NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Zanubrutinib for treating Waldenstrom's macroglobulinaemia

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

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

The appraisal 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 race, sex, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

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

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 26 May 2022

Second appraisal committee meeting: 07 June 2022

Details of membership of the appraisal committee are given in section 5

1 Recommendations

1.1 Zanubrutinib is not recommended, within its marketing authorisation, for treating Waldenstrom's macroglobulinaemia in adults after at least 1 therapy or as first-line treatment when chemoimmunotherapy is unsuitable.

1.2 This recommendation is not intended to affect treatment with zanubrutinib 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

Standard care for Waldenstrom's macroglobulinaemia varies but typically includes chemoimmunotherapy combinations such as bendamustine and rituximab, or dexamethasone, rituximab and cyclophosphamide. When chemoimmunotherapy is unsuitable, rituximab or chlorambucil monotherapy are typically offered. Ibrutinib is available for people with previously-treated Waldenstrom's macroglobulinaemia via the Cancer Drugs Fund. However, because it is not approved for routine commissioning in the NHS, it could not be considered in this appraisal.

Clinical evidence suggests that people with Waldenstrom's macroglobulinaemia may live longer and have a better quality of life with zanubrutinib than with standard care. However, the results are uncertain because zanubrutinib has only been indirectly compared with standard care, and there is no clinical evidence directly comparing zanubrutinib with usual NHS treatments. Also, long-term evidence on the effectiveness of zanubrutinib is not yet available. So, it is unclear how much longer people having zanubrutinib live.

The most likely cost-effectiveness estimate for zanubrutinib is higher than what is normally considered a cost-effective use of NHS resources. So, zanubrutinib cannot be recommended.

2 Information about zanubrutinib

Marketing authorisation indication

2.1 Zanubrutinib (Brukinsa, BeiGene) has a marketing authorisation in the UK for 'the treatment of adult patients with Waldenström's macroglobulinaemia (WM) in adults who have received at least one prior therapy, or in first-line treatment for patients unsuitable for chemo-immunotherapy'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for zanubrutinib.

Price

2.3 The list price of zanubrutinib 120x80 mg capsules is £4,928.65 (excluding VAT; company submission). The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee considered evidence submitted by BeiGene, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

Current management

Bendamustine and rituximab (BR) and dexamethasone, rituximab and cyclophosphamide (DRC) are the key comparators for zanubrutinib

3.1 Waldenstrom's macroglobulinaemia is an incurable form of non-Hodgkin's lymphoma. It typically affects older people and has a long trajectory, with median overall survival of 16 years in people with symptoms. Because the condition progresses slowly, many people die from causes other than Waldenstrom's macroglobulinaemia. The clinical experts explained that

although there is variation in the clinical pathway, the first treatment options are commonly BR and DRC if chemoimmunotherapy is suitable. Although purine analogues such as fludarabine were included in the NICE scope, their use is no longer recommended because of toxicity concerns and the risk of secondary malignancies. This is reflected in the latest clinical guidelines on managing Waldenstrom's macroglobulinaemia from the British Society of Haematology. An autologous stem cell transplant is also an option for younger people. However, because Waldenstrom's macroglobulinaemia mainly affects older people, this is not suitable for most. When the condition has relapsed after or is refractory to first-line treatment, most people are currently offered ibrutinib (a Bruton's tyrosine kinase inhibitor). This is only available via the Cancer Drugs Fund. Other second-line treatment options include rituximab-containing regimens (including either BR or DRC, if not used as a first-line treatment). When chemoimmunotherapy is unsuitable, treatment options include rituximab or chlorambucil monotherapy, or best supportive care. While there is variation in the treatment pathway for people with Waldenstrom's macroglobulinaemia, particularly when it is relapsed or refractory, the committee concluded that BR and DRC represent the 2 most relevant comparators in this appraisal. Ibrutinib could not be considered as a comparator because it only available through the Cancer Drugs Fund and not approved for routine commissioning in the NHS. This means it cannot be considered to be established practice.

