NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pegcetacoplan for treating paroxysmal nocturnal haemoglobinuria

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pegcetacoplan 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 people 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 technology appraisal guidance on treating PNH, NHS England commissions the C5 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]

The technology

Pegcetacoplan (brand name unknown, Apellis Pharmaceuticals) is a is a PEGylated cyclic peptide inhibitor of complement C3 that prevents the

complement-mediated destruction of red blood cells. It is administered by subcutaneous injection.

Pegcetacoplan does not currently have a marketing authorisation in the UK for treating PNH. It has been studied in a randomised clinical trial, compared with eculizumab in adults with PNH who have previously received treatment with eculizumab and who have a haemoglobin level <10.5 g/dL.

Intervention(s)	Pegcetacoplan
Population(s)	Adults with paroxysmal nocturnal haemoglobinuria whose anaemia is not controlled after treatment with a C5 complement inhibitor
Comparators	• Eculizumab • Ravulizumab [subject to NICE appraisal]
Outcomes	The outcome measures to be considered include: • overall survival • intravascular haemolysis • extravascular haemolysis • breakthrough haemolysis • transfusion avoidance • haemoglobin • thrombotic events • 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. 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.

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	Appraisals in development (including suspended appraisals) Ravulizumab for treating paroxysmal nocturnal haemoglobinuria NICE technology appraisal ID1457. Expected publication date to be confirmed
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Highly specialised services 2018 NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). 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 February 2021.

2 Kings College Hospital NHS Trust (2013) Paroxysmal nocturnal haemoglobinuria. Accessed February 2021.

3 Orphanet Paroxysmal nocturnal hemoglobinuria. Accessed February 2021.

4 NHS England (2018) Highly Specialised Services 2018. Accessed February 2021.

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.