NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ravulizumab for treating paroxysmal nocturnal haemoglobinuria

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ravulizumab within its marketing authorisation for treating paroxysmal nocturnal haemoglobinuria.

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 and increased further for those with PNH and who are pregnant. PNH can also lead to extravascular haemolysis (haemolysis taking place in the liver, spleen, bone marrow, and lymph nodes). 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[3]. It is estimated that there are about 650 to 900 people in England with PNH.[3,4] 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]

Although there is currently no NICE guidance for treating PNH, current clinical management for people with PNH can include treatment with 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.[6] 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 • 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	• Eculizumab
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).
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. 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	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) NHS England (2013) NHS standard contract for paroxysmal nocturnal haemoglobinuria service (adults and adolescents) Ref. B05/S(HSS)/a Department of Health and Social Care (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

References

1 PNH National Service. Accessed July 2020.

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

3 Orphanet Paroxysmal nocturnal hemoglobinuria. Accessed July 2020.

4 NHS England (2018) Highly Specialised Services 2018. Accessed July 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 Schubert J, Röth A. Update on paroxysmal nocturnal haemoglobinuria: on the long way to understand the principles of the disease. Eur J Haematol. 2015;94(6):464-473

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