NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Ravulizumab for treating atypical haemolytic uraemic syndrome (aHUS)

Draft scope (pre-referral)

Draft remit/evaluation objective

To evaluate the benefits and costs of ravulizumab within its marketing authorisation for treating atypical haemolytic uraemic syndrome for national commissioning by NHS England.

Background

Atypical haemolytic uraemic syndrome (aHUS) is a chronic and rare disease that causes severe inflammation of blood vessels and the formation of blood clots, leading to organ damage in children and adults. In approximately 70% of people, aHUS is associated with an underlying genetic or acquired abnormality of proteins in the immune system called complement. There are currently around 143 people with a diagnosis of aHUS in England,[1] but there may be many more people who remain undiagnosed.

The prognosis for people with aHUS is poor, with early mortality rates ranging from 10% to 15%, and with the majority of people progressing to end stage renal failure. People with aHUS may experience a considerable impact on their daily living and quality of life and can experience significant kidney impairment, thrombosis, heart failure and brain injury.

Most people who develop aHUS for the first time are treated with daily plasma exchange. However, approximately 50% of people do not respond to treatment and develop permanent kidney failure, requiring treatment with long-term dialysis. Some people may have a kidney or combined kidney-liver transplantation; however there is a high risk of organ rejection following recurrent disease. NICE highly specialised technologies 1 recommends eculizumab as an option for treating aHUS in children and adults.

The technology

Ravulizumab (Ultomiris, Alexion Pharma UK) is a monoclonal antibody that binds to terminal complement protein C5 and prevents the complement-mediated destruction of red blood cells. It is administered by intravenous infusion.

Ravulizumab does not currently have a marketing authorisation in the UK for treating atypical haemolytic uraemic syndrome (aHUS). It has been studied in single-arm clinical trials in adults and children with aHUS who have not previously received treatment with a complement inhibitor (e.g. eculizumab),

and in children and adolescents who have had previous complement inhibitor therapy.

Intervention(s)	Ravulizumab
Population(s)	Children and adults with atypical haemolytic uremic syndrome (aHUS)
Comparators	• plasma infusion and/or exchange Previously treated people with kidney impairment: • kidney dialysis • kidney or kidney/liver transplantation
Outcomes	The outcome measures to be considered include: • overall survival • time to disease recurrence • response to treatment • avoidance of dialysis • avoidance of plasma therapy • maintenance or improvement of kidney function • other major non-renal clinical outcomes • eligibility for/success of transplantation • development of antibodies and resistance • adverse effects of treatment • health related quality of life (for patients and carers).
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options

Clinical Effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• Cost effectiveness using incremental cost per quality-adjusted life year • Patient access schemes and other commercial agreements • The nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	• Guidance will only be issued in accordance with the marketing authorisation. • Guidance will take into account Managed Access Arrangements
Related NICE recommendations and NICE Pathways	Related highly specialised technologies guidance: Eculizumab for treating atypical haemolytic uraemic syndrome (2015) NICE highly specialised technologies guidance 1. Review date January 2018 Related NICE Pathways: Chronic Kidney Disease pathway available at http://pathways.nice.org.uk/pathways/chronic-kidney-disease.

Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2017) Atypical haemolytic uraemic syndrome (aHUS) (all ages): Service specification. Reference number: 170008/S NHS England (2013) Clinical Commissioning Policy: Eculizumab for atypical haemolytic uraemic syndrome. E03/PS(HSS)/a.

Questions for consultation

Have all relevant comparators for ravulizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for aHUS?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

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 the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which ravulizumab 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 have any adverse impact on people with a particular disability or disabilities.

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

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.

References

1. NHS England: Highly Specialised Services 2018. Accessed June 2019