NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pegcetacoplan for previously treated paroxysmal nocturnal haemoglobinuria

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pegcetacoplan within its marketing authorisation for previously treated 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 guidance for treating PNH, current clinical management for patients with PNH can include 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]

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 randomised clinical trials, compared with best supportive care in adults with PNH, and 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)	People with previously treated paroxysmal nocturnal haemoglobinuria
Comparators	• Eculizumab • 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.
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	None
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

Questions for consultation

To whom would pegcetacoplan be offered in the NHS?

Have all relevant comparators for pegcetacoplan been included in the scope? Which treatments are considered to be established clinical practice in the NHS for PNH? How should best supportive care be defined?

Do people stop treatment with eculizumab if their haemoglobin level is <10.5 g/dL? If not, does pegcetacoplan have the potential to displace eculizumab in this group?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom pegcetacoplan is expected to be more clinically effective and cost effective 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 pegcetacoplan 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 pegcetacoplan 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 pegcetacoplan 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.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

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.