The availability of an effective and well-tolerated oral therapy is highly valued and addresses a significant unmet need

3.2 The patient expert explained that Waldenstrom's macroglobulinaemia and its treatment can have a profound effect on quality of life. The condition itself can cause severe pain, fatigue, reduced mobility and increased susceptibility to infections. Current chemotherapy treatments can cause severe adverse reactions and the need for frequent hospital visits. Even though Waldenstrom's macroglobulinaemia may respond well to first-line treatment, the constant threat of relapse can put a huge burden on people

with the condition and their families. Also, chemoimmunotherapy is unsuitable for some people, and treatment options are very limited for this group. The patient expert said that people with the condition are acutely aware that there are a limited number of treatment options. Also, there is a desire among the patient community to have additional options as their condition progresses. The committee noted that zanubrutinib is a Bruton's tyrosine kinase inhibitor and has a different mechanism of action to existing chemoimmunotherapy treatments. Both the patient and clinical experts emphasised that zanubrutinib is highly effective and better tolerated than existing chemoimmunotherapy options. It is also an oral therapy, which is greatly valued by people with the condition because it avoids the need for hospital visits and infusions. The patient expert said that zanubrutinib had rapidly and dramatically made him "feel better" and improved his quality of life. He explained that it had allowed him to participate in general day-to-day activities and return to the normal life he had enjoyed before diagnosis. He explained that this was in stark contrast to his experience with chemoimmunotherapy treatments, with which he had had significant intolerance issues and side effects, some of which were persistent. The committee concluded that the availability of an effective and well-tolerated oral therapy would be highly valued by people with Waldenstrom's macroglobulinaemia and would address a significant unmet need.

Clinical effectiveness

The ASPEN study provides generalisable evidence for zanubrutinib but its comparator, ibrutinib, is not relevant for this appraisal

3.3 The clinical evidence for zanubrutinib came from the ASPEN study, a randomised clinical trial that compared zanubrutinib with ibrutinib. The committee noted that ibrutinib was not a comparator in this appraisal (see section 3.1). The trial included:

- 187 people with relapsed or refractory Waldenstrom's macroglobulinaemia who had had 1 or more previous treatments

- 42 people who had not had any previous treatment and for whom chemoimmunotherapy was unsuitable.

The people in the trial were divided into 2 cohorts. Cohort 1 included 201 people with Waldenstrom's macroglobulinaemia who had a mutation in the myeloid differentiation primary response gene (MYD88^{MUT} type). The people in this cohort were randomised to either zanubrutinib or ibrutinib. Cohort 2 included 28 people with Waldenstrom's macroglobulinaemia (MYD88^{WT} type) and they were all assigned to zanubrutinib. One clinical expert explained that the trial was designed this way because earlier studies had suggested that ibrutinib may work less well in people without the MYD88 mutation. The committee understood that about 90% of people with Waldenstrom's macroglobulinaemia have the MYD88 mutation. But, overall, they expected that zanubrutinib would work equally well in people who did and did not have the MYD88 mutation. The company stated that comparing the data for zanubrutinib from the 2 cohorts supported the assumption that there was no difference in outcomes. The committee considered that the trial data from cohort 1 (which the company used in its model) was generalisable to both people with and without the MYD88 gene mutation. The median age of people in the trial was 70. Also, almost everyone had an Eastern Cooperative Oncology Group performance status of 0 or 1, and many had had a lot of previous treatments. One clinical expert noted that the trial population reflected the patient population in the NHS. The committee concluded that the ASPEN study provided clinical evidence for zanubrutinib that is generalisable to UK clinical practice. However, it concluded that it had not compared zanubrutinib with the relevant comparators for this appraisal.

