NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Belimumab for treating active autoantibody-positive systemic lupus erythematosus

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using belimumab 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, gender, 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 belimumab 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: 25 June 2021

Second appraisal committee meeting: To be confirmed.

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

1 Recommendations

1.1 Belimumab is not recommended, within its marketing authorisation, as an add-on therapy for active autoantibody-positive systemic lupus erythematosus in people 5 years and older when there is a high degree of disease activity (for example, positive anti-double-stranded DNA, low complement) and despite standard therapy.

1.2 People who started belimumab as part of the managed access agreement can continue until NICE publishes its final guidance. If the final guidance does not recommend belimumab for use in the NHS, they and their clinician will need to decide on an NHS-funded treatment and change to this within 1 year.

Why the committee made these recommendations

This appraisal reviews the additional evidence collected as part of the managed access agreement for belimumab for systemic lupus erythematosus (NICE technology appraisal guidance 397).

Standard therapies include non-steroidal anti-inflammatory drugs, corticosteroids, antimalarials and immunosuppressants. Other treatments include biological disease-modifying antirheumatic drugs such as rituximab.

Clinical trial evidence suggests that, after a year of treatment, belimumab plus standard therapy reduces disease activity more than standard therapy alone. However, the results are uncertain because the trials were short. Also, the long-term benefit of belimumab compared with standard therapy or rituximab is unknown.

The cost-effectiveness estimates are also uncertain, and the most likely estimates are higher than what NICE normally considers an acceptable use of NHS resources. So, belimumab is not recommended for use in the NHS.

2 Information about belimumab

Marketing authorisation indication

2.1 The intravenous formulation of belimumab (Benlysta, GlaxoSmithKline) 'is indicated as add-on therapy in patients aged 5 years and older with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy'. The subcutaneous formulation 'is indicated as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy'.

Dosage in the marketing authorisation

2.2 The dosage schedule for the intravenous formulation of belimumab is available in this summary of product characteristics and for the subcutaneous formulation in this summary of product characteristics.

Price

2.3 The list price of belimumab for the intravenous infusion is £121.50 for a 120 mg vial and £405.00 for a 400 mg vial (excluding VAT; BNF online accessed May 2021). The list price for the subcutaneous injection is confidential. The company has a commercial arrangement for both formulations, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee considered evidence submitted by GlaxoSmithKline, 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.

This review looks at data collected using the British Isles Lupus Assessment Group-Biologics Registry (BILAG-BR) and additional clinical trial evidence presented in the company's updated submission to address uncertainties identified during the original appraisal. Further information can be found in NICE's original technology appraisal guidance on belimumab for treating active autoantibody-positive systemic lupus erythematosus. As a condition of the managed access arrangement, the company was required to collect real-world data from the BILAG registry after treatment with belimumab, including on its efficacy, safety and effect on health-related quality of life.

The committee agreed that some of the issues raised in the ERG report had been resolved after technical engagement. These included that there is no evidence for using belimumab in people with severe active central nervous system lupus (key issue 1), that cyclophosphamide is not a relevant comparator (key issue 2), and that intravenous and subcutaneous formulations of belimumab are likely comparable (key issue 7).

The committee agreed that there is unresolved uncertainty with the issues raised in the ERG report about the uncertainty on organ damage utility multipliers (key issue 12) and the sampling order of organ damage and death in the model (key issue 13). However, it thought that it was unlikely that these issues would have a significant effect on the cost-effectiveness results.

