NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Mosunetuzumab for treating relapsed or refractory follicular lymphoma

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using mosunetuzumab in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using mosunetuzumab in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 31 January 2023
- Second evaluation committee meeting: 14 March 2023
- Details of membership of the evaluation committee are given in section 4

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 most likely 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 more data would not sufficiently resolve the high level of uncertainty. Also, mosunetuzumab is not likely to be cost effective.

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

Nature of the condition

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. 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, patients 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, 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 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. Of people who had mosunetuzumab, 58% had a complete response (March 2021 data cut). 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. 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 most common adverse event in the single-arm study of mosunetuzumab was cytokine release syndrome, 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. 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 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 in itself, but whether it is representative of other types of rituximab plus chemotherapy is highly uncertain.

Company's approach for 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 they 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 effect 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. It 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 excluded some important variables, making it highly uncertain with a potential for bias.

Company's approach for 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. It 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, fewer 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 comparators studies. 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 sections 3.8 and 3.11) 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 were not available. Both the company and EAG selected a Weibull function to model overall survival in the mosunetuzumab and rituximab plus lenalidomide arms. The company modelled the 2 arms separately. The EAG preferred to pool the treatment arms, which removed the treatment difference for overall survival. The committee noted that the EAG's pooling of overall survival data changed the cost-effectiveness estimate from that of the company's base case for mosunetuzumab compared with rituximab plus lenalidomide. 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 company modelled the 2 arms separately. The EAG again preferred to pool the arms, removing the treatment difference for overall survival. The committee noted that compared with the company's approach in its base case, the EAG's preference to pool overall survival 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 both treatments have the same overall survival whereas the clinical experts expected people to live longer with mosunetuzumab.The committee concluded that the company and EAG took different approaches to model survival for the 2 comparisons, and the EAG preferred to pool overall survival. It also concluded that it would consider both approaches.

Plausibility of the company's survival modelling

3.11 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 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 sections 3.10). 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 (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. The committee

concluded that 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.

Post-progression utility values

3.12 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. The committee concluded that the company's approach was acceptable but was associated with some uncertainty.

Subsequent therapy assumptions

3.13 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 equal for the comparators, but not for mosunetuzumab. In the company's model, the distribution of subsequent treatments was informed by clinical advice and included rituximab plus lenalidomide (35%), rituximab plus chemotherapy (25%) and other non-rituximab-based chemotherapy (10%) for all treatment arms. The EAG suggested that in clinical practice, people who had disease progression on rituximab plus lenalidomide would be unlikely to have rituximab plus lenalidomide as subsequent therapy. The EAG preferred to assume in its base case that subsequent treatment types in the rituximab plus

lenalidomide arm included rituximab plus chemotherapy (50%) and other non-rituximab-based chemotherapy (20%). It did not change the subsequent therapy assumptions in the mosunetuzumab or rituximab plus bendamustine arms. It 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 had not been accounted for in the EAG's preferred base case. The committee noted that the EAG's adjustment changed the cost-effectiveness estimate from that of the company's base case for mosunetuzumab compared with rituximab plus lenalidomide. The committee concluded that the company's subsequent treatment assumptions may not all reflect clinical practice. It added that the cost-effectiveness estimate for mosunetuzumab is sensitive to changes in subsequent therapy assumptions.

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

3.14 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. 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 both the company and EAG's preferred base cases. For the comparison with rituximab plus bendamustine, the mosunetuzumab ICERs were above £30,000 per quality-adjusted life year (QALY) gained in the company base case and substantially higher than £30,000 per QALY gained in the EAG base case. The committee noted that the ICERs for the EAG base cases do not include any potential overall survival benefit for mosunetuzumab, which is likely to be too conservative. 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

3.15 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 as the primary source of clinical evidence for mosunetuzumab (see section 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 section 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 3.11)
- robustness of the data used to inform post-progression utility (see section 3.12)
- subsequent treatment assumptions (see section 3.13).

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

Mosunetuzumab is not cost effective

3.16 The committee noted that in the company and EAG base cases for the comparison with rituximab plus lenalidomide, mosunetuzumab was more expensive and less effective (see section 3.14). For the comparison with rituximab plus bendamustine (see section 3.15), mosunetuzumab was not plausibly cost effective because both the company and EAG base cases

were greater than £30,000 per QALY gained (see section 3.14). 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

3.17 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. The company also proposed another source of data collection but considered all details relating to it confidential so this cannot be reported here. 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 demonstrate an overall survival benefit, which is one of the key uncertainties (see section 3.11). 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 UK-based patients. The company also proposed that it could do additional data collection on comparators, including through SACT. It suggested that this would allow more robust indirect treatment comparisons. The committee 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. It 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 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 3.15). Also, it had not seen evidence that mosunetuzumab had plausible potential to be cost effective as the company and EAG base cases were both greater than £30,000 per QALY gained (see section 3.16). The committee concluded that mosunetuzumab did not meet the criteria to be considered for a recommendation with managed access.

Other factors

Equality issues

3.18 No equality or social value judgement issues were identified.

Innovation

3.19 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

3.20 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

Technical adviser

Louise Jafferally

Project manager

ISBN: [to be added at publication]