Highly Specialised Technology Evaluation

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

Thank you for agreeing to give us your views on the condition, the technology and the way it should be used in the NHS.

Patients, carers and patient organisations can provide a unique perspective on the condition and the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Where appropriate, please provide case studies of individual patients, their families or carers. Please do not exceed 30 pages.

About you

Your name:

[redacted]

Name of your organisation:

aHUSUK

Brief description of the organisation:

AHUSUK is a support group for patients with aHUS in UK, their families and caregivers. Formed in September 2011 as an unincorporated charitable association, it is registered as a charity with the Charity Commission in England and Wales.(No 1145953).

It is an independent voluntary organisation managed by eight trustees. It has 95 adult members, each of whom either has aHUS or is related to or caring for someone who has. Although the precise number is unknown, the last national survey by Newcastle University in 2011 suggested that there were 140 diagnosed aHUS cases in England in a population of 56m, a frequency of 2.4 per 1M or a ratio of 1:400000.

AHUSUK supports its members and their families by offering information, advice and advocacy. It provides a patient card for relatives to aid early diagnosis. It seeks to increase awareness of the disease among the public and clinicians by providing information and interviews to local and national media. It has campaigned vigorously for access to eculizumab for all diagnosed patients in England. It has petitioned Parliament and Government, met with parliamentarians and ministers, given evidence to parliamentary committees at both Westminster and Holyrood.

It is funded by unrestricted educational grants from Alexion Pharmaceuticals UK, donations from Newcastle University and Yeowart Holdings Ltd (a member's company) and its own fundraising activities, which include sale of merchandise and proceeds from events. Its income in the period 1 11 2011 – 31 10 2012 was £32,000.

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Are you (tick all that apply):

- a patient with the condition for which NICE is considering this technology?

X a carer of a patient with the condition for which NICE is considering this technology?

X an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, member, etc)

- other? (please specify)

I am a founder voluntary trustee and secretary of aHUSUK. My wife was diagnosed with aHUS in April 2011 and while I was her carer for a time, since she received eculizumab in August 2011, as part of a clinical trial, the improvement in her condition has meant I have not had to do so since October 2011.

How does the condition impact on patients, their families or carers?

1(i). Please describe whether patients experience difficulties or delays in receiving:
- a diagnosis
- appropriate treatment
- helpful information about the condition

and the impact these difficulties have on patients and their families or carers.

We would like to present our answers to Q1&2 in the form of an attachment entitled "**The Life Experience of aHUS Patients, their Families and Carers in England and Wales"** This is based on a Report commissioned by NHS in England in 2012 and organised by [redacted], a trustee of aHUSUK. It derives from interviews with 14 aHUS patients and carers conducted by consultants appointed by NHS to assist aHUSUK and has been updated with material from later patient and carer interviews carried out by aHUSUK. It is an evolving document which has been updated to show the continuing stark reality of life for aHUS patients, their families and caregivers.

Sections 2 -5 answer Q 1(i) above and Q 1(ii) below in detail.

Section 6 expands on our answers to Q2 (i) and (ii) below, and includes three case studies which describe the actual beneficial effect of Eculizumab on patients' lives.

(ii) Please describe how patients and their families or carers have to adapt their lives as a result of the condition, and the impact the condition has on the following aspects:
- physical health
- emotional wellbeing
- everyday life (including if applicable: ability to work, schooling, relationships, social functioning)
- other impacts not listed above

See Q1(i) above.

What do patients, their families or carers consider to be the advantages and disadvantages of the technology for the condition?

2. Advantages
(i) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make for patients, their families or carers.

Eculizumab will allow aHUS patients to resume a normal life, free from the burden of the onerous and less than fully effective alternative existing treatments and their medical risks and side effects. (These are listed in detail in our answer to Q6 below). The three case studies in Section 6 of the attachment describe the benefits of eculizumab in three patients recently prescribed the drug.

(ii) Please list any short-term and long-term benefits that patients, their families or carers expect to gain from using the technology. These might include the effect of the technology on:
- the course and outcome of the condition
- physical symptoms
- pain
- level of disability
- mental health
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example friends and employers)
- other issues not listed above

Eculizumab halts the complement over-activity which causes aHUS and prevents further decline in kidney function and if given soon enough, in some circumstances, will even reverse it.

Transplanted patients with aHUS may expect to get the same benefit from a donated organ as other transplanted patients.

Although in some aHUS patients some additional medication may be necessary to counter, say, hypertension, it is likely that patients on eculizumab will have no pain and no disability.

The enhanced quality of life which will follow treatment with eculizumab should give rise to better work prospects, better social and leisure opportunities and an improvement in psychological well-being. As they return to work, many patients will cease to be dependent on state benefits and will become tax contributors.

The improvement in family life will be equally dramatic, particularly for caregivers and close relatives as normal family life resumes. Family breakups, which are more frequent in households where there is serious illness, may be avoided.

The effect on children will be marked, and not just on those with the disease, who will be able to resume studies and other activities, but also on siblings who will get a chance to thrive in an improved home environment, free from the strained atmosphere surrounding serious illness.