Belimumab as a treatment option

People with systemic lupus erythematous would welcome belimumab as a continuing treatment option

3.1 Systemic lupus erythematosus is a chronic autoimmune condition that causes inflammation in the body's tissues and can affect the whole body. The patient experts explained that people with the condition often have frequent disease flares, and more severe symptoms that can result in hospital admissions. This can affect a person's ability to work, complete everyday activities and socialise with others. The patient experts described how this causes stress and anxiety, which can trigger further

disease flares. They described how the condition can affect fertility by causing recurrent miscarriages and severe disease flares. The patient experts further explained that, even when their condition is clinically stable, they still have symptoms that affect their daily life such as fatigue, headaches, joint pain and reduced mental acuity. These symptoms can make it challenging to care for themselves and others. One patient expert explained that treatment with belimumab as an add on to standard therapy has significantly reduced their disease flares and that they have been able to reduce their daily corticosteroid dose. The patient experts explained that treatment with belimumab has helped to improve other day-to-day symptoms of the condition, and this has improved their overall quality of life. They explained the burden of having to travel long distances to have belimumab intravenous infusions administered in hospital, and that they have nausea from the preinfusion medication. However, they continue with the treatment because they think that their condition is responding well to it. One patient expert also described the benefits of using the new subcutaneous formulation of belimumab because of being able to self-administer it at home with little disruption to daily life and the minimal side effects. The committee concluded that people with systemic lupus erythematous would welcome belimumab continuing to be a treatment option.

Treatment pathway and positioning

The company's updated population is appropriate

3.2 The marketing authorisation for belimumab states that it is indicated for systemic lupus erythematosus that has a high disease activity despite standard therapy. The committee discussed that, in the original appraisal, belimumab was recommended for systemic lupus erythematosus with high disease activity (HDA-1) despite standard therapy. HAD-1 is a Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of greater

than or equal to 10 and 2 serological biomarkers (positive anti-double-stranded DNA and low complement). The company and clinical experts explained that, based on the data collected through the BILAG registry, this HDA-1 population was too restrictive in clinical practice. This is because people will often have high levels of disease activity but only 1 of the 2 defined serological biomarkers. So, the company presented a broader high disease activity population (HDA-2) as part of its base case. This included people with a SELENA-SLEDAI score of greater than or equal to 10 and only 1 serological biomarker. The clinical experts considered that the company's new high disease activity population was clinically relevant and would allow more people access to belimumab. The committee concluded that the company's updated population was appropriate for decision making.

Comparators

Standard therapy is a relevant comparator

3.3 The committee heard that standard therapy for treating systemic lupus erythematosus is likely to consist of non-steroidal anti-inflammatory drugs, corticosteroids, antimalarials and immunosuppressants. It was aware that some standard therapies are not licensed for use in systemic lupus erythematosus but are used off label in clinical practice. The committee noted that belimumab is indicated as an add-on therapy to standard care. It understood that standard therapy was included in the scope for the appraisal and concluded that it was a relevant comparator.

Rituximab is a relevant comparator

3.4 The committee discussed the updated NHS England clinical commissioning policy on rituximab for refractory systemic lupus erythematosus in adults and post-pubescent children. It noted that, while rituximab is currently not licensed for treating systemic lupus erythematous, it is available as a treatment option through this

commissioning policy. The committee discussed the eligibility criteria for rituximab outlined in the commissioning policy, which recommends considering using licensed and NICE approved treatments, such as belimumab, first. The clinical experts explained that, based on the data collected from the BILAG registry, only a very small number of people on rituximab would be eligible for belimumab because of the differences in the eligibility criteria. They explained that people having belimumab will generally have more severe disease because of the current eligibility criterion of a SELENA-SLEDAI score of greater than or equal to 10. However, they pointed out that people with renal or central nervous system complications would not be eligible for belimumab and would have rituximab instead. The committee heard that, if belimumab is not recommended for routine commissioning, more people would potentially have treatment with rituximab in its absence. The committee noted that rituximab was included in the final scope for the appraisal and is being used in clinical practice through the commissioning policy. It concluded that rituximab was a relevant comparator.