Zanubrutinib is clinically effective, but data are immature for progression-free and overall survival

3.4 The committee noted that, at a median follow up of 19.5 months in the ASPEN trial, the very good partial response rate in the zanubrutinib arm was 28.4% and 19.2% in the ibrutinib arm. This response occurred at a median time of 4.8 months in the zanubrutinib arm. It was noted that there

was not a complete response in anyone. However, 1 clinical expert said that this was not unexpected because it is acknowledged that this class of drugs is not curative. The clinical expert also noted that it was important to consider the durability of that response, and not just its depth. Median progression-free and overall survival had not been reached at the point of data cut-off, so the survival data for zanubrutinib was currently immature. This was expected because Waldenstrom's macroglobulinaemia is a slowly progressing condition. At 12 months, 97.0% (95% CI 90.9 to 99.0) of people in the zanubrutinib arm were alive and the condition had not yet progressed in 89.7% (95% CI 81.7 to 94.3). Although ibrutinib was not a comparator in this appraisal, the committee noted that overall (93.9%) and progression-free survival (87.2%) was similar to that with zanubrutinib at 12 months. The committee was aware that, although it is not routinely commissioned, people have had ibrutinib through the Cancer Drugs Fund and there is longer-term clinical data available for ibrutinib. The clinical experts explained that zanubrutinib would be expected to have similar clinical efficacy to ibrutinib in clinical practice because they are in the same class of drug. The committee concluded that zanubrutinib is clinically effective, but that data on progression-free and overall survival was immature.

Zanubrutinib is more clinically effective than chemoimmunotherapy treatment, but the exact size of the benefit remains uncertain

3.5 Clinical evidence for the comparators came from 2 main studies:

- The clinical evidence for BR came from a single-arm study of 71 people with relapsed or refractory Waldenstrom's macroglobulinaemia (Tedeschi et al., 2015).
- The clinical evidence for DRC came from a single-arm trial of 72 people with Waldenstrom's macroglobulinaemia who had not had previous treatment but for whom chemoimmunotherapy was considered suitable (Dimopoulos et al., 2007; Kastritis et al., 2015).

The committee noted that the populations in these studies differed from that in ASPEN (see section 3.3). The company attempted to match the populations used in the indirect treatment comparisons and make to adjustments to minimise bias in the results. It presented results of zanubrutinib compared with BR in a population whose condition was relapsed or refractory and compared it with DRC in a population who had not had previous treatment. The company's original submission used a matching-adjusted indirect comparison (MAIC). The ERG noted the limited patient data available for the comparator studies. It thought that this may have led to differences in clinically relevant risk factors between the comparator groups that could not be adjusted for. In response to technical engagement, the company used another method for indirect comparison, a simulated treatment comparison (STC). The company explained that the STC was its preferred approach because it meant that a larger sample size could be maintained, more data used and covariates adjusted for more effectively. Using either the STC or MAIC approach for the indirect comparison, there was improved overall and progression-free survival with zanubrutinib compared with both BR and DRC. The specific results of the analysis are confidential and cannot be shared here. The committee noted that the hazard ratios for progression-free and overall survival were low compared to those typically seen in cancer treatments, suggesting that zanubrutinib is a highly effective treatment. While the hazard ratio point-estimates generated by the MAIC and the STC were different, the confidence intervals had substantial overlap. The committee agreed that this showed some consistency in the results generated by the 2 methods. The clinical experts confirmed that the hazard ratios generated in the analyses to compare zanubrutinib with BR and DRC seemed plausible. The committee considered that there were uncertainties and limitations for both approaches (MAIC and STC). However, it noted that MAIC methods are more transparent and that there was insufficient justification given by the company to switch from the original MAIC to the STC. The committee concluded its preferred approach was therefore the original MAIC approach but acknowledged that this was an area of uncertainty. The committee agreed that zanubrutinib is more clinically effective than chemoimmunotherapy treatments. However, it

concluded that there was a high degree of uncertainty in the size of the treatment effect in the NHS patient population because of the limitations of the indirect comparisons.

