NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Voclosporin with immunosuppressive therapies for treating lupus nephritis [ID3962]

Final scope

Final 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 (I to VI), based on glomerular pathology, following a kidney biopsy[1]. 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 structures[2]. People with lupus nephritis are at increased risk of developing end-stage renal disease[3], which will need dialysis or kidney transplantation[4]. Lupus nephritis has an increased mortality risk compared with SLE without lupus nephritis[3].

There are currently around 60,000 people with SLE in England and Wales and around 3,000 people are diagnosed with SLE each year[5]. 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 backgrounds[8]. Lupus nephritis is also more prevalent in women than in men[8].

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 survival[6]. Recommended initial treatment is mycophenolate with corticosteroids or cyclophosphamide with corticosteroids[6]. A calcineurin inhibitor (especially tacrolimus) can be added to mycophenolate plus corticosteroids, particularly in people with nephrotic-range proteinuria[6]. If the disease responds to initial treatment, maintenance treatment with mycophenolate or azathioprine in combination with corticosteroids is recommended[6]. Rituximab may be considered for treating people whose disease is relapsed or refractory to other treatments[6]

The technology

Voclosporin (Lupkynis, Otsuka Pharmaceuticals) is a calcineurin-inhibitor immunosuppressant that suppresses lymphocyte proliferation, T-cell cytokine production, and expression of T-cell activation surface antigens. In addition, voclosporin is associated with the stabilisation of the renal podocyte actin cytoskeleton. Voclosporin is administered orally.

Voclosporin does not currently have a marketing authorisation in the UK for treating lupus nephritis. It has been studied in a in a randomised, placebo-controlled clinical trial in combination with mycophenolate mofetil and low-dose oral corticosteroids in adults with class III, IV or V (including mixed class III/V and IV/V) active lupus nephritis.

Intervention(s)	Voclosporin with immunosuppressive therapies
Population(s)	Adults with active lupus nephritis
Comparators	Standard therapy for lupus nephritis without voclosporin including the following induction treatments, followed by maintenance treatment with mycophenolate plus corticosteroids or azathioprine plus corticosteroids: • mycophenolate plus corticosteroids • cyclophosphamide plus corticosteroids • azathioprine plus corticosteroids • rituximab • a calcineurin inhibitor plus mycophenolate and corticosteroids.
Outcomes	The outcome measures to be considered include: • 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	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	The availability and cost of biosimilar and generic products should be taken into account. 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' (2021). NICE Technology Appraisal TA752. Review date December 2024. Appraisals in development (including suspended appraisals) 'Anifrolumab for treating active autoantibody-positive systemic lupus erythematosus' NICE technology appraisals guidance [ID3804]. Publication expected April 2022 'Prasterone for the treatment of systemic lupus erythematosus' NICE technology appraisals guidance [ID392] (suspended appraisal). 'Belimumab for treating lupus nephritis' Proposed NICE technology appraisals guidance [ID2722]. Suspended. Related Evidence Summaries: 'Systemic lupus erythematosus: oral mycophenolate (ESUOM36)' (2014). NICE Evidence summary
Related National Policy	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

	NHS England (2020) Rituximab for refractory Systemic Lupus Erythematosus (SLE) in adults and post-pubescent children 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

References

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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.

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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.