Clinical effectiveness

Belimumab improves the Systemic Lupus Erythematosus Responder Index (SRI) 4 response rate at 52 weeks compared with standard therapy

3.5 The company submission included the BLISS 52 and BLISS 76 randomised controlled trials comparing intravenous belimumab plus standard therapy (from now, referred to as belimumab) to placebo plus standard therapy (from now, referred to as standard therapy). The company presented results for the new HDA-2 population based on the pooled trials and new evidence from the BLISS SC randomised controlled trial comparing a new subcutaneous formulation of belimumab with standard therapy. The primary outcome of all studies was the response rate at week 52 compared with baseline. This was assessed with the SRI(4), which is a composite measure of disease activity. Belimumab

showed a statistically significant improvement in SRI(4) response rate compared with standard therapy in the HDA 2 population across both the BLISS SC, and pooled BLISS 52 and BLISS 76 trials (actual results are confidential and cannot be reported here). The committee concluded that belimumab improved SRI(4) response rate at 52 weeks compared with standard therapy.

BLISS long-term extension studies do not provide long-term effectiveness evidence for belimumab compared with standard therapy

3.6 The company included new evidence from the BLISS long-term extension studies. These were single-arm continuation studies of people enrolled in the pivotal BLISS randomised controlled trials (see section 3.5). People who had been randomised to have belimumab continued treatment with belimumab, while people in the placebo groups were switched to belimumab in all long-term extension studies:

- The BLISS 76 US long-term extension study included people in the US who had completed the BLISS 76 trial. The primary outcome was the number people whose condition responded according to SRI(4), which was 75.6% in the total population at 7 years.
- The BLISS 52/76 non-US long-term extension study included people not from the US who had completed either BLISS 52 or BLISS 76 trials. The primary outcome was mean Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) change from baseline, which is a measure of organ damage. In the total population, the mean SDI change was 0.2 (standard deviation 0.56) at 8 years.
- The BLISS SC long-term extension study included people who had completed the BLISS SC trial. The primary outcome was the number of people whose condition responded according to the SRI(4), which was 61.4% in the total population at 6 months.

The committee noted that the long-term extension studies did not have comparator arms. It concluded that they did not provide long-term effectiveness evidence for belimumab compared with standard therapy.

An indirect treatment comparison between belimumab and rituximab is preferred

3.7 The company explained that no new evidence directly comparing belimumab with rituximab had been identified after the original appraisal. It also stated that an indirect comparison based on the EXPLORER trial, which compared rituximab with placebo, was not appropriate. This is because the EXPLORER trial did not meet its primary end point and for other reasons such as the trial population included people with more severe disease compared with the BLISS trials. The committee heard that a comparison between belimumab and rituximab was available from the observational prospective cohort BILAG-BR substudy, which was presented as part of the company's submission. This study was designed to fulfil the managed access requirements from the previous appraisal. A multilevel regression analysis done by the University of Manchester compared the efficacy of belimumab with rituximab based on data collected from the substudy. The eligibility criteria in the study reflected the high disease activity (HDA-1) population recommended in the original appraisal and included people having belimumab, rituximab or other non-biological treatments. Outcome measures assessed in the analysis included measures of disease activity (change in BILAG-2004, SLEDAI-2K and SDI scores), and health-related quality of life measured using generic and disease-specific instruments. The results suggested that, for most outcome measures, a similar level of change in disease activity was seen between belimumab and rituximab at 12 months of follow up (actual results are confidential and cannot be reported here). The company considered that there was a high likelihood of confounding and selection bias in this analysis. It thought that the data were not appropriate for comparing treatment efficacy, so did not do an indirect

treatment comparison. The committee noted that using the observational data did provide a comparison in a UK population relevant to the decision problem. It acknowledged that the long-term comparative effectiveness between treatments could not be determined based on the 12 months of data collected in the registry for belimumab. The committee concluded that, because rituximab is a relevant comparator (see section 3.4), it would have preferred to see an indirect treatment comparison between belimumab and rituximab in the relevant population.