Zanubrutinib is expected to have similar effectiveness when chemoimmunotherapy is and is not suitable

3.6 The committee noted that, of the 19 people who had not had previous treatment in the ASPEN study, there was a very good partial response in 26%, compared with 29% in the relapsed or refractory population. The company considered that it was reasonable to consider that the clinical effectiveness of zanubrutinib taken as a first treatment by people for whom chemoimmunotherapy was unsuitable and zanubrutinib taken after chemoimmunotherapy by people whose condition was relapsed or refractory would be similar. The clinical experts stated that, when chemoimmunotherapy is considered unsuitable, it is typically because someone is too frail or has other comorbidities, and that these factors may affect outcome. The clinical experts expected people having zanubrutinib as their first treatment would do at least as well as people whose condition was relapsed or refractory. The committee noted that the comparator data for people who had not had a previous treatment was from the comparison with DRC. The clinical experts said that rituximab or chlorambucil monotherapy would not work as quickly or have the same durability as standard combined chemoimmunotherapy regimens. The committee noted that the proportion of people in the ASPEN study for whom chemoimmunotherapy was not suitable was small, and considered whether this would be the same in clinical practice. The clinical experts advised that the proportion of people for whom chemoimmunotherapy is considered unsuitable may depend, to some degree, on the alternative treatment options that are available. They estimated that the figure could be up to 15% if effective options were available that better suited that group (for example, oral therapy that avoided the need for hospital visits). The committee concluded that there was remaining uncertainty about whether Waldenstrom's macroglobulinaemia responds to treatment in the

same way in people who have not had previous treatment as in those whose condition is relapsed or refractory. However, it noted that the assumption of equivalent efficacy by the company was likely to be a conservative one. This was based on the clinical experts' expectation that people having zanubrutinib as their first treatment would do at least as well as those whose condition was relapsed or refractory. Also, the monotherapy treatment options used when chemoimmunotherapy is unsuitable may be less effective than chemoimmunotherapy, increasing the potential benefit of zanubrutinib compared with the comparators for this group.

The company's economic model

The structure of the company's model is appropriate for decision making

3.7 The company developed a cohort partitioned survival model (PSM) to project the long-term clinical and economic consequences. The PSM consisted of 3 mutually exclusive health states: preprogression; postprogression; and death. The committee noted the ERG's concerns that this type of model relies on estimating progression-free and overall survival over a long period. This can be uncertain if the trial data for these outcomes is immature, as was the case in ASPEN. However, overall, the committee concluded that it was acceptable for decision making.

The extrapolations of overall and progression-free survival are plausible but uncertainties remain

3.8 To estimate progression-free and overall survival beyond the data collection periods for zanubrutinib and its comparators, the company used parametric models to extrapolate the data over a 30-year time horizon. The models generated 5- and 10-year survival estimates, which are confidential and cannot be shared here. The clinical experts explained that long-term overall survival on zanubrutinib and ibrutinib was likely to be similar (see section 3.4). So, the committee compared the modelled 5-year overall survival estimates in the zanubrutinib arm with long-term

trial data from study 118E for ibrutinib. The 5-year overall survival data for ibrutinib was broadly consistent with the 5-year overall survival data estimated for zanubrutinib. The committee noted that, in the comparison with BR, the modelled estimates based on the STC indirect comparison were slightly higher and those based on the MAIC approach slightly lower than the 5-year estimates for ibrutinib. The committee accepted that the extrapolated survival estimates for zanubrutinib were appropriate for decision making, noting that there were remaining uncertainties in the data that underpinned them.

Utility values in the economic model are appropriate given the available evidence

3.9 The utility value for preprogression was obtained from EQ-5D collected during the ASPEN study. The committee noted that the value was higher than that for the general UK population, which was felt to be unrealistic. However, it noted that this is commonly seen when comparing trial populations with the general population. There was not enough data in the ASPEN study to estimate the utility value for progressed Waldenstrom's macroglobulinaemia. So, the company and ERG agreed a reduction of 0.18 on the preprogression value. This was based on previous NICE technology appraisal guidance on ibrutinib for treating relapsed or refractory mantle cell lymphoma and on ibrutinib for treating Waldenstrom's macroglobulinaemia. The committee acknowledged that this value was uncertain but was suitable for decision making. It also noted that adjusting this value did not have a big effect on the cost-effectiveness results.

