NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ravulizumab for treating atypical haemolytic uraemic syndrome (aHUS)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ravulizumab within its marketing authorisation for treating atypical haemolytic uraemic syndrome.

Background

Atypical haemolytic uraemic syndrome (aHUS) is a 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 with the condition, aHUS is associated with an underlying genetic or acquired abnormality of proteins in the immune system called complement.[1]

The prognosis for people with aHUS historically was poor if without treatment. Early mortality rates ranged from 10% to 15%, and the majority of people progressed to end stage renal failure.[2] 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. The prevalence of aHUS is estimated to be about 5.5 per million and it is estimated that around 150 to 180 people with the condition are receiving treatment in England.[3,4]

The current treatment for people who develop aHUS is eculizumab. NICE highly specialised technologies (HST) guidance 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 activation, therefore blocking blood clots formation and destruction of red blood cells. It is administered by intravenous infusion.

Ravulizumab has been granted positive opinion by the Committee for Medicinal Products for Human Use for the “treatment of patients with a body weight of 10 kg or above with atypical haemolytic uremic syndrome (aHUS) who are complement inhibitor treatment-naive or have received eculizumab for at least 3 months and have evidence of response to eculizumab.”

Ravulizumab has a marketing authorisation in the UK for the treatment of paroxysmal nocturnal haemoglobinuria.

Intervention(s)	Ravulizumab
Population(s)	People who weigh 10 kg or more with atypical haemolytic uremic syndrome (aHUS) and: • who have not had complement inhibitor treatment, or • who have had eculizumab for at least 3 months and whose disease has responded to eculizumab.
Comparators	Eculizumab
Outcomes	The outcome measures to be considered include: • overall survival • disease recurrence • response to treatment • cessation or avoidance of dialysis • 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
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
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. 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 atypical haemolytic uremic syndrome?

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 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)?

Do you consider that the use of ravulizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

References

1. Noris et al. Relative role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. Clin J Am Soc Nephrol 2010;5(10):1844-59

2. National renal complement therapeutics centre – atypical Haemolytic uraemic syndrome (aHUS) Accessed May 2020

3. NHS England – Service specifications aHUS Accessed May 2020

4. National renal complement therapeutics centre: The Annual Report of the National Renal Complement Therapeutics Centre 2018/19. Accessed May 2020