NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Ravulizumab for treating paroxysmal nocturnal haemoglobinuria

Draft scope (pre-referral)

Draft remit/evaluation objective

To evaluate the benefits and costs of ravulizumab within its marketing authorisation for treating paroxysmal nocturnal haemoglobinuria for national commissioning by NHS England.

Background

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare blood condition in which red blood cells are attacked by the body's immune system. It is characterised by intravascular haemolysis (rupturing of red blood cells) with resultant anaemia often leading to transfusion dependence, severe disabling symptoms of haemolysis and, frequently, thrombosis (blood clotting). The risk of thrombosis is increased in people with PNH who are pregnant. PNH can also lead to extravascular haemolysis. It is an acquired condition, meaning it is not inherited so cannot be passed on from parent to child. PNH is a chronic condition that is associated with complications that can be severely debilitating and life threatening including abdominal pain, kidney problems, fatigue, shortness of breath, bleeding and blood clots, dysphagia, organ damage and premature mortality.[1,2]

The incidence of PNH in Great Britain has been estimated as approximately 1 in 770,000 each year, with a predicted prevalence of approximately 1 in 62,500, suggesting that there are currently approximately 896 people living with PNH in England (1/62,500x55,977,178).[3] It has also been estimated that there are about 650 people in England with PNH.[4] However, the severity of PNH is heterogeneous and not everyone with the condition will be eligible for treatment. The number of patients treated with alternative complement inhibitor eculizumab in the UK as of December 2018 was 239.[4] PNH can occur at any age but is most frequently diagnosed between the ages of 30-40 years old.[3,5] Ten-year survival after diagnosis and without treatment with a complement-inhibitor has been estimated to range between 65% and 78%.[6]

There is currently no NICE guidance for treating PNH. Current clinical management for patients with PNH includes treatment with complement inhibitor eculizumab. Allogeneic stem cell transplantation may be curative but is associated with significant risks and is only considered for patients with severe bone marrow failure.[7] Other interventions, notably red blood cell transfusions, folic acid, iron tablets and anti-coagulant treatments are offered to prevent or treat complications.[2]

© National Institute for Health and Care Excellence 2020. All rights reserved.

The technology

Ravulizumab (Ultomiris, Alexion Pharmaceuticals) 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 has a marketing authorisation in the UK for treating PNH in adults who have haemolysis with clinical symptoms indicative of high disease activity, or whose disease is clinically stable after having eculizumab for at least 6 months. It has been studied in randomised clinical trials compared with eculizumab, in adults with PNH who have not previously received treatment with a complement inhibitor (e.g. eculizumab), and in adults who have had eculizumab for at least 6 months.

Intervention(s)	Ravulizumab
Population(s)	Adults with paroxysmal nocturnal haemoglobinuria • who have haemolysis with clinical symptom(s) indicative of high disease activity or • whose disease is clinically stable after having eculizumab for at least 6 months
Comparators	• Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • haemolysis (measured by lactate dehydrogenase [LDH] level) • breakthrough haemolysis • transfusion avoidance • stabilised haemoglobin • thrombotic events • 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

© National Institute for Health and Care Excellence 2020. All rights reserved.

	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 any Managed Access Arrangements for the intervention under evaluation
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2018) Highly specialised services 2018. NHS England (2017) Manual for Prescribed Specialised Services 2018/19. Chapter 86, Paroxysmal nocturnal haemoglobinuria service (adults and adolescents)

© National Institute for Health and Care Excellence 2020. All rights reserved.

	Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

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 paroxysmal nocturnal haemoglobinuria? How should best supportive care be defined?

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-

© National Institute for Health and Care Excellence 2020. All rights reserved.

guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.

References

1 PNH National Service. Accessed February 2020.

2 Kings College Hospital NHS Trust (2013) Paroxysmal nocturnal haemoglobinuria. Accessed February 2020.

3 Orphanet Paroxysmal nocturnal hemoglobinuria. Accessed February 2020.

4 NHS England (2018) Highly Specialised Services 2018. Accessed February 2020.

5 Al-Ani F, Chin-Yee I, and Lazo-Langner A. (2016) Eculizumab in the management of paroxysmal nocturnal hemoglobinuria: patient selection and special considerations. Therapeutics and Clinical Risk Management. 12:1161-70. doi: 10.2147/TCRM.S96720.

6 Martí-Carvajal AJ, Anand V, Cardona AF, Solà I. Eculizumab for treating patients with paroxysmal nocturnal hemoglobinuria. Cochrane Database of Systematic Reviews 2014, Issue 10

7 Hill A, DeZern AE, Kinoshita T, Brodsky RA. (2017) Paroxysmal nocturnal haemoglobinuria. *Nat Rev Dis Primers.* 3:17028

© National Institute for Health and Care Excellence 2020. All rights reserved.