3. Disadvantages

Please list any problems with or concerns you have about the technology. Disadvantages might include:
- aspects of the condition that the technology cannot help with or might make worse
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient or their family (for example cost of travel needed to access the technology, or the cost of paying a carer)

Eculizumab has no disadvantages compared to the other treatments of plasma exchange (PEX) and renal dialysis. Administration of eculizumab is by fortnightly infusion in hospital. This takes 35 minutes followed by 60 minutes observation. It has no reported side effects although patients may have to have a meningitis vaccination at least 2 weeks before commencing treatment. We know of only one occurrence of meningococcal meningitis in a UK aHUS patient, when it occurred after a booster had been given and prior to the commencement of treatment by eculizumab.

Patients report a beneficial effect almost immediately and experience noticeable improvement after just a few infusions. In pre-dialysis patients, provided aHUS is diagnosed and eculizumab administered before the patient has lost all kidney function, it would appear to be effective in every case.

4. Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.
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We know of no difference of opinion about its usefulness among patients receiving eculizumab. In fact, among our members either receiving the drug themselves or as parents of children receiving the drug there is unanimous agreement about its effectiveness. They often use terms such as “miracle drug” and “magic bullet” to describe the dramatic effect it has on their condition and quality of life.

5. Are there any groups of patients who might benefit **more** from the technology than others? Are there any groups of patients who might benefit **less** from the technology than others?

Every single aHUS patient should benefit from eculizumab. The extent to which they will do so will depend on their condition and current treatment. It is likely that those who have had to endure dialysis, sometimes for years, and may now be prescribed eculizumab in support of a renal transplant, will see the most marked improvement. To a lesser extent, those undergoing PEX will still see huge benefits and of course the uncertainty surrounding the long term effectiveness of PEX will be removed. All should be able to return to a normal life, which will mean resumption of family life, resumption of careers and education opportunities and the chance to lift their horizons and aspire to much more than just short term survival. They should all enjoy improved life expectancy.

All this will of course be less marked in newly diagnosed patients, where the disease is diagnosed and eculizumab administered at an early stage, that is before they suffer significant loss of kidney function. They will be spared the trauma of PEX and dialysis. In one sense they could be said to be the greatest beneficiaries of all.

Finally those with a known genetic predisposition will benefit from the knowledge that eculizumab will be made available and they need not have their lives ruined by this disease.

6. Comparing the technology with alternative available treatments or technologies

NICE is interested in your views on how the technology compares with existing treatments for this condition in the UK.

(i) Please list current standard practice (alternatives if any) used in the UK.

The following summary of the burdens of current conventional treatments was included in aHUSUK's recent patient submission to the Clinical Priorities Advisory Group and was extracted from information supplied in the Report attached to Q1&2 above and from an on-line survey completed in May 2013 by aHUSUK members. To fully appreciate the huge improvement in treatment that eculizumab brings it is necessary to understand the two existing treatments.

"In recent years plasma exchange (PEX), that is the replacement of the body's entire blood plasma in one session, has been the standard pre-dialysis treatment for adults and children. It is not pleasant. Patients have told us about daily treatment sessions lasting several hours.

The side effects and risks as follows:

- Oedema causing shortness of breath and mobility problems ,
- Hives, allergic reactions and anaphylactic shock,
- Hypotension,
- Nausea and fatigue ,
- Inconvenience and risk of fixed lines becoming dislodged or causing infection.

Although there were occasional reports of patients going spontaneously into temporary remission, these are rare, and when PEX failed to maintain kidney function, as it often did over the longer term, dialysis was the only remaining option.

Dialysis is required when kidney function is lost. It is a replacement therapy and not a complete substitute for a functioning kidney. Patients are subjected to a strict diet and fluid restrictions of 500 ml a day. Dialysis can be done in hospital or at home. Many patients resigned to a lifetime of dialysis prefer the flexibility of being able to dialyse at home; but that requires space, equipment and training in its use. All patients found treatment a huge burden.

They reported the physical and mental effects as follows:

• Requirement for operations to create access points for treatment and surgery to maintain effective fistulas and avoid catastrophic bursts, but knowing that these access points are finite;
• Risk of tesio line in jugular vein becoming infected, splitting or becoming detached;
• Those dialysing with a fistula having to place two large and sharp needles into their own arm;
• CAPD dialysis requires a permanent catheter into the abdomen, which results in scarring and body image issues
• Having to cope with technical faults/power cut/water supply issues in the equipment in mid treatment on home dialysis (with the risk of losing 400ml of blood volume)
• Constant vigilance required to spot infection and possible air entry into lines
• On CAPD it is inconvenient and tying to exchange dialysis fluid every four hours every day
• Extremely low blood pressure causing patients to 'crash ‘and lose consciousness during treatment
• High blood pressure causing seizures and migraine headaches
• Cramps, nausea, faintness and/or headaches during and following a dialysis session
• Fatigue due to anaemia and requiring blood transfusions or self injection of EPO
• Fear of fluid overload causing respiratory failure and drowning in your own body
• Fear of potassium levels so high they can cause a heart attack
• Greater risk of heart and blood vessel disease including strokes and fluid around the heart and severe damage to the heart valves requiring open heart by-pass surgery
• Steal syndrome associated with fistulas causing pain and requiring surgery
• Losing hair because of blood thinning drugs required for dialysis
• Episodes of extremely painful and life threatening peritonitis
• CAPD treatment causing encapsulating Sclerosing peritonitis which requires major abdominal surgery and on-going treatment which can cause ovarian cysts
• Anxiety and depression resulting in need for counselling and medication
• Body image problems resulting from scarring and from unsightly fistulas and from weight gain and loss from treatment
• Parathyroid problems
• Pulmonary Hypertension
• Carpal tunnel syndrome
• Gall stones and gall bladder removal
• Renal bone disease causing joint pain and need for hip replacements
• Restless legs syndrome
• Dry and extremely itchy skin