Assuming that zanubrutinib suddenly stops working at 5 years is clinically implausible

3.10 The committee heard that the company's base case assumed life-long treatment effectiveness. However, the ERG thought that this was not realistic and implemented a 5-year treatment effect cut-off. This was based on NICE's technology appraisal guidance on lenalidomide with

rituximab for previously treated follicular lymphoma. Once people had been on zanubrutinib for 5 years, the hazard ratio for progression-free and overall survival was assumed to become equal to that in the comparator arms. The people in the model continued to take zanubrutinib until their condition progressed rather than a stopping rule being applied. The clinical lead for cancer drugs in the NHS stated that the risk of people's condition progressing while they were on treatment was already accounted for in the model. So, it was overly pessimistic to apply a sudden treatment effect cut-off. The clinical experts agreed with this view. They explained they have experience in other indications in which people have been taking the same type of drug, ibrutinib, for many years and are still deriving benefit. The committee concluded that there was insufficient evidence to justify this treatment effect cut-off. It noted that 'treatment waning effects' (meaning a reduced treatment effect over time) are typically applied after treatment has stopped, not while people are still on treatment. The committee concluded that a treatment effect cut-off was implausible and should not be applied in the absence of any evidence to support this assumption.

Ibrutinib should not be included as a subsequent treatment

3.11 Although ibrutinib was not considered as a comparator, the company base case included ibrutinib as a subsequent treatment option. This was based on the company's assumption that ibrutinib will be available via routine commissioning in the NHS by the time people move to their next treatment. However, ibrutinib is not currently approved for routine commissioning in the NHS. So, the committee agreed that it should be removed as a subsequent treatment, as the ERG had done in its exploratory base case. The company stated that some implicit treatment benefits from ibrutinib were included in the modelled overall survival in the comparator arms. The committee noted that people in the clinical trials of BR and DRC were unlikely to have had follow-on treatment with ibrutinib because they were done before ibrutinib was licensed. So, it noted that extrapolating overall survival from this trial data would not have captured a

benefit of having ibrutinib after these treatments. The company explained that it had sought clinical opinion on the expected outcomes for the people in the BR and DRC arms of the trials. This was to select a modelled distribution that gave clinically plausible long-term survival outcomes. This opinion would have been based on current practice, in which people might have had ibrutinib after BR or DRC via the Cancer Drugs Fund. So, although the patient population in the BR and DRC trials did not have ibrutinib, the company claimed that overall survival beyond the end of the study period did include some expected benefit from ibrutinib. The committee concluded that ibrutinib costs should be removed from the model. It was doubtful that there was any need for adjustment of postprogression survival in the BR or DRC modelled arms.

Cost-effectiveness results comparing zanubrutinib with BR and DRC separately and with a 'blended comparator' are appropriate

3.12 The company used a blended comparator in its cost-effectiveness model, That is, it compared zanubrutinib with a combination of BR and DRC. The company did separate cost-effectiveness analyses for each comparator. It then produced a weighted average of these results using the estimated proportions of who would have each treatment in clinical practice. The company used data from the Rory Morrison Registry to estimate that, in the absence of ibrutinib, 49% of people would have BR and 51% would have DRC. The clinical experts agreed that it was reasonable to estimate that about 50% of people would have each treatment. This was because typically people would initially be treated with either BR or DRC, and their second-line treatment would be whichever they had not had first line (BR followed by DRC, or DRC followed by BR). The committee recalled that the comparison of zanubrutinib with BR had been in people whose condition was relapsed or refractory. It also recalled that the comparison of zanubrutinib with DRC had been in people who had not had previous treatment. The committee agreed that the comparison of zanubrutinib with BR may have been more reliable than the comparison with DRC, although both BR and DRC were comparators. This was because, in ASPEN, most

people had Waldenstrom's macroglobulinaemia that was relapsed or refractory. The committee concluded that it would take into account the cost-effectiveness results comparing zanubrutinib with the blended comparator of BR and DRC in its decision making. However, it also concluded that it would take into account the cost-effectiveness results of the 2 pairwise comparisons separately.

