NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Iptacopan for treating paroxysmal nocturnal haemoglobinuria

Final scope

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, chronic blood condition caused by an acquired mutation (a mutation that is not present from birth) of the PIG-A gene within stem cells in the bone marrow. The body's immune system attacks and ruptures red blood cells. The breakdown of red cells can happen within the blood vessels (intravascular haemolysis) or outside the blood vessels (extravascular haemolysis). This often results in anaemia, and can lead to transfusion dependence, severe disabling symptoms of haemolysis and thrombosis (blood clotting). The risk of thrombosis is further 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, It is estimated that there are about 650 to 900 people living with PNH in England.[3,4] PNH can occur at any age but is most frequently diagnosed between the ages of 30 and 40 years old.[2]

The severity of PNH is varied and not everyone with the condition will need treatment. The National PNH service is commissioned by NHS England as a specialised service. Clinical management includes treatment with complement inhibitors, although some people will experience haemolysis despite treatment with complement inhibitors (breakthrough haemolysis):

- Eculizumab, a C5 inhibitor, is commissioned for PNH with high disease activity.[6]

- Ravulizumab, a C5 inhibitor, is recommended 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, a C3 inhibitor, is recommended 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 PNH. 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 anaemia despite treatment with a C5 inhibitor.

Intervention(s)	Iptacopan
Population(s)	Adults with paroxysmal nocturnal haemoglobinuria
Subgroups	If the evidence allows the subgroups based on previous treatment with complement inhibitors will be considered: • treatment naïve • treatment experienced • treatment experienced with anaemia despite previous treatment
Comparators	• Eculizumab • Ravulizumab • Pegcetacoplan • Danicopan with a C5 inhibitor (subject to NICE ongoing 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. 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.

References

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

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

3. Orphanet (2023) Paroxysmal nocturnal hemoglobinuria. Accessed July 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. NHS England (2013) NHS standard contract for paroxysmal nocturnal haemoglobinuria service (adults and adolescents) Ref. B05/S(HSS)/a.