• Impaired cognitive function
• Coping with aftermath of miscarriage and premature births during episode of aHUS."

The contrast between the above treatments and a simple 35 minute infusion of eculizumab every fortnight, free from the associated medical risks and side effects, coupled with the certainty of a return to better quality of life, could not be more pronounced.

(ii) If you think that the new technology has any **advantages** for patients over other current standard practice, please describe them. Advantages might include:
- improvement of the condition overall
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in hospital)
- side effects (please describe nature and number of problems, frequency, duration, severity etc)

The advantages are enormous and can be summarised as follows:

• Dramatic improvement in medical condition
• Ease of use
• Absence of side effects and treatment risk (which are described fully in the answer to Q6 above) .
• Improvement in longevity
• Improvement in social, work, leisure and travel opportunities
• Improvement in family life
• Recovery of confidence and self esteem
• Relaxation of dietary controls
• Freedom from strict fluid input restrictions

But the overwhelming advantage will be the certainty of a return to a better quality of life which eculizumab will bring.

(iii) If you think that the new technology has any **disadvantages** for patients compared with current standard practice, please describe them. Disadvantages might include:
- worsening of the condition overall
- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

We are unaware of any incidence of disadvantage to a patient receiving eculizumab compared to PEX or dialysis.

7. Research evidence on patient, family or carer views of the technology
(i) If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their care reflects that observed under clinical trial conditions.

We have no research evidence to prove this point but we know of no reason for there to be any difference in the experience of patients on a trial or otherwise. .

ii) Are there any adverse effects that were not apparent in the clinical trials but have come to light since the treatment has become available?

Again we have no research evidence but again we know of no adverse effects between trials and normal usage.

(iii) Are you aware of any research carried out on patient, family or carer views of the condition or existing treatments that is relevant to an evaluation of this technology? If yes, please provide references to the relevant studies.

No

8. Availability of this technology to patients

(i) What key differences, if any, would it make to patients, their families or carers if this technology was made available?

The difference to a patient's life after starting treatment with eculizumab cannot be overstated. It is truly life changing. It provides the chance, which many may have thought had been lost, to enjoy a longer life free from the huge physiological and psychological burdens imposed by other treatments, which have been described elsewhere. It offers a chance for them to resume a normal life and make a full contribution to society. The beneficial effect on family life is correspondingly huge.

(ii) What implications would it have for patients, their families or carers if the technology was **not** made available?

If eculizumab were to be removed from existing patients, they would inevitably suffer acute kidney injury and would have to revert immediately to treatment by PEX or dialysis, with all the medical and social difficulties associated with these. This is not to mention the depressive effect of seeing themselves condemned to an increasingly blighted life and early death, from which they thought they had escaped.

If only patients currently receiving eculizumab were to continue treatment and all others, including newly diagnosed patients were to be denied it, this would perpetuate all the current difficulties experienced by these patients and create an obvious injustice within the cohort. .

If only current recipients and the newly diagnosed were to receive the drug, it would perpetuate the injustice suffered by the majority of the aHUS cohort, some of whom have been and still are discriminated against because of age, weight and disability. .

(iii) Are there groups of patients that have difficulties using the technology?

No

Equality

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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 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.

We believe that all aHUS patients should be treated as one cohort and given the opportunity to receive this drug in accordance with their clinical need. Failure to provide it for a notional sub-cohort would constitute an inequality bordering on discrimination.

Other Issues

Please consider here any other issues you would like the Evaluation Committee to consider when evaluating this technology.

AHUS patients have waited a long time for this drug to be made freely available in England for all who need it and the medical condition of several on existing treatments has deteriorated in the meantime. In the past 3 years the drug has been looked at twice, by AGNSS and CPAG, both of which acknowledged its clinical effectiveness and recommended that it be centrally commissioned in England.

It is commissioned centrally in England for another condition, PNH, and has been since 2010. .

It is freely available from state health services in Italy, Spain, France and Belgium for aHUS patients in these countries.

Although the manufacturers maintain that the drug has to be taken in the prescribed dose for life, CPAG recommended recently that NHS investigate whether flexibility in dosing might be possible. We have evidence that in at least one European country, Italy, where the drug has been freely available for years, that flexible dosing, based on strict clinical criteria and patient monitoring, is working successfully.

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