NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus

Final 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 15,000 people in England and Wales with SLE and approximately 2000 people are diagnosed with SLE each year. The prevalence of SLE is significantly higher in African-Caribbean, South Asian and Chinese populations compared with European white populations. Although the severity of the disease is greater in the male population, SLE is significantly more common in women (90% of SLE) than men (10% of SLE) and mainly affects people aged 15-60 years old. After the age of 50 the percentage of women with lupus falls to 75% and the percentage of men with the disease rises to 25%.

The aim of current treatments for SLE is to control and ease symptoms. Standard therapy currently includes the use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, disease-modifying drugs such as hydroxychloroquine and immunosuppressive agents such as cyclophosphamide, azathioprine, methotrexate and mycophenolate mofetil.

Rituximab and cyclophosphamide are also considered as treatment options, particularly in the case of more severe disease. Prednisolone and hydroxychloroquine are the only drugs specifically licensed for the treatment of SLE. There is currently no NICE guidance on the treatment of SLE.

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.

Belimumab does not currently have UK marketing authorisation for the treatment of active autoantibody-positive systemic lupus erythematosus. It has been studied in clinical trials at different doses compared with placebo plus standard care, as an add on to standard therapy (NSAIDs, corticosteroids, disease-modifying drugs such as hydrocychloroquine and immunosuppressive agents) in people with active SLE on a stable SLE treatment regimen.

Intervention(s)	Belimumab as an add on to standard therapy
Population(s)	Adults 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 • incidence and severity of flares • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows, reduction in supportive treatments, for example steroid use, will be captured in the evidence base. Standard therapy includes, but is not limited to: prednisolone, hydroxychloroquine, cyclophosphamide, azathioprine, methotrexate and mycophenolate mofetil.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal (suspended appraisal), June 2004, 'Prasterone for the treatment of systemic lupus erythematosus.'