The results of the propensity score-matched analysis is biased in favour of belimumab

3.8 The company's long-term extension studies did not have comparator arms. So, it did a propensity score-matched analysis to compare results from people who had belimumab in the BLISS 76 US long-term extension study with people who had standard therapy in the external Toronto Lupus Cohort (n=99 in each cohort). The primary end point of the propensity score-matched analysis was to compare organ damage progression (mean change in SDI score) from baseline to year 5 in people having treatment with belimumab or standard therapy with 5 or more years of follow up. The results showed that people having treatment with belimumab had statistically significantly less organ damage (5-year SDI change of 0.283, 95% confidence interval [CI] 0.166 to 0.400) compared with people having standard therapy alone (5-year SDI change of 0.717, 95% CI 0.500 to 0.934). The committee noted that several important variables were not included in the matching, including measures of socio-economic outcomes, disease progression and disease activity over time. It discussed the ERG's critique that there were also differences between the populations in the cohorts before matching. These included differences in the rates of smoking, which were higher in the Toronto Lupus Cohort. Because of this, the committee considered that it was likely that people from the Toronto Lupus Cohort would have had worse outcomes, even after matching, because of the influence of these

unmatched variables on organ damage progression. The committee heard that most people withdrew from the BLISS 76 US long-term extension study before 5 years. So, people who continued having belimumab at 5 years were likely to have progressed less or had a better response than people who had belimumab for 1 to 4 years before stopping treatment. The committee recalled testimony from a patient expert, who described the burden of attending hospital for regular intravenous infusions of belimumab. It agreed that it was likely that people who stayed on belimumab for 5 years had low disease activity, a good response to treatment or both. The committee noted that, in the long-term extension studies, reasons for withdrawal other than because of adverse events included lack of efficacy, physician choice, lack of compliance and withdrawal of consent. The committee concluded that the results of the propensity score-matched analysis was biased in favour of belimumab.

Cost effectiveness

The model structure remains unchanged from the original appraisal and is suitable for decision making

3.9 The company presented a microsimulation model with an annual cycle length and lifetime horizon. The model structure remained unchanged from the original appraisal. Two separate models were presented for each formulation of belimumab. It used the new HDA-2 population (see section 3.2), with patient baseline characteristics drawn from the pooled BLISS 52 and BLISS 76 trials for the intravenous belimumab model and BLISS SC for the subcutaneous belimumab model. The company used the average patient weight from the BILAG registry for the intravenous model. In the original appraisal, this was taken from the pooled BLISS 52 and BLISS 76 trials. The committee concluded that, because the model structure remained unchanged from the original appraisal, it was suitable for decision making.

Using a calibration factor to adjust for long-term organ damage is not suitable for decision making

3.10 In the original appraisal, the company simulated long-term effects of belimumab on disease progression using the natural history model based on the Johns Hopkins lupus cohort. In this review, the BLISS long-term extension studies (BLISS 52 and BLISS 76) were used to extrapolate long-term effects on disease progression. The company considered that, compared with results from the propensity score-matched analysis, its model overestimated organ damage progression in the belimumab arm but underestimated progression in the standard therapy arm (see section 3.8). So, the company simulated its model using several calibration factors until the results matched the observed results from the propensity score-matched analysis. The chosen calibration factor was then applied to the belimumab arm only for up to 6 years and used to adjust the time-to-event risk equations for organ damage probabilities in the models. The ERG noted that this implied that the annual risk of organ damage for belimumab was adjusted downwards by 50.9%. The ERG noted that the main issue with applying the calibration factor was that the propensity score-matched analysis it was based on had several methodological issues (see section 3.8). Another concern was that the model assumptions in the previous appraisal assumed a constant treatment effect of belimumab on disease activity reduction after 1 year (based on the trial data). The committee considered that this was already an optimistic assumption in terms of the long-term treatment effect with belimumab. This was particularly so when taking into account that some people stopped treatment in the long-term extension studies because of a lack of efficacy. The committee also considered that adding the calibration factor would have further increased the treatment benefit with belimumab. It concluded that using a calibration factor to adjust for long-term organ damage was not suitable for decision making.

