

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Voclosporin with immunosuppressive therapies for treating lupus nephritis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of voclosporin with immunosuppressive therapies 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, particularly the filtering units called glomeruli, resulting in inflammation. This complication is called lupus nephritis. Lupus nephritis is divided into classes, based on glomerular pathology, following a kidney biopsy¹. Common signs and symptoms of lupus nephritis include blood or foam in urine, swelling in extremities, and high blood pressure. Untreated lupus nephritis can permanently damage kidney structures². People with lupus nephritis are at increased risk of developing end-stage renal disease³, which will need dialysis or kidney transplantation⁴. Lupus nephritis has an increased mortality risk compared with SLE without lupus nephritis³.

There are currently around 60,000 people with SLE in England and Wales and around 3,000 people are diagnosed with SLE each year⁵. Around 40% to 60% of people with SLE develop lupus nephritis^{6,7}. Compared with people who are described as white, the prevalence of lupus nephritis is around 4, 18 and 19 times higher, respectively, among those with Indo-Asian, Afro-Caribbean and Chinese family backgrounds⁸. Lupus nephritis is also more prevalent in women than in men⁸.

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 survival⁶. Recommended initial treatment is mycophenolate with corticosteroids or cyclophosphamide with corticosteroids⁶. Azathioprine is an alternative to mycophenolate and cyclophosphamide in people without adverse prognostic factors, or when these treatments are contraindicated or not tolerated⁹. A calcineurin inhibitor (especially tacrolimus) can be added to mycophenolate plus corticosteroids, particularly in people with nephrotic-range proteinuria⁶. Rituximab may also be considered as initial treatment for people with pure Class V (membranous) lupus nephritis, or for treating people whose disease is relapsed or refractory to other treatments⁹. If the disease responds to initial treatment, maintenance treatment with mycophenolate or azathioprine in combination with corticosteroids is recommended⁶.

The technology

Voclosporin (Lupkynis, Otsuka Pharmaceuticals) is a calcineurin-inhibitor immunosuppressant that results in inhibition of lymphocyte proliferation, T-cell cytokine production, and expression of T-cell activation surface antigens.

Voclosporin 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 mycophenolate mofetil and initial treatment with methylprednisolone, followed by a reducing course of oral corticosteroids compared with placebo in people with active lupus nephritis.

Intervention(s)	Voclosporin with immunosuppressive therapies
Population(s)	Adults with active lupus nephritis
Comparators	<p>Standard therapy for lupus nephritis without voclosporin including the following induction treatments, followed by maintenance treatment with mycophenolate plus corticosteroids or azathioprine plus corticosteroids:</p> <ul style="list-style-type: none"> • mycophenolate plus corticosteroids • cyclophosphamide plus corticosteroids • azathioprine plus corticosteroids • rituximab • a calcineurin inhibitor plus mycophenolate and corticosteroids.
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • renal response • rate and severity of renal-related events (e.g., flares) • rate and duration of remission • incidence of end-stage renal disease • corticosteroid use • mortality • adverse effects of treatment • health-related quality of life.

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>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.</p>
Other considerations	<p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>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.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>‘Belimumab for treating active autoantibody-positive systemic lupus erythematosus’ (2016). NICE Technology Appraisal TA397. Review date June 2021.</p> <p>Appraisals in development (including suspended appraisals)</p> <p>‘Belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus’ NICE technology appraisals guidance [ID1591]. Publication expected November 2021</p> <p>‘Anifrolumab for treating active autoantibody-positive systemic lupus erythematosus’ NICE technology appraisals guidance [ID3804]. Publication expected April 2022</p> <p>‘Prasterone for the treatment of systemic lupus erythematosus’ NICE technology appraisals guidance [ID392] (suspended appraisal).</p> <p>‘Belimumab for treating lupus nephritis’ Proposed NICE technology appraisals guidance [ID2722]. Publication date to be confirmed.</p> <p>Related Evidence Summaries:</p> <p>‘Systemic lupus erythematosus: oral mycophenolate (ESUOM36)’ (2014). NICE Evidence summary</p>

<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 5. Adult highly specialist rheumatology services</p> <p>NHS England (2020) Rituximab for refractory Systemic Lupus Erythematosus (SLE) in adults and post-pubescent children</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2,4,5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>
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Questions for consultation

Have all relevant comparators for voclosporin with immunosuppressives been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for lupus nephritis?

Are the outcomes listed appropriate?

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

Should different classes of lupus nephritis be considered as specific subgroups?

Where do you consider voclosporin with immunosuppressives will fit into the existing NICE 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 voclosporin with immunosuppressives 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 voclosporin with immunosuppressives 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 voclosporin with immunosuppressives 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 Weening, J.J et al. (2004) The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited. *J Am Soc Nephrol* 15:241-250
- 2 Lupus Foundation of America. [What is lupus nephritis?](#) Accessed August 2021.
- 3 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.
- 4 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.
- 5 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.
- 6 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.
- 7 Saxena R, Mahajan T and Mohan C. (2011). Lupus nephritis: current update. *Arthritis research & therapy* 13(5):240
- 8 Patel M, Clarke AM, Bruce IN and Symmons DPM, The prevalence and incidence of biopsy-proven lupus nephritis in the UK: Evidence of an ethnic gradient. *Arthritis & Rheumatism* 54(9):2963-2969.

Draft scope for the appraisal of voclosporin with immunosuppressives for treating lupus nephritis

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Page 5 of 6

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9 Gordon C, Amissah-Arthur M, Gayed M et al. (2018). The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. *Rheumatology*. 57(1):1-45