Clinical Commissioning Policy Statement: Eculizumab in the prevention of recurrence of C3 glomerulopathy post kidney transplant

NHS England Reference: A06/PS/a

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Additional Circulation List	Regional Medical Directors; Regional Directors of Specialised Commissioning; Regional Clinical Directors of Specialised Commissioning; Regional Directors of Nursing
Description	NHS England will not routinely commission this specialised treatment in accordance with the criteria described in this policy.
Cross Reference	
Superseded Docs (if applicable)	
Action Required	
Timing / Deadlines (if applicable)	
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Document Status

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Plain Language Summary

Kidneys are organs that help filter waste products from the blood. C3 glomerulopathy is an immune disease of the kidneys in which the normal filtering function of the kidneys becomes damaged (by a substance called C3 complement) and protein and blood cells cross through the filters into the urine. Over time, the filters become irreversibly damaged and cannot be repaired, meaning that kidney function eventually declines.

Background

C3 glomerulopathy is a type of glomerulonephritis in which dysregulation of the alternative pathway of the complement system (a component of the immune system) results in abnormal accumulation of the complement protein C3 within the kidney. C3 glomerulopathy includes C3 glomerulonephritis (C3GN) and dense deposit disease (DDD). The incidence of C3 glomerulopathy is 1–2 per million population per year. Renal prognosis is poor, with a 30% risk of end stage renal disease at two years. With some exceptions, the risk of recurrence in the transplanted kidney is over 70%, with more than a 50% chance of graft loss.

The optimal management of people with C3 glomerulopathy (affecting their own and/or a transplanted kidney) is uncertain because existing therapies have not been tested in robust clinical trials. This is most likely due to the inherent difficulties in performing randomised controlled trials in rare disease. In people who have not had a kidney transplant, immunomodulatory agents such as glucocorticoids, mycophenolate mofetil, cyclosporine, tacrolimus and cyclophosphamide have been used. However, evidence for the efficacy of such agents is limited and none are considered to represent definitive therapy. Other proposed treatments include plasma exchange, rituximab (with or without plasma exchange) and eculizumab.

Eculizumab (Soliris, Alexion Pharma UK) is a recombinant humanised monoclonal antibody that binds to complement protein C5, inhibiting its cleavage to C5a (a proinflammatory anaphylatoxin) and C5b and preventing the generation of the terminal complement complex C5b-9 (membrane attack complex), which causes cell lysis and death in pathogens.

Eculizumab has a marketing authorisation in the UK for treating adults and children with atypical haemolytic uraemic syndrome (aHUS) and paroxysmal nocturnal haemoglobinuria (PNH) (summary of product characteristics for Soliris[1]). Like C3 glomerulopathy, aHUS and PNH are complement-mediated diseases, which stimulated interest in using eculizumab to treat this condition. Use of eculizumab to treat people with C3 glomerulopathy, or to prevent recurrence of the condition in a transplanted kidney, is outside the approved indications.

Commissioning Position

Eculizumab as a treatment to prevent recurrence of C3 glomerulopathy post kidney transplant is not routinely commissioned by NHS England.

Effective from

July 2015

Evidence Summary

The National Institute for Health and Care Excellence (NICE) has published an Evidence Summary on the use of eculizumab to prevent recurrence of C3 glomerulopathy post-kidney transplant.[2]

NICE concluded that: '*no evidence was found to determine whether prophylactic use of eculizumab is effective and safe for preventing recurrence of C3 glomerulopathy after kidney transplantation*'.

NICE found no studies or case reports of eculizumab to prevent recurrence of C3 glomerulopathy after a kidney transplant.

There are case reports and a single small study examining the effect of eculizumab on post-transplant recurrent disease, either on histological or clinical criteria.

A small open-label study (n=6, 3 post-transplant) and 7 reports of single cases who had recurrence of C3 glomerulopathy post-transplant and were using eculizumab to prevent progression of the disease were found.

Of the 10 cases relating to eculizumab post kidney transplant, eculizumab improved or stabilised signs of C3 glomerulopathy in 7 cases. A partial response was seen in 1 case, and it was ineffective in 2 cases.

Overall, although eculizumab improved or stabilised signs of C3 glomerulopathy in most cases, improvements in both renal function (proteinuria and serum creatinine) and histology were not always found. In addition, it is possible that cases in which eculizumab was unsuccessful are under reported in the literature.

NICE concluded that '*more evidence is needed to better assess the safety and efficacy of eculizumab in this heterogeneous condition and to determine which patients are most likely to respond treatment*'.

Cost

The cost of one vial of eculizumab 300 mg concentrate solution for infusion is £3150.00 excluding VAT.

According to the summary of product characteristics, in people weighing 40 kg or more, the usual dose given by intravenous infusion is:

- initially 900 mg weekly for 4 weeks, then 1200 mg for 1 week and subsequently every 2 weeks in aHUS
- initially 600 mg weekly for 4 weeks, then 900 mg for 1 week and subsequently every 2 weeks in PNH.

In people weighing less than 40 kg, the dose is adjusted according to weight.

The optimal dosage regimen for eculizumab in C3 glomerulopathy is unclear.

The dose of eculizumab used in the majority of cases with C3 glomerulopathy was 900 mg weekly for four weeks, then 1200 mg for one week and subsequently every two weeks. Based on this dosing regimen, the cost of the five-week initiation phase is £50,400 and the cost of four weeks' maintenance treatment is £25,200 (excluding VAT), not including any other costs incurred when eculizumab is, for example, diluted and administered. The annual cost of treatment in the maintenance phase is £327,600 (excluding VAT).

Equality Impact

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998.

This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

Responsible CRG

Renal Dialysis Clinical Reference Group

Date approved

July 2015

Policy review date

July 2018

References

1. Alexion Pharma UK Limited (2015) Soliris summary of product characteristics.

2. National Institute for Health and Care Excellence (2015) Prevention of recurrence of C3 glomerulopathy post-transplant: eculizumab. NICE evidence summary: unlicensed off-label medicine 44 which can be found at http://www.nice.org.uk/advice/esuom44/chapter/Key-points-from-the-evidence