NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus (review of TA397)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of belimumab within its licensed indication for the treatment of active autoantibody-positive systemic lupus erythematosus.

Background

Systemic lupus erythematosus (SLE) is a chronic autoimmune condition that causes inflammation in the body's tissues. SLE affects the whole body including the skin, joints, internal organs and serous membranes and results in chronic debilitating ill health. The cause of SLE is unknown though a combination of genetic, environmental and hormonal factors is thought to play a role in disease development and progression. Disease activity varies over time and, at the onset, symptoms are very general and may include unexplained fever, extreme fatigue, muscle and joint pain and skin rash. Active SLE involves frequent flares and more severe symptoms compared with inactive disease which is when the disease is in remission. SLE can lead to arthritis, kidney failure, heart and lung inflammation, central nervous abnormalities and blood disorders. Over 90% of people with SLE develop problems with their joints and muscles such as athralgia (joint pain) and myalgia (muscle pain). Renal disease also occurs in 40-75% of people with SLE and significantly contributes to morbidity and mortality. Long-term damage accrues as a result of persistent disease activity and also due to cumulative effects of steroids.

There are currently around 60,000 people with SLE in England and Wales and approximately 3000 people are being diagnosed with SLE each year.[1] The prevalence of SLE is significantly related to ethnicity, and is highest among people of African-Caribbean ethnicity. Although the severity of the disease is greater in the male population, SLE is approximately 7 times more common in women than men. It mainly affects people between 15 and 60 years of age. However, when SLE presents in childhood it may have more severe disease presentation than in adults, with a higher incidence of major organ involvement and a more aggressive disease course.[2]

There is no cure for SLE. The aim of current treatments is to control and ease symptoms, and prevent organ damage and long-term complications. Standard therapy currently includes using:[3]

- non-steroidal anti-inflammatory drugs (NSAIDs),
- corticosteroids such as prednisolone or methylprednisolone,

- conventional disease-modifying anti-rheumatic drugs (DMARDs) such as hydroxychloroquine or immunosuppressive agents (for example, cyclophosphamide, azathioprine, methotrexate and mycophenolate mofetil), and
- biological DMARDs such as rituximab and belimumab.

Cyclophosphamide and biologics DMARDs are usually reserved for more severe and/or refractory disease. Prednisolone, hydroxychloroquine and belimumab are the only drugs specifically licensed for the treatment of SLE. People with SLE may receive additional treatments to manage their comorbidities, such as drugs for thrombosis, arthritis, blood pressure, depression, osteoporosis, raised cholesterol and heart disease.[4] There is lack of evidence for therapeutic intervention specific to SLE in children. Treatment options are generally aligned with those for adult SLE.[2]
NICE technology appraisal 397 recommended belimumab as an option as add-on treatment for active autoantibody-positive SLE in adults only if all of the following apply:

- There is evidence for serological disease activity (defined as positive anti-double-stranded DNA and low complement) and a Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of greater than or equal to 10 despite standard treatment.
- Treatment with belimumab is continued beyond 24 weeks only if the SELENA-SLEDAI score has improved by 4 points or more.
- The company provides belimumab with the discount agreed in the patient access scheme.
- Under the conditions for data collection, monitoring, patient eligibility and consent, ongoing treatment, cost to the NHS, and review by NICE as laid out in the managed access agreement.

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 or by subcutaneous injection.

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

Intervention(s)	Belimumab as an add on to standard therapy

Population(s)	People aged 5 years or more with active autoantibody-positive systemic lupus erythematosus
Comparators	• Standard therapy alone For people in whom it is considered appropriate: • Rituximab plus standard therapy • Cyclophosphamide plus standard therapy
Outcomes	The outcome measures to be considered include: • disease activity • rate and duration of response • rate and duration of remission • incidence and severity of flares • incidence of long-term complications and/or organ damage • corticosteroid use • mortality • health-related quality of life, including fatigue • adverse effects of treatment
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. 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. Costs will be considered from an NHS and Personal Social Services perspective. 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	Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: 'Belimumab for treating active autoantibody-positive systemic lupus erythematosus'. NICE Technology Appraisal 397. Review date April 2020. Related Evidence Summaries: 'Systemic lupus erythematosus: oral mycophenolate (ESUOM36)' (2014) Evidence summary Appraisals in development (including suspended appraisals): 'Prasterone for the treatment of systemic lupus erythematosus.' NICE Technology Appraisal (suspended appraisal).

Questions for consultation

Is the burden of childhood SLE adequately described?

Have all relevant comparators for belimumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for SLE (for both paediatric and adult population)?

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 current standard care pathway?

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 is 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?

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).

References

[1] Rees F, Doherty M, Grainge M et al. The incidence and prevalence of systemic lupus erythematosus in the UK, 19992012. Ann Rheum Dis 2016;75:13641.

[2] Lupus UK. Juvenile-onset lupus.

[3] Gordon, C., Amissah-Arthur, M.B., Gayed, M., Brown, S., Bruce, I.N., D'Cruz, D., Empson, B., Griffiths, B., Jayne, D., Khamashta, M. and Lightstone, L., 2018. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. Rheumatology, 57(1), pp.e1-e45.

[4] Lupus Trust. How lupus is treated.