

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Ravulizumab for treating paroxysmal nocturnal haemoglobinuria

Final scope

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 ($1/62,500 \times 55,977,178$).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 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 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. Eculizumab is commissioned for this indication by NHS England through the national PNH highly specialised service.⁷ As such, eculizumab has not been through a health technology assessment, and the current value of eculizumab to the NHS has not been evaluated. Therefore, if ravulizumab were to be recommended for NHS use on the basis of comparing ravulizumab with eculizumab this could lead to an unacceptable use of NHS resources. Allogeneic stem cell transplantation may be curative but is associated with significant risks and is only considered for patients with

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Issue Date: April 2020

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severe bone marrow failure.⁸ Other interventions, notably red blood cell transfusions, folic acid, iron tablets and anti-coagulant treatments are offered to prevent or treat complications.²

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 <ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Best supportive care
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life

	<ul style="list-style-type: none"> • extent and nature of current treatment options
Clinical Effectiveness	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<p>NHS England (2018) Highly specialised services 2018.</p> <p>NHS England (2017) Manual for Prescribed Specialised Services 2018/19. Chapter 86, Paroxysmal nocturnal haemoglobinuria service</p>

	<p>(adults and adolescents)</p> <p>NHS England (2013) NHS standard contract for paroxysmal nocturnal haemoglobinuria service (adults and adolescents) Ref. B05/S(HSS)/a</p> <p>Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.</p>
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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.
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- 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 NHS England (2013) [NHS standard contract for paroxysmal nocturnal haemoglobinuria service \(adults and adolescents\) Ref. B05/S\(HSS\)/a](#)
- 8 Hill A, DeZern AE, Kinoshita T, Brodsky RA. (2017) Paroxysmal nocturnal haemoglobinuria. *Nat Rev Dis Primers*. 3:17028