NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Iptacopan for treating complement 3 glomerulopathy [ID6283]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of iptacopan within its marketing authorisation for treating complement 3 (C3) glomerulopathy.

Background

Glomerulonephritis is a condition where there is inflammation in the kidney. C3 glomerulopathy is a type of glomerulonephritis. It is an autoimmune condition, but can also be caused by gene variants.[1] In C3 glomerulopathy there are issues with the regulation of a part of the immune system (the 'complement system'). This results in the build-up of the C3 protein in the kidneys. C3 glomerulopathy includes C3 glomerulonephritis (C3GN) and dense deposit disease (DDD).[2]

The major features of C3 glomerulopathy include high levels of protein in the urine (proteinuria), blood in the urine (haematuria), reduced amounts of urine, low levels of protein in the blood, and swelling in many areas of the body.[3] The kidney problems associated with C3 glomerulopathy tend to worsen over time.

About half of affected people develop kidney failure within 10 years of their diagnosis. People with kidney failure usually require dialysis or kidney transplantation to stay alive. However, after transplantation, there is a high risk of C3 glomerulopathy recurrence. C3 glomerulopathy may also affect tissues other than the kidney, such as fatty tissues under the skin and can cause visual disturbances due to deposits in the retina.

Each year, around 1 to 2 people per million of the UK population develop C3 glomerulopathy.[4] The median age at which C3 glomerulopathy is diagnosed is 21 to 23 years.[4,5] Point prevalence estimates from studies in the UK and other countries range from 0.05 to 1.4 cases per 10,000 people.[1]

There are currently no NICE recommended treatments for C3 glomerulopathy. People usually have treatment to reduce proteinuria, manage hypertension, and to reduce inflammation. This includes angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists (ARBs), in addition to immunosuppressants, including corticosteroids. In late-stage kidney disease, people will need dialysis or kidney transplant, but there is a high-risk of C3 glomerulopathy recurrence after a kidney transplant.[1] The Kidney Disease Improving Global Outcomes 2021 Clinical Practice Guideline for the Management of Glomerular Diseases recommends that, in people with moderate-to-severe disease, C3 glomerulopathy should be treated with mycophenolate mofetil plus corticosteroids (in addition to ACE inhibitors/ARBs), and if this does not work, eculizumab should be considered.[6] NHS England has published a clinical commissioning policy that commissions eculizumab for the treatment of highly aggressive C3 glomerulopathy that recurs after kidney transplant in adults and children.[2]

The technology

Iptacopan (Fabhalta, Novartis) does not currently have a marketing authorisation in the UK for treating complement 3 glomerulopathy. It is an oral treatment.

Iptacopan has been studied in a randomised controlled trial compared with placebo in people aged 12 to 60 years with complement 3 glomerulopathy. Its efficacy and safety has also been studied in a non-randomized open-label study in adults who have and have not had a kidney transplant.

Intervention(s)	Iptacopan
Population(s)	Adults with complement 3 glomerulopathy
Subgroups	If evidence allows, the following subgroups will be considered: • People who have and have not had a kidney transplant • People with C3 glomerulonephritis • People with dense deposit disease • People with CFHR5 nephrology

Comparators	• Established clinical management without iptacopan, which may include:
	  ○ Angiotensin converting enzyme inhibitors
	  ○ Angiotensin II receptor antagonists
	  ○ Corticosteroids
	  ○ Mycophenolate mofetil
	  ○ Sodium-glucose co-transporter-2 (SGLT2) inhibitors
	In people who have previously had a kidney transplant and who have highly aggressive C3 glomerulopathy recurrence as specified in the NHS England clinical commissioning policy for eculizumab:
	• Eculizumab

Outcomes	The outcome measures to be considered include: • kidney function (for example, stabilisation of deterioration in eGFR) • Proteinuria • Disease progression (need for kidney transplant and/or dialysis) • 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 use of iptacopan is conditional on the results of renal biopsy. The economic modelling should include the costs associated with diagnostic testing in people who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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 NICE guidelines:** Chronic kidney disease: assessment and management (2021) NICE guideline NG203. **Related quality standards:** Chronic kidney disease in adults (2011, updated 2017) NICE quality standard 5. **Other NICE products:** C3 glomerulopathy in the native kidney: eculizumab (2015) NICE evidence summary ESUOM49 Prevention of recurrence of C3 glomerulopathy post-transplant: eculizumab (2015) NICE evidence summary ESUOM44
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024)

	NHS England (2017) Clinical Commissioning Policy: Eculizumab in the treatment of recurrence of C3 glomerulopathy post-kidney transplant (all ages)

References

1. Smith RJH, Appel GB, Blom AM, et al. (2019) C3 glomerulopathy - understanding a rare complement-driven renal disease. Nat Rev Nephrol. 15(3):129-143.

2. NHS England (2017) Clinical Commissioning Policy: Eculizumab in the treatment of recurrence of C3 glomerulopathy post-kidney transplant (all ages) [Accessed November 2024]

3. The National Kidney Foundation (2024) Complement 3 Glomerulopathy (C3G) [Accessed November 2024]

4. Medjeral-Thomas NR, O'Shaughnessy MM, O'Regan JA, et al. (2014) C3 glomerulopathy: clinicopathologic features and predictors of outcome. Clinical Journal of the American Society of Nephrology 9:46-53

5. Martín B, Smith RJH (2007) C3 Glomerulopathy. GeneReviews® [Internet]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1425/ [Accessed November 2024]

6. KDIGO (2021) Clinical Practice Guideline for the Management of Glomerular Diseases [Accessed November 2024]