NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Iptacopan for treating complement 3 glomerulopathy ID6283

Draft scope

Draft 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. 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).[1]

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. The kidney problems associated with C3 glomerulopathy tend to worsen over time. About half of affected people develop end-stage renal disease (ESRD) within 10 years of their diagnosis. People with ESRD usually require dialysis or kidney transplantation to stay alive. Dense deposit disease 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.[2] Point prevalence estimates from studies in the UK and other countries range from 0.05 to 1.4 cases per 10,000 people.[3]

There are currently no NICE recommended treatments for C3 glomerulopathy. People usually have treatment to improve kidney function 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.[3] 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 initially with mycophenolate mofetil plus corticosteroids, and if this does not work, eculizumab should be considered. NHS England has published a clinical commissioning policy that routinely commissions eculizumab for treatment of C3 glomerulopathy that recurs after kidney transplant.[1]

The technology

Iptacopan (Fabhalta, Novartis) does not currently have a marketing authorisation in the UK for treating complement 3 glomerulopathy. Iptacopan has been studied in a clinical trial compared to 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)	People 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

Comparators	• Established clinical management without iptacopan, which may include:
	  ○ Angiotensin converting enzyme inhibitors
	  ○ Angiotensin II receptor antagonists
	  ○ Corticosteroids
	  ○ mycophenolate mofetil
	In people who have previously had a kidney transplant and who have 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 (including proteinuria reduction, improvement in eGFR and progression to ESRD) • need for kidney 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. 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)

Questions for consultation

Are all relevant comparators included? Would iptacopan be used alongside or instead of ACE inhibitors, ARBs, corticosteroids and mycophenolate mofetil?

Is eculizumab ever used in the NHS for people with C3 glomerulopathy who have not previously had a kidney transplant?

How is moderate-to-severe C3 glomerulopathy defined in clinical practice?

Does diagnosis of C3 glomerulopathy in order to be eligible for iptacopan require biopsy or other diagnostic testing in people that would otherwise not have been tested?

Where do you consider iptacopan will fit into the existing care pathway for C3 glomerulopathy?

Please select from the following, will iptacopan be:
A. Prescribed in secondary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in secondary care
C. Other (please give details):
For comparators please detail if the setting for prescribing and routine follow-up differs from the intervention.

Are the subgroups listed appropriate?

Are the outcomes listed appropriate? Is it anticipated that iptacopan would be effective in reducing non-renal symptoms in dense deposit disease? If so, are there any further outcomes which should be considered?

Would iptacopan be a candidate for managed access?

Do you consider that the use of iptacopan 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 iptacopan 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 is considering evaluating this technology through its Highly Specialised Technologies Evaluation Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on NICE's health technology evaluation processes is available at: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).

References

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

2. 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

3. 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.

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