validated.

Subsequent therapy assumptions

- 3.14 The company's model applied subsequent treatment costs from the point of disease progression for all treatment arms. The EAG noted that this reflected what might happen in clinical practice. It added that this approach produced a bias towards lower costs in favour of mosunetuzumab. This is because progression-free survival and time on treatment is assumed to be equal for the comparators, but not for mosunetuzumab. After the first committee meeting, the company and EAG agreed on the distribution of subsequent treatments. These included rituximab plus lenalidomide (35%), rituximab plus chemotherapy (25%) and other non-rituximab-based chemotherapy (10%) for the mosunetuzumab and rituximab plus bendamustine treatment arms. In the rituximab plus lenalidomide arm it was assumed that people would not have rituximab plus lenalidomide as their subsequent therapy. So, in this arm subsequent treatment types included rituximab plus chemotherapy (50%) and other non-rituximab-based chemotherapy (20%). The committee noted that the subsequent therapy assumptions were informed by clinical advice. The EAG noted that it was possible that some people would have previous treatment with rituximab plus lenalidomide but not have it as their most recent previous therapy. This was not accounted for in the EAG's and company's updated base cases. The committee concluded that the company's subsequent treatment assumptions are likely to reflect clinical practice.

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

- 3.15 The company submitted incremental cost-effectiveness ratios (ICERs) for mosunetuzumab compared with rituximab plus lenalidomide and rituximab plus bendamustine incorporating a patient access scheme discount. The deterministic and probabilistic ICERs were broadly similar. The ICERs cannot be presented because they include confidential discounted prices for lenalidomide and rituximab. For the comparison with rituximab plus lenalidomide, mosunetuzumab was more costly and less effective in the company's updated base case. Also,

mosunetuzumab was more costly and marginally less effective than rituximab plus lenalidomide in the EAG's preferred base case. The committee noted that in the company's model, people had lower life-years gained with mosunetuzumab compared with rituximab plus lenalidomide (see [section 3.12](#)). It also noted that in the EAG's preferred model, life-years gained were the same for mosunetuzumab and rituximab plus lenalidomide. For the comparison with rituximab plus bendamustine, the mosunetuzumab ICER was above £30,000 per quality-adjusted life year (QALY) gained in the company's updated base case and substantially higher than £30,000 per QALY gained in the EAG base case. In a scenario analysis, the EAG explored the impact on its preferred base case of changing the utility values (see [section 3.13](#)) for the comparison of mosunetuzumab and rituximab plus bendamustine. The committee noted that using the utility values from Wild et al. reduced the cost-effectiveness estimate of the EAG's preferred base case by a large amount, but the ICER remained substantially above £30,000 per QALY gained. The committee noted that for both comparisons the ICERs for the EAG base cases do not include any potential overall survival benefit for mosunetuzumab, which may be plausible but conservative (see [section 3.12](#)). The committee concluded that, based on the ICERs presented, mosunetuzumab does not represent a cost-effective use of NHS resources.

Cost-effective estimates are highly uncertain

3.16 [NICE's guide to the methods of technology appraisal](#) notes that above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will specifically consider the degree of certainty and uncertainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted the high level of uncertainty in the cost-effectiveness estimate caused by:

- a single-arm trial being the primary source of clinical evidence for mosunetuzumab (see [sections 3.3 and 3.4](#))

- issues with the indirect treatment comparisons including the comparators and the representativeness of rituximab plus bendamustine for other types of rituximab plus chemotherapy (see [section 3.5](#)), variables included (see [sections 3.6 and 3.7](#)), differences between the study populations included and the reliability and plausibility of the results (see [section 3.8](#))
- immaturity and sparsity of efficacy estimates included in the model (see [section 3.12](#))
- limitations in the data used to inform the utility values (see [section 3.13](#)).

The committee concluded that the cost-effectiveness estimates are highly uncertain.

Mosunetuzumab is not cost effective

- 3.17 The committee noted that in the company's updated and EAG's base cases for the comparison with rituximab plus lenalidomide, mosunetuzumab was more expensive and less effective (see [section 3.15](#)). For the comparison with rituximab plus bendamustine, mosunetuzumab was not plausibly cost effective because both the company's updated and EAG's base cases were greater than £30,000 per QALY gained (see [section 3.15](#)). The estimates are also associated with considerable uncertainty. The committee concluded that mosunetuzumab did not represent a cost-effective use of NHS resources so could not be recommended for routine commissioning.

