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Highly Specialised Technology Evaluation

Eculizumab for the treatment of atypical haemolytic uraemic syndrome (aHUS)

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed 12 pages.

About you

Your name: Rodney D Gilbert

Name of your organisation: University Hospital Southampton NHS Foundation Trust

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? **Yes**
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

aHUS was traditionally treated with plasma exchange or sometimes plasma infusion. Since eculizumab became available most places have started using it. There was significant variation initially as funding was applied for to individual PCTs. More recently NHS England have established a vetting and approval process under the auspices of Prof Tim Goodship in Newcastle. Clinicians can apply to Prof Goodship and his team for approval. The greates variability currently is in diagnosis. The only alternative treatment is plasma exchange which is significantly less efficacious.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

Paediatric patients with CD46 mutations generally do better than others but adults with the same mutation have as bad a prognosis as other patients. Some patients e.g. those with CD46 may need a shorter course of treatment than others e.g. with activating mutations of factor B but there is no good data on this as yet.

What is the likely impact of the technology on the delivery of the specialised service? Would there be any requirements for additional staffing and infrastructure, or professional input (for example, community care, specialist nursing, other healthcare professionals)?

The treatment is much easier to administer than plasma exchange and can in fact be given at the patient's home.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

As far as I am aware it is used according to the manufacturer's instructions for aHUS. It may have been used off-label for other indications such as antibody mediated rejection and C£ nephropathies but I am unable to comment on this.

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

We currently follow the manufacturer's guidelines.

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The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

Eculizumab is considerably easier to use than plasma exchange, particularly in young children. It can be used at home in stable patients.

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

We are very familiar with the indications for starting eculizumab: Start early, on clinical suspicion of aHUS if necessary. Need to measure ADAMTS13 and look for evidence of *E. coli* infection. Genetic testing is not necessary to make the diagnosis or start treatment (it takes at least 8 weeks for the result) but testing for *DKGE* mutations should be performed in infants/young children as these patients don't respond well to eculizumab. More work is required to determine those patients in whom it can safely be stopped. Possibilities include children with isolated CD46 abnormalities and those with factor H antibodies.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

The published data reflects clinical practice.

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

Side efffects are generally very minor except for the risk on meningococcal infection (around 0.5 per 100 patient years.)

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Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

I have one case report accepted for publication but not yet published on the beneficial effects with cardiac and cerebral involvement. I recently reviewed a manuscript reporting a child who was dialysis dependent but whose GFR improved to over 70 ml/min/1.73m^2 on eculizumab.

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Implementation issues

Following a positive recommendation, NICE will recommend that NHS England provide funding for the technology within a specified period of time.

If the technology is unlikely to be available in sufficient quantity or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within the specified period of time, NICE may advise NHS England to vary this direction.

The drug should be readily available in sufficient quantities.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

No

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Equality and Diversity

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 this evaluation:

- Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which eculizumab is/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 lead to recommendations that have any adverse impact on people with a particular disability or disabilities

Please tell us what evidence should be obtained to enable the Evaluation Committee to identify and consider such impacts

I cannot forsee any problems with equality or diversity issues.