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

Final scope

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 a secondary cause of complement dysregulation has not been identified.[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, but this progression can be more rapid for some people. 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] 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] The incidence and prevalence of primary IC-MPGN is unknown, but is thought to be similarly uncommon.

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. 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 angiotensin converting enzyme [ACE] inhibitors and angiotensin II

receptor blockers [ARBs]), and if this does not work, eculizumab should be considered.[7] Eculizumab does not have a marketing authorisation for C3 glomerulopathy or IC-MPGN. Despite this, 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. 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 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 a subcutaneous treatment.

Pegcetacoplan has been studied in a randomised controlled trial compared with placebo in people older than 12 years (weighing at least 30 kg) with primary C3 glomerulopathy or primary IC-MPGN.

Intervention(s)	Pegcetacoplan
Population(s)	People aged 12 years and older with primary 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 ○ For people with C3 glomerulopathy, further subgroups could include C3 glomerulonephritis, dense deposit disease, and any specific genetic subtypes of these • People with immune-complex membranoproliferative glomerulonephritis • Age (12 to 18 years or over 18 years) – if consideration is given to these subgroups, the committee will consider any equalities implications.

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 (in people older than 18 years)

	○ Iptacopan (subject to NICE evaluation; in people older than 18 years, for C3G) ○ Other immunomodulatory treatments 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 (including 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)

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]