Managed access

Criteria for managed access not met

- 3.18 Having concluded that mosunetuzumab could not be recommended for routine use, the committee then considered if it could be recommended with managed access for treating relapsed or refractory follicular lymphoma after 2 or more systemic therapies. The committee discussed the criteria for a managed access recommendation by NICE (see [NICE's webpage on managed access](#)). It noted that the company had submitted a proposal for managed access. The company considered that additional

data collection could resolve some of the uncertainties associated with its cost-effectiveness modelling. It noted that this would include further data collection from the GO29781 study cohort, which would continue until at least June 2024. It also proposed that if recommended with managed access, the company would do a prospective study collecting real-world evidence on mosunetuzumab. This would include progression-free survival data. The committee noted that longer-term data from the GO29781 study cohort would be helpful to inform the survival modelling and post-progression utilities. But, this would depend on how much data can be collected to resolve some uncertainties. Also, the timeframe for data collection with managed access may not be long enough to show an overall survival benefit, which is one of the key uncertainties (see [section 3.12](#)). The committee noted that the Systemic Anti-Cancer Dataset (SACT) would provide useful UK-based data to explore the generalisability of the GO29781 study cohort to patients in the UK. It noted that it was unlikely SACT data would sufficiently resolve the high uncertainty associated with the indirect treatment comparisons. It added that SACT would not provide any information on previous treatment lines. It would also be unlikely to provide any overall survival data with a long enough duration to reduce uncertainty by very much. The committee noted that additional data collection would not resolve any uncertainty about whether rituximab plus bendamustine is representative of other types of rituximab plus chemotherapy (R-CHOP, R-CVP). The company proposed a potential new source of evidence on comparator treatments. It considers all details related to this confidential so it cannot be described here. It suggested that this would allow more robust indirect treatment comparisons. Stakeholders commented on the draft guidance that clinical studies completing during 2023 to 2026 may provide additional data on standard care. The committee noted these may provide useful information on comparators, but any comparison with mosunetuzumab would still be unanchored. Also, when adjusting for prognostic factors and effective modifiers the effective sample size may be small. It also noted that comparator studies cannot form part of a managed access agreement. The company confirmed that there are no ongoing comparative trials to provide more robust, controlled evidence on mosunetuzumab monotherapy at third line or later for relapsed or refractory follicular lymphoma. The committee highlighted that, because the indirect treatment comparisons were highly uncertain, a trial

comparing mosunetuzumab with standard care comparators is needed. The committee appreciated that managed access is designed to resolve uncertainties, but it did not think that it would sufficiently resolve the high level of uncertainty in this submission (see [section 3.14](#)). Also, it had not seen evidence that mosunetuzumab had plausible potential to be cost effective, because the company and EAG base cases were both greater than £30,000 per QALY gained (see [section 3.15](#)). The committee concluded that mosunetuzumab did not meet the criteria to be considered for a recommendation with managed access.

Other factors

Potential equality issue

- 3.19 Stakeholders commented on the draft guidance that not recommending mosunetuzumab may disadvantage older or frailer people with follicular lymphoma because they do not have access to the full range of immunochemotherapy treatment options. They also noted that these people have an even greater need for novel therapies earlier in the disease course. The committee acknowledged that some people have a greater unmet need for new treatment options. It also noted that its recommendation applies to all people within the marketing authorisation indication for mosunetuzumab (see [section 2.1](#)). The committee concluded that this is not an equality issue.
- 3.20 NICE's advice about conditions with a high degree of severity did not apply.

Innovation

- 3.21 The committee noted that mosunetuzumab is the first of a new class of drugs in this setting with a unique mode of action. New treatment options would be welcomed by patients and clinicians (see [section 3.1](#)) in an area where there is no current standard care (see [section 3.2](#)). Clinical experts advised that mosunetuzumab can be used after multiple previous treatments and in chemotherapy-resistant relapsed or refractory follicular lymphoma. The committee considered whether

mosunetuzumab was innovative. It recalled that the economic modelling of mosunetuzumab was highly uncertain. Because of this, it was possible that there were some benefits of mosunetuzumab not captured in the modelling. So, it concluded that mosunetuzumab may be innovative but there is a high level of uncertainty in the evidence presented. It would like to consider innovation together with the exploration of other uncertainties in the model, along with evidence of any uncaptured benefits.

Conclusion

- 3.22 Mosunetuzumab is not recommended for treating relapsed or refractory follicular lymphoma after 2 or more systemic therapies.

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The [minutes of each evaluation committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Professor Stephen O'Brien

Chair, technology appraisal committee C

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical and a project manager.

Catherine Spanswick

Technical lead

Louise Crathorne and Christian Griffiths

Technical adviser

Louise Jafferally

Project manager

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Accreditation