It is unclear whether the modelled response to treatment for belimumab 'non-responders' is consistent with the BLISS trials

3.11 In the model, people on belimumab with a reduction of 4 or more points in the SELENA-SLEDAI score at week 24 were classified as 'responders'. Actual SELENA-SLEDAI scores were estimated based on a regression model, given that there was not a 24-week time point in the model. The committee noted that, at 24 weeks, 34.1% of people from the HDA-2 subgroup were classified as 'non-responders' using the regression model and stopped treatment with belimumab. The committee did not think it was clinically plausible that nearly half of these 'non-responders' would have had a SELENA-SLEDAI score reduction of 4 or more at 52 weeks on standard therapy alone. The ERG noted that the model could have underestimated belimumab costs compared with clinical practice because people having a response to belimumab were classified as 'non-responders' and therefore modelled to stop treatment with belimumab. The company explained that this observation did not mean that these people were incorrectly classified in the model as 'non-responders'. It highlighted that no one classed as a belimumab 'non-responder' at 24 weeks had a SELENA-SLEDAI reduction of 4 or more points. The clinical experts explained that standard of care for lupus treatments in clinical trials include a combination of immunosuppressants, hydroxychloroquine and high-dose corticosteroids. Because of this, they considered that it was possible for some people to have a benefit with standard therapies, particularly because regular care in clinical trials is usually better than clinical practice. The clinical experts considered that people whose condition has not responded to belimumab would have their standard therapy adjusted, for example, by dose escalation. This may result in an improvement in disease activity within 3 to 6 months of changing treatments for some people. The ERG explained that, because it did not have the company's regression model from which these assumptions were derived, it was unable to validate whether the

company's assumption had been implemented in line with the BLISS trials. The committee considered that a 6-month cycle length may have been more appropriate to use in the model to align with the 24-week continuation rule. It further noted that the company should have submitted the regression model so that it could have been validated by the ERG. The committee was not convinced that people whose condition has not responded to belimumab at 24 weeks would have a significant improvement in disease activity at 52 weeks on standard therapy alone. It concluded that it was unclear whether the modelled response to treatment for belimumab 'non-responders' was consistent with the BLISS trials.

Disease activity should be based on the BLISS trials for the first 52 weeks for people whose condition has not responded to belimumab

3.12 The ERG suggested that there was an error in the company's model because 'non-responders' had the same reduction in disease activity as people having standard therapy at 52 weeks. It considered that this likely meant the treatment benefit of belimumab was overestimated. This is because the BLISS trials showed that people whose condition did not respond to belimumab had a smaller reduction in disease activity than people having standard therapy in the first 52 weeks. The company considered that this was not an error in the model, but an assumption that 'non-responders' took the average standard therapy score from week 52 onwards. The company explained that this assumption was made because 'non-responders' to belimumab at week 24 switched to standard therapy for the remainder of the modelled time horizon (see section 3.11). The ERG explained that, because the model had a yearly cycle, this assumption did not capture any disadvantage that 'non-responders' to belimumab may have in the first 52 weeks, and was not in line with the BLISS trials. The company's scenario analysis assumed a return to standard therapy efficacy for 'non-responders' after 1 full year of standard therapy alone. The committee noted that this had a small effect on the incremental cost-effectiveness ratio (ICER). It discussed the ERG's base

case, which used the BLISS evidence to incorporate the difference in disease activity between 'non-responders' and people having standard therapy in the first 52 weeks. The committee preferred the ERG's approach and concluded that disease activity for people whose condition has not responded to belimumab should be based on the BLISS trials for the first 52 weeks.

A re-estimated utility regression model would resolve the uncertainty in the cost-effectiveness results

3.13 The ERG explained that the company's utility regression model used to estimate utility values excluded key organ damage coefficients without re-estimating the remaining coefficients used in the regression equation. The company agreed that this was an error but were unable to provide a re-estimated model during technical engagement. Instead, the company presented scenario analyses to explore the effect of varying the regression utility coefficients (log of age, constant, SLEDAI score, black ethnicity) in the regression equation by 1 standard deviation in each direction. The committee considered that company scenarios likely explored the full effect but noted that ICERs increased or decreased by around £3,000 per quality-adjusted life year (QALY) gained with only 1 of the coefficients varied. It noted the ERG's critique that the ICERs could increase or decrease further with combinations of coefficients varied but that the variation by 1 standard deviation was likely substantial. The committee concluded that it would have preferred the company to provide a re-estimated model to resolve the uncertainty in the cost-effectiveness results.

