NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Targeted-release budesonide for treating primary IgA nephropathy (review of TA937)

Final scope

Remit/evaluation objective

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

Background

IgA nephropathy (also known as Berger's disease) is a chronic autoimmune kidney disease. It causes a build up of IgA containing immune complexes in the glomeruli of the kidneys. This causes inflammation and damage in the glomeruli and reduces their function, eventually leading to scarring of the whole kidney. In IgA nephropathy, both kidneys are affected equally. The condition is commonly classified as primary or secondary, with secondary disease associated with comorbidities such as IgA vasculitis and chronic liver disease. The presentation of IgA nephropathy varies considerably and, in its early stages, may have no symptoms. The most common symptoms are blood or protein in the urine (haematuria or proteinuria). IgA nephropathy is also associated with complications from reduced kidney function including high blood pressure, high cholesterol and cardiovascular problems. The rate of progression is variable, although ongoing decline in glomerular function may eventually lead to kidney failure, requiring transplant or life-long dialysis. A particularly severe form, known as rapidly progressive IgA nephropathy, has been reported in a small proportion of people who are at higher risk of progressive kidney function loss.

It is estimated that around 4 in 10,000 people have primary IgA nephropathy in Europe.[1] Most people progress to ESRD within 10 to 15 years of diagnosis with all at risk of ESRD within their expected lifetime unless an eGFR rate loss ≤1 ml/min per 1.73 m^2 per year can be maintained from diagnosis.[2]

There is no cure for IgA nephropathy. 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 enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are given at the maximum tolerated licensed doses. Supportive care also includes dietary modification and exercise with or without diuretics to remove extra fluid from the blood and reduce cholesterol levels. Some people are at risk of progressive loss of kidney function. People with over 1 gram (g) of protein in their urine daily have treatment to reduce IgA buildup, protect kidneys and manage damage from IgA nephropathy. Second-line treatments may include glucocorticoids, sodium-glucose cotransporter-2 (SGLT2) inhibitors or entry into a clinical trial. Clinical experts explained that the use of glucocorticoids is rare or limited because of safety concerns associated with systemic use. SGLT2 inhibitors are being increasingly used since NICE technology appraisal guidance 775 was published. NICE technology appraisal guidance 937 recommends targeted-release budesonide as an add on to standard care when there is a risk of rapid disease progression in

adults with a urine protein-to-creatinine ratio of 1.5 g/gram or more. People with severely reduced kidney function may need dialysis or a kidney transplant.

The technology

Targeted-release budesonide (Kinpeygo, Genus Pharmaceuticals) has been studied in clinical trials and has a marketing authorisation from the European Medicines Agency for the treatment of adults with primary IgA nephropathy with a urine protein excretion ≥ 1.0 g/day or urine protein-to-creatinine ratio ≥ 0.8 g/gram.

Intervention(s)	Targeted-release budesonide as an add-on to standard care
Population(s)	Adults with primary IgA nephropathy with a urine protein-to-creatinine ratio of 0.8 g/gram or more
Subgroups	If the evidence allows the following subgroup will be considered: • People at risk of rapidly progressive IgA nephropathy (urine protein-to-creatinine ratio of 1.5g/gram or more)

Comparators	Individually optimised standard care without targeted-release budesonide:
	Standard care is defined as:
	• ACE inhibitors and ARBs at the maximum tolerated licensed doses, diuretics, and dietary and lifestyle modification, with or without:
	  ○ SGLT2 inhibitors
	  ○ Sparsentan (subject to NICE evaluation)

Outcomes	The outcome measures to be considered include: • proteinuria (for example, change from baseline in urine protein creatine ratio) • kidney function (eGFR) • disease progression (dialysis and/or transplant) • 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.
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	**Related technology appraisals:** Dapagliflozin for treating chronic kidney disease (2022) NICE technology appraisal 775. Targeted-release budesonide for treating primary IgA nephropathy (2023) NICE technology appraisal guidance 937 **Related technology appraisals in development:** Sparsentan for treating primary IgA nephropathy. NICE technology appraisal guidance [ID 6308] Publication expected April 2025 **Related interventional procedures:** Chronic kidney disease: assessment and management (2021) NICE guideline NG203
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017 NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication

References

1. European Medicines Agency (EMA). (2020) Orphan designation for the treatment of primary IgA nephropathy. (Accessed February 2024)

2. Pitcher D, Braddon F, Hendry B, et al. Long-Term Outcomes in IgA Nephropathy. Clinical journal of the American Society of Nephrology: CJASN. 2023; 18(6): 727-38