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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: Dr Marie Scully

Name of your organisation : UCLH. On behalf of RCPath and BSCH

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? X
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? X
- 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)

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

What is the expected place of the technology in current practice?
The technology would be expected to be used as soon as a HUS is confirmed acutely (once secondary causes are excluded and ADAMTS 13 levels are confirmed as not severely reduced), in patients currently refractory to PEX or in whom PEX is required to stabilise disease chronically and to cover renal transplant.

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?

The current therapy is Plasma exchange, throughout the UK. However, the way this is delivered is variable. The disadvantages are the poor response to therapy, specifically renal function, effects of central line insertion and acute and chronic effects of plasma, including analphylaxis and potential transmission of known or unknown pathogens.

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?
The response and outcome will depend on the underlying complement mutation. Factor H related disease is associated with 25% mortality and a high rate of renal replacement therapy. However, MCP mutations are unlikely to need long term renal replacement and have a low mortality rate. However, between 30-50% of patients will not have a mutation identified.

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)?
All patients require genetic analysis and ADAMTS 13 measurement at presentation. Confirmation to proceed with the technology will need to be centrally agreed, eg a group in north and south UK who need to confirm proceeding with therapy-given the cost and complexity of the disorder.
Availability of out patient services for therapy infusion and specialist follow up clinics

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?
Currently dictated by NHS England and central medical review of the case as defined above

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.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

NHS England guidance in accordance with Central medical review of cases have clearly defined cases for whom the technology is appropriate. There are guidelines but they do not incorporate the technology

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 technology is safer, more efficacious and easier to administer than the current alternative (plasma exchange). Patients need to be aware of the risk of meningococcal infection and ideally it should be run from regional central experts to monitor with local trusts response to therapy and the need to continue.

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.
Depending on presentation +/-the underlying genetic abnormality, there is definitely patients who will not need continuous therapy. Acute exacerbations eg infections, will require immediate access to therapy, but those who have normalisation of renal function may not need continuous treatment eg MCP mutations

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

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

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?
Clinical trial practice does reflect routine clinical practice. However, not all patients may require continuous therapy. The most important outcome is normalisation of renal function.

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?

The side effect profile is very acceptable and relatively fewer than PEX

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.

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Highly Specialised Technology Evaluation

All trial evidence submitted

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.

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

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

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)?

As described above. NICE need to be mindful that the currently available therapy (PEX) is inferior and not without associated cost and complications

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;

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

- 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

NICE must not put further hurdles to access the technology, otherwise it will result in significant disadvantages to a HUS patients