NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pegcetacoplan for treating primary complement 3 glomerulopathy and primary immune-complex membranoproliferative glomerulonephritis in people 12 years and over ID6489

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pegcetacoplan within its marketing authorisation for treating primary complement 3 (C3) glomerulopathy and primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN) in people 12 years and over.

Background

Glomerulonephritis is a condition where there is inflammation in the kidney. Both C3 glomerulopathy and IC-MPGN are types of glomerulonephritis, and share similar pathogenesis.[1] In both conditions, there are issues with regulation of a part of the immune system (the 'complement system'). In C3 glomerulopathy, this results in the build-up of C3 protein in the kidneys, with little or no immunoglobulin. IC-MPGN is characterised by build-up of both complement proteins and immunoglobulin.[1] C3 glomerulopathy can be further subdivided into C3 glomerulonephritis (C3GN) and dense deposit disease (DDD).[2] 'Primary' C3 glomerulopathy and IC-MPGN means that the underlying cause of complement dysregulation is not known.[1] Secondary C3 glomerulopathy and IC-MPGN can occur due to multiple reasons, including infection, autoimmune conditions, and cancer.

The major features of C3 glomerulopathy and IC-MPGN 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 associated kidney problems 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 recurrence.

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] The incidence of primary IC-MPGN is unknown. Point prevalence estimates for C3 glomerulopathy from studies in the UK and other countries range from 0.05 to 1.4 cases per 10,000 people.[6]

There are currently no NICE recommended treatments for C3 glomerulopathy or IC-MPGN. People usually have treatment to reduce proteinuria, manage hypertension, and to reduce inflammation. This may include angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists (ARBs), in addition to immunosuppressants, including corticosteroids, and sodium-glucose co-transporter-2 (SGLT2) inhibitors. In late-stage kidney disease, people will need dialysis or kidney transplant, but there is a high-risk of recurrence after a kidney transplant. The Kidney Disease Improving Global Outcomes (KDIGO) 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.[7] 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] For primary IC-MPGN, the KDIGO guidelines also recommend ACE inhibitors and ARBs, with the addition of corticosteroids and other immunosuppressive treatment for people with severe disease.

The technology

Pegcetacoplan (Aspaveli, Swedish Orphan Biovitrum) does not currently have a marketing authorisation in the UK for treating primary C3 glomerulopathy or primary IC-MPGN. It is an intravenous treatment.

Pegcetacoplan has been studied in a randomised controlled trial compared with placebo in people older than 12 years with primary C3 glomerulopathy or primary IC-MPGN.

Intervention(s)	Pegcetacoplan
Population(s)	People with complement 3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis
Subgroups	If evidence allows, the following subgroups will be considered: • People who have and have not had a kidney transplant • People with C3 glomerulopathy • People with immune-complex membranoproliferative glomerulonephritis • Age (12 to 18 years or over 18 years)

Comparators	• Established clinical management without pegcetacoplan, which may include:
	  ○ Angiotensin converting enzyme inhibitors
	  ○ Angiotensin II receptor antagonists
	  ○ Corticosteroids
	  ○ Mycophenolate mofetil
	  ○ Sodium-glucose co-transporter-2 inhibitors
	  ○ Iptacopan (subject to NICE evaluation)
	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 availability and cost of biosimilar and generic products should be taken into account. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of pegcetacoplan 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 technology appraisals in development:**

	Iptacopan for treating complement 3 glomerulopathy. NICE technology appraisal guidance [ID6283] Publication expected January 2026. **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

In NHS practice, what are the main differences in how primary C3 glomerulopathy and IC-MPGN are treated?

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

Would budenoside or sparsentan ever be used as treatment for C3 glomerulopathy or IC-MPGN and if so, would they be considered a comparator or a concomitant treatment?

Would there be any other concomitant treatments that should be accounted for in the modelling?

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

Where do you consider pegcetacoplan will fit into the existing care pathway for C3 glomerulopathy and IC-MPGN?

Would the existing care pathway differ between people aged between 12 and 18 years and people over 18 years? If so, how?

Please select from the following, will pegcetacoplan be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. 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? Are there any further outcomes which should be considered?

Would pegcetacoplan be a candidate for managed access?

Do you consider that the use of pegcetacoplan 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 pegcetacoplan 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. (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. Bomback AS, Charu V, Fakhouri F. (2024) Challenges in the Diagnosis and Management of Immune Complex-Mediated Membranoproliferative Glomerulonephritis and Complement 3 Glomerulopathy. Kidney Int Rep. 10(1):17-28.

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 (2025) Complement 3 Glomerulopathy (C3G) [Accessed March 2025]

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 March 2025]

6. 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.

7. KDIGO (2021) Clinical Practice Guideline for the Management of Glomerular Diseases [Accessed March 2025]

