Specialised Services Circular

Issue date:	11 May 2015
ID	SSC 1522
Category:	Commissioning
Status:	For action
Public & Press:	Not applicable

NICE Highly Specialised Technology guidance 1: Eculizumab for treating atypical haemolytic uraemic syndrome

Circulation

For action	**For information**
Local Team Assistant Directors of Specialised Commissioning Regional Team IFR Leads Finance Leads Local Team Pharmacists Local Teams to circulate to: Acute Trust Chief Executives; Acute Trust Medical Directors Acute Trust Chief Pharmacists Clinical Reference Group Chairs: onward circulation relevant CRG members.	Regional Directors of Specialised Commissioning Regional Medical Directors Regional Clinical Directors of Specialised Commissioning Director of Nursing Specialised Commissioning Regional Nursing Directors of Specialised Commissioning

Background

Atypical haemolytic uraemic syndrome (aHUS) is a chronic, rare, progressive condition that causes severe inflammation of blood vessels and the formation of blood clots in small blood vessels throughout the body, a process known as systemic thrombotic microangiopathy. In around 70% of patients, aHUS is associated with an

underlying genetic or acquired abnormality of the proteins of the complement system, which is part of the body's defence against infection. The prognosis for people with aHUS is poor. Patients are at constant risk of sudden and progressive damage, and failure of vital organs. Mortality rates range from 10–15% in the acute phase of the disease and, within a year of diagnosis, up to 70% of patients progress to end-stage renal failure and need dialysis or die. One patient in 5 has aHUS affecting organs other than the kidneys, most commonly the brain or heart.

aHUS can occur at any age. Onset occurs in childhood more frequently than in adulthood (around 60% and 40% of all cases respectively). Most children (70%) who develop aHUS will experience the disease for the first time before the age of 2 years. The true incidence and prevalence of aHUS in England is uncertain because some patients remain undiagnosed. Worldwide, the prevalence of aHUS ranges from 2.7–5.5 per million population, with an incidence of about 0.40 per million population.

Before eculizumab became available, plasma therapy was traditionally the first line treatment for aHUS. Guidelines published by the British Committee for Standards in Haematology and the British Transplantation Society (2009; before the availability of eculizumab) recommend offering all patients with aHUS a trial of plasma exchange and/or plasma infusion. However, response to plasma therapy is variable, and up to 40% of patients may die or progress to end-stage renal failure and need dialysis with the first clinical aHUS manifestation, despite the use of plasma therapy. Some patients may be eligible for a kidney or combined kidney-liver transplantation; however, there is a high risk of organ rejection after recurrent disease.

Eculizumab (Soliris, Alexion Pharma UK) is a human monoclonal antibody that binds to complement C5 and blocks prothrombotic and pro-inflammatory processes. It is produced from murine myeloma cells by recombinant DNA technology. Eculizumab has a marketing authorisation in the UK 'in adults and children for the treatment of patients with atypical haemolytic uraemic syndrome (aHUS)'. It is also licensed for use in people with paroxysmal nocturnal haemoglobinuria.

Summary

NICE in their Highly Specialised Technology Guidance published 28 January 2015 have stated that:

Eculizumab, within its marketing authorisation, is recommended for funding for treating atypical haemolytic uraemic syndrome, only if **all** the following arrangements are in place:

- coordination of eculizumab use through an expert centre
- monitoring systems to record the number of people with a diagnosis of atypical haemolytic uraemic syndrome and the number who have eculizumab, and the dose and duration of treatment
- a national protocol for starting and stopping eculizumab for clinical reasons
- a research programme with robust methods to evaluate when stopping treatment or dose adjustment might occur.

The Newcastle upon Tyne Hospitals NHS Trust has been operating as an interim

expert centre with funding for the service held centrally. The model of care is such that the expert centre confirms that the patient has a diagnosis of aHUS and that they meet the criteria for eculizumab. They initiate treatment with eculizumab but the ongoing prescribing of the drug is generally passed to a centre more local to the patient but which has expertise in treating patients with renal disease. The cost of eculizumab will therefore be met by local specialised commissioning teams through usual contractual arrangements. There is no longer a central budget for the drug – this was passed to Area Teams in April 2014.

NHS England is seeking expressions of interest (EoI) from providers to become the expert centre:

https://www.contractsfinder.service.gov.uk/Notice/0de6c928-c942-42ed-83b4-4bd01133433c

The EoI criteria are based on those set out in the NICE guidance and a more detailed service specification is also being developed. This will be progressed through the usual Programme of Care and Clinical Priorities Advisory Group mechanisms. In the meantime, Newcastle will continue to provide the aHUS service. Once any EoIs are received, the Highly Specialised Commissioning Team will liaise with any local specialised commissioning colleagues to discuss the EoIs and put in place appropriate contracting arrangements.

A database of patients on eculizumab has already been established and currently includes 82 patients (some of whom are no longer receiving eculizumab) as of February 2015. Summary information will be sent to local specialised commissioning colleagues in order for them to cross-reference against their records. There are also a small number of patients who are still receiving the product through the trial or through compassionate arrangements. The details of these patients will be sent to the relevant teams.

Some work has already been initiated on stopping criteria and a research programme is being explored.

NICE has stated that the long-term budget impact of eculizumab for treating atypical haemolytic uraemic syndrome is uncertain but will be considerable. The NICE guidance states that NHS England and the company (Alexion Pharma UK) should consider what opportunities might exist to reduce the cost of eculizumab to the NHS.

Eculizumab is given intravenously in adults as initial treatment at a dose of 900 mg for 4 weeks, then as maintenance treatment at a dose of 1200 mg on week 5 and then every 12–16 days. The summary of product characteristics for eculizumab states that “treatment is recommended to continue for a patient's lifetime, unless discontinuation of treatment is clinically indicated”. Patients under 18 years with a body weight of 40 kg or more are treated in line with the adult dosing recommendations. Paediatric patients with a body weight below 40 kg have their dose adjusted by body weight. Eculizumab costs £3150 per 30 ml (10 mg/ml) vial (excluding VAT; British national formulary, online July 2014). The total cost of eculizumab per adult is estimated to be about £340,200 (initial and maintenance treatment) in the first year of treatment and about £327,600 for 1 year of treatment on the recommended maintenance dose. Eculizumab inhibits terminal complement activation and therefore makes patients vulnerable to meningococcal infections. Life-threatening and fatal infections have occurred in patients who have received

eculizumab. Due to this increased risk, meningococcal vaccination is recommended at least two weeks prior to receiving eculizumab, unless the risks of delaying eculizumab therapy outweigh the risk of developing a meningococcal infection, in which case the vaccine should be given as soon as possible. The cost of these vaccinations should be funded by NHS England.

NHS England will commission eculizumab for aHUS according to the full criteria contained within this circular from 28th April 2015.

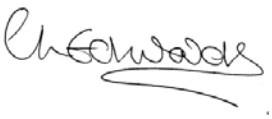
Action

Area Teams are asked to note this position and to work with providers to ensure that eculizumab for treating atypical haemolytic uraemic syndrome is made available in its NICE approved indication as set out above.

Further Information

NICE Highly Specialised Technology Guidance 1: Eculizumab for treating atypical haemolytic uraemic syndrome can be found at https://www.nice.org.uk/guidance/hst1

James D Palmer
National Clinical Director
Specialised Services



Cathy Edwards
Operational Delivery Director
Specialised Commissioning