NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Anifrolumab for treating active autoantibody-positive systemic lupus erythematosus

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of anifrolumab within its marketing authorisation for treating active autoantibody-positive systemic lupus erythematosus.

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. SLE can result 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. SLE can lead to mucocutaneous disease, 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 arthralgia (joint pain) and myalgia (muscle pain). Up to 40% develop renal disease, which significantly contributes to morbidity and mortality.[1] 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 disease that is inactive or under control (in remission). Persistent disease activity and side effects from cumulative doses of corticosteroids contribute significantly to the accrual of irreversible long-term organ damage.

It is estimated that in 2019 there were around 60,000 people with SLE in England and Wales and around 3,000 people are being diagnosed with SLE each year.[2,3] The prevalence of SLE is significantly related to ethnicity, and is highest among people of African-Caribbean family background. The prevalence of renal disease is also higher in Black, Asian and Hispanic populations, compared with the white population.[4] Although the disease is more severe in men, SLE is around 6 to 9 times more common in women than men.[1,5]

There is no cure for SLE. The aim of current treatments is to control and ease symptoms, prevent organ damage and long-term complications. Standard therapy currently includes using:[6,7]

- non-steroidal anti-inflammatory drugs (NSAIDs),
- corticosteroids such as oral prednisolone, and
- conventional disease-modifying anti-rheumatic drugs (DMARDs) such as antimalarials (for example, hydroxychloroquine) or immunosuppressive agents (for example, cyclophosphamide, azathioprine, methotrexate and mycophenolate mofetil).

Around 10 to 15% of people with SLE continue to have high disease activity despite standard therapy and are treated with rituximab or belimumab.[8] Prednisolone,

hydroxychloroquine and belimumab are the only drugs specifically licensed for the treatment of SLE.

NICE technology appraisal 397 recommends belimumab, via a managed access agreement, as an add-on treatment option 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 Erythematosus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 10 or more despite standard treatment.
- Treatment with belimumab is continued beyond 24 weeks only if the SELENA-SLEDAI score has improved by 4 points or more.

An NHS England clinical commissioning policy recommends rituximab as a treatment option for moderate or severe refractory SLE that has not responded to 2 or more immunosuppressive therapies if the following apply:

- Either there is disease activity with at least 1 British Isles Lupus Assessment Group index (BILAG) A score, 2 BILAG B scores or a SLEDAI-2K score of 6 or more, or the disease needs unacceptably high levels of oral glucocorticoids.
- The person is not eligible for clinical trials or belimumab.

The technology

Anifrolumab (brand name unknown, AstraZeneca) is a fully human monoclonal antibody that binds to the type I interferon receptor, blocking the activity of all type I interferons which are involved in inflammatory pathways. These include IFN-alpha, IFN-beta and IFN-omega. Between 60% and 80% of adults with SLE have an increased type I interferon gene signature, which has been shown to correlate with disease activity. Anifrolumab is administered intravenously.

Anifrolumab does not currently have a marketing authorisation in the UK for systemic lupus erythematosus. It has been studied in clinical trials in combination with standard care compared with placebo (plus standard care) in adults with active autoantibody-positive SLE.

Intervention(s)	Anifrolumab as an add-on to standard therapy
Population(s)	Adults with active autoantibody-positive SLE
Comparators	• Standard therapy alone • Belimumab plus standard therapy (subject to ongoing NICE appraisal) • Rituximab 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 • rate and duration of corticosteroid-free remission • mortality • health-related quality of life • 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 technologies and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar products should be taken into account.
Other considerations	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: 'Belimumab for treating active autoantibody-positive systemic lupus erythematosus' (2016). NICE Technology Appraisal 397. Review date June 2021. Appraisals in development (including suspended appraisals): 'Belimumab for treating autoantibody-positive systemic lupus erythematosus (Review of TA397)' NICE technology appraisals guidance [ID1591]. Publication date to be confirmed.

	'Prasterone for the treatment of systemic lupus erythematosus' NICE technology appraisals guidance [ID392] (suspended appraisal). Related NICE Pathways: Systemic connective tissue conditions (2016) NICE pathway
Related National Policy	NHS England (2020) Rituximab for refractory Systemic Lupus Erythematosus (SLE) in adults and post-pubescent children NHS England (2013) 2013/14 NHS Standard Contract for Specialised Rheumatology Services (Adult). A13/S/a. NHS England (2013) 2013/14 NHS Interim Clinical Commissioning Policy Statement: Rituximab for the treatment of Systemic Lupus Erythematosus in adults. A13/PS/a. The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 5. Adult highly specialist rheumatology services. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

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2 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

3 Office for National Statistics (2020) Population estimates. Accessed: October 2020 https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates

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

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6 Gordon C, Amissah-Arthur MB, Gayed M et al. (2018). The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. Rheumatology 57(1), pp.e1-e45

7 Fanouriakis A, Kostopoulou M, Alunno A et al. (2019) 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. Ann Rheum Dis 78:736-745

8 NICE (2016) Final appraisal determination – Belimumab for treating active autoantibody-positive systemic lupus erythematosus