NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Anifrolumab for treating active autoantibody-positive systemic lupus erythematosus

Draft scope

Draft 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 dose 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 approximately 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 ethnicity. The prevalence of renal disease is also higher in Black, Asian and Hispanic populations, compared with the white population.[4] Although the severity of the disease is greater in the male population, SLE is approximately 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, and 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,
- conventional disease-modifying anti-rheumatic drugs (DMARDs) such as antimalarials (for example, hydroxychloroquine) or immunosuppressive agents (for example, cyclophosphamide, azathioprine, methotrexate and mycophenolate mofetil), and
- biological DMARDs such as rituximab and belimumab.

Approximately 10 to 15% of people with systemic lupus erythematosus 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 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 Erythematosus 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 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 including 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 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 in adults with active autoantibody positive systemic lupus erythematosus.

Intervention(s)	Anifrolumab in combination with standard care
Population(s)	Adults with active autoantibody positive SLE
Comparators	• Standard therapy alone • Standard therapy with belimumab • Standard therapy plus rituximab

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.
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 in development publication expected July 2021. Related NICE Pathways: Systemic connective tissue conditions (2016) NICE pathway
Related National Policy	NHS England (2014) 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) 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

Questions for consultation

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

Is cyclophosphamide used to treat active autoantibody positive SLE in clinical practice in the NHS?

Which treatments are considered to be established clinical practice in the NHS for active autoantibody positive SLE?

Are people with active SLE clinically identifiable and distinguishable? What are the clinical criteria for active SLE?

Are the outcomes listed appropriate?

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

Where do you consider anifrolumab will fit into the existing NICE pathway, systemic connective tissue conditions?

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 anifrolumab 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 anifrolumab 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 anifrolumab 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. 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
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
5. 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
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