## Appendix B

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

# Belimumab for treating lupus nephritis

**Draft scope**

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of belimumab within its marketing authorisation for treating lupus nephritis.

### Background

Systemic lupus erythematosus (SLE) is a chronic autoimmune condition that causes inflammation in the body's tissues. The manifestations of SLE vary greatly between people and can affect the whole body including the skin, joints, internal organs and serous membranes.

In some people with SLE, the body's immune system targets kidney cells resulting in inflammation. This complication is called lupus nephritis. Common symptoms of lupus nephritis include blood or foam in urine, swelling in extremities, and high blood pressure. Untreated lupus nephritis can permanently damage kidney structures.[1] People with lupus nephritis are at increased risk of developing end-stage renal disease[2], which may need dialysis or kidney transplantation.[3] Lupus nephritis has an increased mortality risk compared with SLE without lupus nephritis.[4]

There are currently around 60,000 people with SLE in England and Wales and around 3,000 people are diagnosed with SLE each year.[5] Up to 40% of people with SLE develop lupus nephritis.[6] The prevalence of lupus nephritis is also higher among those with Black, Asian or Hispanic family backgrounds.[7] Although SLE is approximately 6 to 9 times more common in women than men,[6,8] men are more likely to develop lupus nephritis and kidney failure.[7]

There is no cure for lupus nephritis. The aim of current treatments for lupus nephritis is to preserve renal function, prevent disease flares, improve quality of life, and improve survival.[6] Recommended initial treatment includes mycophenolate with corticosteroids, cyclophosphamide with corticosteroids, or mycophenolate with calcineurin inhibitors.[6] Rituximab or calcineurin inhibitors may be considered as alternatives to mycophenolate or cyclophosphamide for people whose disease has not responded.[6] Mycophenolate or azathioprine in combination with corticosteroids may be considered for maintenance therapy.[6]

### The technology

Belimumab (Benlysta, GlaxoSmithKline) is a human monoclonal antibody that inhibits the biological activity of B-lymphocyte stimulator (BLyS). BLyS promotes survival and development of B-lymphocyte cells into antibody-producing mature plasma B cells. In SLE, elevated BLyS levels contribute to the production of autoantibodies and have been associated with increased SLE disease activity. Belimumab is administered intravenously.

## Appendix B

Belimumab has a marketing authorisation as an add-on therapy in people aged 5 and older with active, autoantibody-positive SLE with a high degree of disease activity (for example, positive anti-dsDNA and low complement) despite standard therapy.

Belimumab does not currently have a marketing authorisation in the UK for treating lupus nephritis. It has been studied in a clinical trial in combination with standard therapy compared with placebo (plus standard therapy) in adults with active lupus nephritis.

| | |
|---|---|
| **Intervention(s)** | Belimumab as an add-on to standard therapy |
| **Population(s)** | Adults with active lupus nephritis |
| **Comparators** | Standard therapy without belimumab including the following induction regimens, with or without maintenance:<br>• cyclophosphamide plus corticosteroids<br>• mycophenolate plus corticosteroids (mycophenolate does not currently have a marketing authorisation in the UK for this indication)<br>• rituximab (rituximab is does not currently have a marketing authorisation in the UK for this indication)<br>• calcineurin inhibitors as monotherapy or in combination with mycophenolate. |
| **Outcomes** | The outcome measures to be considered include:<br>• renal response<br>• time to death or renal-related event<br>• disease activity<br>• rate and duration of remission<br>• incidence and severity of flares<br>• incidence of long-term complications and/or organ damage<br>• corticosteroid use<br>• rate and duration of corticosteroid-free remission<br>• mortality<br>• adverse effects of treatment<br>• health-related quality of life. |

## Appendix B

| | |
|---|---|
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br><br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account. |
| **Other considerations** | The availability and cost of biosimilar and generic products should be taken into account.<br><br>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br><br>'Belimumab for treating active autoantibody-positive systemic lupus erythematosus' (2016). NICE Technology Appraisal 397. Review date May 2021.<br><br>Appraisals in development (including suspended appraisals)<br><br>'Belimumab for treating active autoantibody-positive systemic lupus erythematosus (Review of TA397)' NICE technology appraisals guidance [ID1591]. Publication expected July 2021.<br><br>'Prasterone for the treatment of systemic lupus erythematosus.' NICE technology appraisals guidance [ID392] (suspended appraisal).<br><br>Related Evidence Summaries:<br><br>'Systemic lupus erythematosus: oral mycophenolate (ESUOM36)' (2014). NICE Evidence summary |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 5. Adult highly specialist rheumatology services<br><br>NHS England (2020) Rituximab for refractory Systemic Lupus Erythematosus (SLE) in adults and post-pubescent children<br><br>Department of Health and Social Care, NHS Outcomes |

## Appendix B

| | |
|---|---|
| | Framework 2016-2017: Domains 2, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 |

**Questions for consultation**

Have all relevant comparators for belimumab been included in the scope? In particular, should the following be considered as comparators?

- Azathioprine
- Calcineurin inhibitors

Are the outcomes listed appropriate?

Are there any subgroups of people in whom belimumab is expected to be more clinically effective and cost effective, or other groups that should be examined separately?

Where do you consider belimumab will fit into the existing treatment pathway for lupus nephritis?

To what extent does the patient population covered in NICE Technology Appraisal 397 overlap with the patient population in the proposed appraisal of belimumab for treating lupus nephritis?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which belimumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider belimumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of belimumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

## Appendix B

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

## Appendix B

### References

1 Lupus Foundation of America. What is lupus nephritis? Accessed April 2021.

2 Hanly J G, O'Keefe, A G, Su L, Urowitz M R, Romero-Diaz J (2016) The frequency and outcome of lupus nephritis: results from an international inception cohort study. Rheumatology 55:252-262.

3 Bertsias GK, Tektonidou M, Amoura Z, Aringer M, Bajema I, Berden JHM, et al. (2012) Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. Annals of the Rheumatic Diseases 71(11):1771.

4 Rees F, Doherty M, Grainge M et al. (2016) The incidence and prevalence of systemic lupus erythematosus in the UK, 1999-2012. Ann Rheum Dis 75:13641.

5 Fanouriakis A, Kostopoulou M, Cheema K et al. (2020) 2019 Update of the Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA–EDTA) recommendations for the management of lupus nephritis. Annals of the Rheumatic Diseases 79:713-723.

6 Parikh SV, Almaani S, Brodsky S, Rovin BH (2020) Update on Lupus Nephritis: Core Curriculum 2020. American Journal of Kidney Diseases.

7 Weckerle CE, Niewold TB (2011) The unexplained female predominance of systemic lupus erythematosus: clues from genetic and cytokine studies. Clinical reviews in allergy & immunology 40(1):42-49.

8 Almaani S, Meara A, Rovin B H (2017) Update on Lupus Nephritis. Clinical Journal of the American Society of Nephrology 12(5):825-835.