Clinical Commissioning Policy Statement: Eculizumab for atypical haemolytic uraemic syndrome

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**Document Status**

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Policy Statement
NHS England will commission in accordance with the criteria outlined in this document.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population in England.

Equality Statement
Throughout the production of this document, due regard has been given to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited in under the Equality Act 2010) and those who do not share it.

Plain Language Summary
Atypical haemolytic uraemic syndrome is a very rare condition which affects small blood vessels throughout the body. It is life threatening and a particular problem is kidney failure. Most patients end up on kidney dialysis and transplant is not possible because the disease destroys the transplanted kidney. In many cases the disease is genetic and several members of the same family are affected.

The disease is caused by the body’s complement system. Eculizumab is a drug which effectively blocks the complement system and so prevents progression of the disease. Eculizumab is not a cure so treatment is for life.

NHS England will commission eculizumab for new patients with atypical haemolytic syndrome (defined to include those with a functioning kidney) and for existing patients who are on dialysis and are suitable for a kidney transplant. A commissioning for evaluation scheme will be developed for patients who are not suitable for transplant.
1. Introduction

Eculizumab (Soliris®) is a humanised monoclonal IgG2/4κ antibody produced from murine myeloma cells by recombinant DNA technology.

Eculizumab is marketed by Alexion and has an orphan drug designation in Europe. The drug received marketing authorisation from the European Medicines Agency for the treatment of paediatric and adult patients with aHUS in September 2011. The drug was launched in the UK in November 2011 but is not currently in mainstream use in the NHS.

One 30mL (300mg) vial of Eculizumab (concentrate for intravenous infusion) currently costs £3,150.00.24

Eculizumab also holds full EMA marketing authorisation for the treatment of paroxysmal nocturnal haemoglobinuria (PNH).

Eculizumab has been approved in the EU for the first line treatment of patients diagnosed with aHUS.

2. Definitions

Atypical haemolytic uraemic syndrome is a complement activation disease which is defined and diagnosed clinically, though a proportion of patients have an identifiable genetic mutation.

3. Aim and objectives

The aim of this interim commissioning policy is to provide treatment with eculizumab for those patients indicated by this policy, whilst NICE guidance is developed.

4. Epidemiology and needs assessment

Atypical haemolytic uraemic syndrome (aHUS) is a rare disease affecting approximately 170 people in the UK. It is a condition that develops due to dysregulation of the innate immune system. In children the illness initially causes poor feeding, vomiting and fatigue, whilst adults initially complain of fatigue and general distress. As the illness progresses complications can develop such as anaemia, oedema, hypertension, and acute kidney failure. Current treatment options include plasma therapy (infusion and/or exchange) and liver-kidney transplantation. The outcome is often poor, with approximately 53% of familial cases and 37% of sporadic cases resulting in end stage renal failure (ESRF) or death. Eculizumab (Soliris®) is a new therapy used in patients with aHUS. It is a monoclonal antibody to complement C5 that inhibits the disease process by blocking pro-thrombotic and pro-inflammatory processes which in aHUS can lead to cellular damage in the blood vessels and renal failure.

5. Evidence base

In 2012, the Advisory Group for National Specialised Services (AGNSS)
commissioned a Health Technology Assessment (HTA) from an External Reference Group.

**Clinical effectiveness**

The HTA critically appraised the manufacturer’s submission to AGNSS and also included an independent systematic review of the evidence which covered a broader evidence base as it also included evidence on plasma therapy (not considered by the manufacturer), as well as more information regarding the adverse event profile associated with Eculizumab.

Three studies of Eculizumab were identified. Two single arm prospective studies (C08-002 and C08-003) and one single arm retrospective study (C09-001R) were included in both the manufacturer’s submission and in the independent systematic review. No randomised or controlled studies were identified. Outcomes were assessed in terms of the change from baseline to endpoint at approximately 26 weeks. Thrombotic microangiopathy (TMA) activity, as measured by TMA event free status, was achieved in at least 80% of patients in the prospective studies. Normalisation of platelet count was achieved in 82% of patients in Study C08-002 and in 90% of patients in Study C08-003. Adverse events were frequent with hypertension and upper respiratory tract infection affecting about a third of patients in the prospective studies, although these may be complications of aHUS. No deaths occurred during the prospective studies. The results of the study extension phases suggest that the benefits of treatment are sustained.

**Cost-effectiveness**

The economic analysis presented within the submission suggests that the discounted incremental cost-effectiveness ratio for Eculizumab versus standard care is around £521,000 per QALY gained for a 23-year old cohort and around £376,000 per QALY gained for a 2-year old cohort.

The revised model submitted by Alexion suggests that the discounted incremental cost-effectiveness ratio for Eculizumab versus standard care is around £439,000 per QALY gained for a 23-year old cohort and around £348,000 per QALY gained for a 2-year old cohort.

The ERG had a number of concerns regarding the validity of the model, particularly with respect to the appropriateness of the methods used to derive parameter values for the standard care group, the incorrect implementation of probabilistic sensitivity analysis, the inclusion of a number of assumptions which appear to favour Eculizumab, reliance on modeller’s assumptions rather than expert elicitation, and a lack of clarity regarding the methods used to identify and select evidence to inform the model.

Additional analysis undertaken by the ERG suggests that changing many of the model parameters has little impact upon the incremental cost-effectiveness of Eculizumab. However, changing assumptions regarding the standard care probabilities indicates that the incremental cost-effectiveness ratios for Eculizumab may be considerably higher than the estimates presented within the manufacturer’s submission.
6. Rationale behind the policy statement

The evidence base regarding the clinical effectiveness, cost effectiveness and safety of eculizumab for treating atypical haemolytic uraemic syndrome has been used as a basis for this interim commissioning policy.

7. Criteria for commissioning

Eculizumab has been referred to NICE by Ministers of Health as the first topic for evaluation in their new Highly Specialised Technologies Programme. This review will be undertaken during 2013/14.

In the interim, given the serious nature of the disease, NHS England will fund Eculizumab in patients outlined below.

Eculizumab for the treatment of aHUS is not routinely commissioned for patients currently diagnosed with aHUS who have not received approval for Eculizumab from an existing commissioning body.

NHS England will commission eculizumab for new patients with atypical haemolytic syndrome (defined to include those with a functioning kidney) and for existing patients who are on dialysis and are suitable for a kidney transplant. A commissioning for evaluation scheme will be developed for patients who are not suitable for transplant.

8. Patient pathway

It is proposed to deliver the service locally to patients but with co-ordination from the expert centre in Newcastle.

9. Governance arrangements

Diagnosis will be through the Newcastle Centre and in accordance with the pathway described in this policy.

10. Mechanism for funding

From August 2013 NHS England is responsible for commissioning Eculizumab in line with this policy on behalf of the resident population of England. Funding will be transacted as per local contract agreements and terms.

11. Audit requirements

Audit will be in line with requirements for audit of Highly Specialised Services

12. Documents which have informed this policy

Report to Advisory Group for National Specialised Services 2012
13. Links to other policies

None

14. Date of review

On issue of NICE guidance

References


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