Appendix G - professional organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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: Comments submitted by [redacted], RCP registrar

Name of your organisation: Royal College of Physicians (RCP)

Comments coordinated by [redacted]

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- 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?

NHS England now approves clinical use, and therefore minimises geographic variation. There is still some uncertainty around the approval and use of the drug around transplantation, and this may influence the decision on usage in individual patients.
There are some differences of clinical opinion based on the specific mutation present, and this is due to a lack of sufficient evidence base of the response of individual mutations to treatment. Ongoing clinical trials and registries with detailed phenotypic data are essential to overcome this problem.
Alternative treatments in most cases are plasma exchange, and in the cases with end stage renal disease, liver-kidney transplantation in certain mutations. The use of the drug peri and post-transplantation is another area that requires more evidence, including the consideration of liver-kidney transplantation as a potential cure for those with a mutation in a soluble complement factor.

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?

Yes, each different complement factor that is mutated could behave in a different way biologically, and needs to be considered individually. Some subgroups may therefore require more or less prolonged treatment to maintain clinical wellbeing, but that is not yet adequately studied.

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)?

Little additional requirements for staffing or infrastructure are required. This type of technology delivery and monitoring is currently well within the remit of the tertiary paediatric units that manage most cases with this condition. Some remote advice may be needed for adult units not as familiar with the protocols for management.

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?

The technology has considerable potential outside its licensed indication, but that requires well designed double-blind trials to evaluate. Unfortunately any plans for these are not yet forthcoming from the company, and the drug is entering clinical practice in some cases as treatment for unlicensed indications. This is particularly true for D+HUS, where there are uncontrolled series of patients published, but also for e.g. MPGN where there are case reports of use published.

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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.

Our experts are not aware of any clinical guidelines yet produced. There is, however, an aHUS Rare Disease Group (an expert group, under the umbrella of the renal Rare Disease Registry, RADAR), tasked to develop clinical guidelines for the UK.

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?

The only current alternative is plasma infusion or exchange, which is expensive and invasive. The technology in principle is easier than this to use, though will require regular hospital visits (currently 2 weekly) to administer, and monitoring for infection, particularly meningococcus, and prophylacticvaccination.

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.

This is an important and unresolved question. The technology is currently licensed for lifelong use, but has not been evaluated for shorter periods of treatment, or for targeted treatment during disease relapses. There are good theoretical reasons for why this may be possible, and for which mutations may be more or less likely to require prolonged treatment regimes. This needs to be formally tested.

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 clinical trials published are of limited scope in that a total of only 37 patients were enrolled over 2 controlled trials. They do however indicate a dramatic benefit in

the patients treated, and the circumstances do reflect UK clinical practice (one trial was on patients resistant to plasma therapy, and one on patients on chronic plasma therapy). The outcome measurements were appropriate, and reflected both disease activity/haematological parameters, and recovery of renal function. The age group was patients over 12 years, so younger patients have not been formally evaluated. Long term follow up was just over a year, and suggests sustained remission up to that point. There are no other markers of longer term outcome at the moment that are predictive.

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 effects include infection (meningitis, peritonitis, URTIs etc) and hypertension, and affect a substantial proportion of patients (32-50%). These are all a potential risk, particularly in the long term, and evaluation and long term follow up of a significantly larger number of patients is required for full perspective. All patients on treatment should be subject to formal registry follow up.

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.

There are aHUS registries set up in Europe and the UK, and these should be consulted for clinical information as detailed above.

Implementation issues

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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.

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)?

In paediatrics the technology could be delivered without significant additional resources, using current tertiary care units. However, resources to collect clinical phenotypic follow up data on an ongoing basis would be essential to continue to evaluate the drug in this rare group of patients. In adult practice, some additional staff training and specialist advice may be necessary, considering the rarity of the condition for any individual unit.

Equality

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 the treatment is 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.

No adverse impacts anticipated