NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Iptacopan for treating paroxysmal nocturnal haemoglobinuria

Draft scope

Draft remit/evaluation objective

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

Background

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare blood condition caused by an acquired mutation of the PIG-A gene that is not present from birth. The body's immune system attacks and ruptures red blood cells, resulting in anaemia. This can lead 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 is a chronic condition that is associated with complications that can be severely debilitating and life threatening. These can include abdominal pain, kidney problems, fatigue, shortness of breath, bleeding and blood clots, dysphagia, organ damage and premature mortality.[1,2]

The annual incidence of PNH in Great Britain has been estimated to be about 1 in 770,000, with a predicted prevalence of about 1 in 62,500, suggesting that there are currently about 905 people living with PNH in England.[3,4] PNH can occur at any age but is most frequently diagnosed at about 30 years old.[2] Ten-year survival after diagnosis has been estimated to range between 65% and 78%.[5]

Clinical management for PNH includes treatment with complement inhibitor eculizumab. Eculizumab is commissioned for this indication by NHS England through the national PNH highly specialised service.[6] For PNH, NICE recommends:

- ravulizumab for adults with haemolysis with clinical symptoms suggesting high disease activity, or whose disease is clinically stable after having eculizumab for at least 6 months (NICE technology appraisal 698), and
- pegcetacoplan for adults who have anaemia after at least 3 months of treatment with a C5 inhibitor (NICE technology appraisal 778).

Allogeneic stem cell transplantation may be curative but is associated with significant risks and is only considered for patients with severe bone marrow failure. 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

Iptacopan (Brand name unknown, Novartis Pharmaceuticals) does not currently have a marketing authorisation in the UK for paroxysmal nocturnal haemoglobinuria. Iptacopan monotherapy has been studied in a single-arm clinical trial in adults with PNH who have not previously had treatment with a complement inhibitor. It has also been compared with eculizumab and ravulizumab in a randomised controlled trial of adults with PNH who previously had stable regimens of anti-C5 antibody treatment.

Intervention(s)	Iptacopan
Population(s)	People with paroxysmal nocturnal haemoglobinuria
Subgroups	If the evidence allows the following subgroups will be considered: • previous treatment: treatment naïve vs treatment experienced • type of haemolysis: extravascular vs intravascular.
Comparators	• Eculizumab • Ravulizumab • Pegcetacoplan • Crovalimab (subject to NICE ongoing appraisal) • Danicopan with a C5 inhibitor (subject to NICE ongoing appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • haemolysis • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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. The availability and cost of biosimilar and generic products should 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	**Related technology appraisals:** Pegcetacoplan for treating paroxysmal nocturnal haemoglobinuria (2022) NICE technology appraisal guidance 778. Ravulizumab for treating paroxysmal nocturnal haemoglobinuria (2021) NICE technology appraisal guidance 698. **Related technology appraisals in development:** Danicopan with a C5 inhibitor for treating paroxysmal nocturnal haemoglobinuria with extravascular haemolysis [ID5088] Publication date to be confirmed. Crovalimab for treating paroxysmal nocturnal haemoglobinuria [ID6140] 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) NHS manual for prescribed specialist services (2018/2019) Chapter 86, Paroxysmal nocturnal haemoglobinuria service (adults and adolescents)

	NHS England (2013/14) Standard Contract for Paroxysmal Nocturnal Haemoglobinuria Service (Adults and Adolescents). Reference B05/S(HSS)/a NHS England (2020) Paroxysmal Nocturnal Haemoglobinuria Service (Adults and Adolescents) blood and infection metric definitions.

Questions for consultation

Where do you consider iptacopan will fit into the existing care pathway for paroxysmal nocturnal haemoglobinuria?

Would iptacopan be a candidate for managed access?

Do you consider that the use of iptacopan can result in any potential 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 committee to take account of these benefits.

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 iptacopan 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-tehnology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. PNH National Service (2023) The National PNH Service. Accessed May 2023.

2. NORD (2023) Paroxysmal Nocturnal Hemoglobinuria. Accessed May 2023.

3. European Molecular Biology Laboratory (2023) OLS Orphanet Rare Disease Ontology Paroxysmal nocturnal hemoglobinuria. Accessed May 2023.

4. Office for National Statistics (2022) Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2021. Accessed May 2023.

5. Martí-Carvajal AJ, Anand V, Cardona AF et al. (2014) Eculizumab for treating patients with paroxysmal nocturnal hemoglobinuria. Cochrane Database of Systematic Reviews Issue 10.

6. NHS England (2013) NHS standard contract for paroxysmal nocturnal haemoglobinuria service (adults and adolescents) Ref. B05/S(HSS)/a.