Cost-effectiveness results

The cost-effectiveness estimates are above the range considered a cost-effective use of NHS resources

3.13 The committee noted that the company had agreed a patient access scheme for zanubrutinib. There were confidential prices for BR and DRC, so the exact incremental cost-effectiveness ratios (ICERs) cannot be reported here. The committee's preferred modelling assumptions were:

- using the MAIC rather than the STC method for indirect comparisons of the clinical data because, although both were uncertain, insufficient justification was given for using the STC and the MAIC was a more transparent approach (see section 3.5)
- excluding the costs of ibrutinib as a subsequent treatment (see section 3.11)
- to not apply any treatment effect cut-off (see section 3.10)

Applying these assumptions resulted in ICERs for zanubrutinib compared with the blended comparator of BR and DRC, compared with BR and compared with DRC. All the ICERs were above £30,000 per quality-adjusted life year (QALY) gained. The committee further noted that the lowest ICER estimate was from the comparison with BR and the highest ICER estimate was from the comparison with DRC. The committee concluded that the cost-effectiveness estimates were above the range usually considered a cost-effective use of NHS resources.

An acceptable ICER would be comfortably under £30,000 per QALY gained

3.14 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 take into account the degree of certainty 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, specifically about:

- the inherent limitations of the indirect comparisons of zanubrutinib with BR and with DRC, compounded by substantial differences in the trial populations (see section 3.5)
- the immaturity of the zanubrutinib data, with median progression-free and overall survival not being met in the study period (see section 3.4)

However, the committee also noted that there is significant unmet clinical need for people with Waldenstrom's macroglobulinaemia. It also noted that the patient and clinical experts are hugely supportive of the medicine, calling it a step-change in treatment. The committee agreed that zanubrutinib had a large treatment effect compared with BR and DRC, although the exact size of the clinical benefit could not be determined. So, it concluded that an acceptable ICER would need to be comfortably below £30,000 per QALY gained.

Innovation

Zanubrutinib is a step-change in managing Waldenstrom's macroglobulinaemia

3.15 The committee accepted that zanubrutinib has several benefits for people, including oral administration, manageable adverse reactions, low toxicity and fewer hospital visits. The committee concluded that zanubrutinib could be considered a step-change in managing Waldenstrom's

macroglobulinaemia compared with the chemoimmunotherapies BR and DRC.

Cancer Drugs Fund

Zanubrutinib cannot be recommended through the Cancer Drugs Fund

3.16 Having concluded that zanubrutinib could not be recommended for routine use, the committee then considered whether it could be recommended for treating Waldenstrom's macroglobulinaemia within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs Fund methods guide (addendum). It covers technologies that have plausible potential to be cost effective and have clinical uncertainty that could be addressed with data collection over the period the technology is in the Cancer Drugs Fund. The most plausible ICERs, including all of the committee's preferred assumptions, were above the range usually considered to be cost effective. The committee concluded that zanubrutinib does not have plausible potential to be cost effective at the current price.

Conclusion

Zanubrutinib is not recommended for treatment Waldenstrom's macroglobulinaemia

3.17 Zanubrutinib is a clinically effective technology compared with chemoimmunotherapy but there is uncertainty about the exact size of its clinical benefits. Zanubrutinib could be considered cost effective if the ICER was comfortably below £30,000 per QALY gained. However, the committee's preferred ICER was considerably above this. So, zanubrutinib is not recommended for treating Waldenstrom's macroglobulinaemia in adults after at least 1 therapy or as first-line treatment when chemoimmunotherapy is unsuitable.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review 3 years after publication of the guidance. NICE welcomes comment on this proposed date. NICE will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Dr Jane Adam
Chair, appraisal committee
April 2022

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

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

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

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

Alex Sampson
Technical lead

Mary Hughes

Technical adviser

Thomas Feist

Project manager

ISBN: [to be added at publication]