NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Danicopan as an add-on treatment to a C5 inhibitor for treating extravascular haemolysis in adults with paroxysmal nocturnal haemoglobinuria

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of danicopan as an add-on treatment to a C5 inhibitor within its marketing authorisation for treating extravascular haemolysis in adults with 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 thrombosis (blood clotting). People with PNH may also experience extravascular haemolysis (EVH; haemolysis taking place in the liver, spleen, bone marrow, and lymph nodes), which can be clinically significant and lead to symptomatic anaemia and ongoing transfusion dependence

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.[1] It is estimated that there are about 650 to 900 people in England with PNH.[2] PNH can occur at any age but is most frequently diagnosed between the ages of 30 and 40 years old.[1,3] The proportion of people with PNH who experience clinically significant EVH is uncertain.

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.[4]

- 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.[5] Other

interventions, notably red blood cell transfusions, folic acid, iron tablets and anti-coagulant treatments are offered to prevent or treat complications.[6]

The technology

Danicopan (brand name unknown, Alexion Pharmaceuticals) does not currently have a marketing authorisation in the UK for PNH. It has been studied in clinical trials in combination with either eculizumab or ravulizumab compared with placebo in combination with either eculizumab or ravulizumab in adults with clinically evident extravascular haemolysis who have been receiving a C5 inhibitor for at least 6 months.

Intervention(s)	Danicopan as an add-on treatment to a C5 inhibitor (eculizumab or ravulizumab).
Population(s)	Adults with paroxysmal nocturnal haemoglobinuria who have signs and symptoms of extravascular haemolysis while on treatment with a C5 inhibitor (eculizumab or ravulizumab).
Comparators	• Pegcetacoplan • Eculizumab • Ravulizumab • Iptacopan (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. 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	**Related technology appraisals:** Pegcetacoplan for treating paroxysmal nocturnal haemoglobinuria (2022) NICE technology appraisal guidance TA778. Ravulizumab for treating paroxysmal nocturnal haemoglobinuria (2021) NICE technology appraisal guidance TA698. **Related technology appraisals in development:** Iptacopan for treating paroxysmal nocturnal haemoglobinuria [ID6176] Expected publication June 2024. 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 (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. NHS England (2018) NHS manual for prescribed specialist services (2018/2019) Chapter 86, Paroxysmal nocturnal haemoglobinuria service (adults and adolescents)

References

1 Orphanet Paroxysmal nocturnal hemoglobinuria. Accessed May 2023.

2 NHS England (2020) Highly Specialised Services 2019/20. Accessed May 2023.

3 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.

4 PNH National Service Indications for Treatment with Eculizumab, Ravulizumab and Pegcetacoplan Accessed May 2023.

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

6 Kings College Hospital NHS Trust (2013) Paroxysmal nocturnal haemoglobinuria. Accessed May 2023.