Cost-effectiveness estimates

Belimumab compared with standard therapy is not cost effective

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. So, the committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The company's probabilistic base-case ICER (using the patient access scheme for belimumab) compared with standard therapy was £30,808 per QALY gained for the intravenous formulation of belimumab and £29,264 per QALY gained for the subcutaneous formulation. The ERG presented analyses including the committee's preferred modelling assumptions which:

- removed the calibration factor (see section 3.10)
- used the BLISS trial evidence to incorporate the difference in disease activity between people whose condition has not responded to belimumab and people having standard therapy in the first 52 weeks (see section 3.12).

The committee's preferred probabilistic ICERs were £53,910 per QALY gained for the intravenous formulation of belimumab and £62,367 per QALY gained for the subcutaneous formulation of belimumab (using the patient access scheme for belimumab). Both of these are above the range that NICE considers to be an acceptable use of NHS resources. The committee therefore could not recommend belimumab as a treatment option for people with active autoantibody-positive systemic lupus erythematosus.

Other factors

There are no equality issues that can be addressed in this technology appraisal

3.15 The committee understood that systemic lupus erythematosus mainly affects women, particularly those of child-bearing age. The patient experts explained that there is a risk of infertility and harm to an unborn baby with most immunosuppressive and biological treatments (if taken during

pregnancy). This can make family planning challenging. The committee heard how the condition is more common in people of African, Caribbean and Asian family background and that they tend to have poorer health outcomes than people from other family backgrounds. It noted a stakeholder comment that double-stranded-DNA antibodies are less common in people from an African family background, and that any recommendation about belimumab use stating this as a criterion could be considered as discriminatory. The committee was aware that the company's updated population meant that only 1 of the 2 biomarkers was needed for someone to be eligible for treatment with belimumab. It also heard that administering intravenous belimumab in a specialist centre may be a barrier to accessing treatment if a person lives far way and has to take time off work to have regular infusions. The committee discussed that having a subcutaneous formulation that can be self-administered may improve access to belimumab. It concluded that issues about differences in prevalence or incidence of a condition and healthcare implementation cannot be addressed in a technology appraisal.

The benefits of belimumab are captured in the cost-effectiveness analysis

3.16 The company considers belimumab as an add on to standard therapy to be innovative because it reduces disease activity and corticosteroid use in people with systemic lupus erythematosus. The committee agreed that these are important benefits and recognised that belimumab is the only medicine specifically licensed for treating systemic lupus erythematosus. However, it concluded that it had not been presented with evidence of any additional benefits that could not be captured in the QALY.

Conclusion

Belimumab is not recommended for routine use

3.17 The committee recognised that people with systemic lupus erythematous have benefitted from treatment with belimumab, and that using the subcutaneous formulation at home is beneficial. It acknowledged that belimumab compared with standard therapy improves disease outcomes, but that comparative long-term evidence is lacking. It considered that some of the assumptions used in the modelling were not appropriate and that there was uncertainty about the cost-effectiveness estimates. The committee agreed that it would like to see analyses that include:

- an indirect comparison with rituximab (see section 3.7)
- removal of the calibration factor (see section 3.10)
- the regression analysis that informs response to treatment at 24 weeks (see section 3.11)
- disease activity at 52 weeks in people whose condition has not responded to belimumab that matches the BLISS trials (see section 3.12)
- a re-estimated utility regression model (see section 3.13).

It considered that the most plausible ICERs were above the range that NICE normally considers to be a cost-effective use of NHS resources. So, the committee concluded not to recommend belimumab, within its marketing authorisation, for treating active autoantibody-positive systemic lupus erythematosus.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based

on information gathered by NICE, and in consultation with consultees and commentators.

Gary McVeigh
Chair, appraisal committee
May 2021

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 D.

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.

Anita Sangha
Technical lead

Victoria Kelly
Technical adviser

Kate Moore

Project manager

ISBN: [to be added at publication]