

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Targeted-release budesonide for treating IgA nephropathy

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of targeted-release budesonide within its marketing authorisation for treating immunoglobulin A (IgA) nephropathy.

Background

IgA nephropathy (also known as Berger's disease) is a chronic autoimmune kidney disease. People with the condition produce abnormal IgA antibody that builds up in the glomeruli of the kidneys, responsible for filtering waste and removing excess fluid from the blood. The abnormal IgA deposits cause inflammation and damage in glomeruli and reduce their function, eventually leading to scarring of the whole kidney.¹ In IgA nephropathy, both kidneys are affected equally.² The condition is commonly classified as primary or secondary, with secondary disease associated with comorbidities such as IgA vasculitis and chronic liver disease.³ The presentation of IgA nephropathy varies considerably and, in its early stages, may have no symptoms. Once symptoms appear, the most common symptoms are blood or protein in the urine (haematuria or proteinuria).² However, diagnosis can only be confirmed by abnormal glomerular deposits on a kidney biopsy.¹ IgA nephropathy is also associated with complications from reduced kidney function including high blood pressure and cholesterol levels, cardiovascular problems and Henoch-Schönlein purpura, a condition affecting the blood vessels that presents as a rash.¹ The rate of progression is variable but is usually slow. However, ongoing decline in glomerular function may eventually lead to kidney failure, requiring transplant or life-long dialysis.² A particularly severe form of the disease known as rapidly progressive IgA nephropathy has been reported in a small proportion of people.⁴

The exact prevalence of primary IgA nephropathy in England is uncertain, however, it is estimated that around 4 in 10,000 people have the condition in Europe.⁵ Between 20% to 40% of people with IgA nephropathy develop kidney failure within 10 to 20 years of diagnosis, leading to end stage kidney disease in around 15% to 50% of people throughout their lifetime.^{1,6} IgA nephropathy is more prevalent in men than in women and also amongst Asian and Caucasian populations.^{1,7} It is most commonly diagnosed in people in their teens to late 30s.¹

There is no cure for IgA nephropathy and no published NICE guidance for the management of the condition. The aim of current treatment is to prevent or delay kidney failure and associated complications. Initial treatment focuses on reducing protein levels in the urine and blood pressure. Antihypertensives such as angiotensin-converting enzymes (ACE) inhibitors or angiotensin receptor blockers (ARBs) are recommended in people with more than 0.5 grams of protein in their urine per day. Supportive care also includes dietary modification and exercise with or without diuretics to remove extra fluid from the blood and reduce cholesterol levels. In people at high risk of progression despite optimised supportive care (defined as urine protein levels above 0.75 grams per day), immunosuppressants in the form of glucocorticoids (steroids) can be used. Cyclophosphamide is also used to treat people with rapidly progressive IgA nephropathy.⁴ Anticoagulants, fish oil, surgical

tonsillectomy, hydroxychloroquine and other immunosuppressants (such as cyclosporin A, azathioprine and mycophenolate mofetil) have also been evaluated in clinical trials. People with severely reduced kidney function may need dialysis or a kidney transplant.¹

The technology

Targeted-release budesonide (Nefecon, Calliditas Therapeutics AB) is a corticosteroid which suppresses the formation of immune complexes (molecules formed from the binding of antigens to antibodies) in the lower small intestine, where most IgA is produced. By reducing the levels of immune complexes circulating in the blood, budesonide aims to stop the transport of abnormal IgA to the kidney and prevent deposits in the glomeruli. It is administered orally.

Targeted-release budesonide does not have a marketing authorisation in the UK for treating IgA nephropathy. It has been studied in clinical trials compared with placebo in people with primary IgA nephropathy who are taking stable doses of ACE inhibitors or ARBs and are at risk of progressing to kidney failure.

Intervention(s)	Targeted-release budesonide
Population(s)	People with primary IgA nephropathy
Subgroups	If the evidence allows the following subgroups will be considered: <ul style="list-style-type: none"> • People with rapidly progressive IgA nephropathy
Comparators	Established clinical management without targeted-release budesonide, including ACE inhibitors, ARBs, diuretics and dietary and lifestyle modification, with or without: <ul style="list-style-type: none"> • Glucocorticoids • Cyclophosphamide (in people with rapidly progressive IgA nephropathy)
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • change from baseline in urine protein creatinine ratio • kidney function • disease progression (dialysis and/or transplant) • 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.</p>
Other considerations	<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	<p>Related Guidelines:</p> <p>Chronic kidney disease: assessment and management (2021) NICE guideline 203. Review date TBC.</p>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 15 'Adult specialist renal services' page 65.</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2</p>

Questions for consultation

How is IgA nephropathy currently treated in the NHS?

Where do you consider targeted-release budesonide will fit into the existing treatment pathway for IgA nephropathy?

Would the following treatments be considered established clinical practice for the treatment of IgA nephropathy:

- Immunosuppressants other than glucocorticoids and cyclophosphamide
- Anticoagulants
- Fish oil
- Surgical tonsillectomy?

Would targeted-release budesonide always be used in people who are taking stable doses of ACE inhibitors or ARBs?

Would targeted-release budesonide only be used in people who are at risk of progressing to kidney failure? How is this population defined in clinical practice?

Would targeted-release budesonide be used in people with rapidly progressive IgA nephropathy?

Have all relevant comparators for targeted-release budesonide been included in the scope?

Would targeted-release budesonide be a candidate for managed access?

Do you consider targeted-release budesonide 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 targeted-release budesonide can result in any potential 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 committee to take account of these benefits.

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 targeted-release budesonide 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

References

1. National Institute of Diabetes and Digestive and Kidney Diseases (2015) [IgA nephropathy](#)
2. IgA Nephropathy Foundation (2021) [IgA Nephropathy – What You Need to Know](#). Accessed January 2022.

3. Wang, M et al (2020) [Secondary IgA Nephropathy Shares the Same Immune Features With Primary IgA Nephropathy](#), Kidney International Reports. 5(2): 165-172.
4. Kidney Disease: Improving Global Outcomes (2021) [Clinical Practice Guidelines for the Management of Glomerular Diseases](#). Kidney International. 100(4s)
5. European Medicines Agency (2016) [Orphan designation](#). Accessed January 2022
6. Vecchio, M et al. [Immunosuppressive agents for treating IgA nephropathy](#). Cochrane Database of Systematic Reviews 2015, Issue 8
7. Kiryluk K, et al. (2012) [Geographic differences in genetic susceptibility to IgA nephropathy: GWAS replication study and geospatial risk analysis](#). PLoS Genet. 8(6):e1002765.