

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Crovalimab for treating paroxysmal nocturnal haemoglobinuria

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of crovalimab 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). 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

Crovalimab (brand name unknown, Roche) does not currently have a marketing authorisation in the UK for PNH. Crovalimab monotherapy has been studied in a single-arm clinical trial in people with PNH who have not previously had treatment with a complement inhibitor. It has also been compared with eculizumab in randomised controlled trials in people with PNH not previously treated with complement inhibitors, and in people with PNH currently treated with complement inhibitors.

Intervention(s)	Crovalimab
Population(s)	People with paroxysmal nocturnal haemoglobinuria
Subgroups	<p>If the evidence allows the subgroups based on previous treatment with complement inhibitors will be considered:</p> <ul style="list-style-type: none"> • people not previously treated with complement inhibitors (treatment naive) • people currently treated with complement inhibitors •
Comparators	<ul style="list-style-type: none"> • Eculizumab • Ravulizumab • Pegcetacoplan • Iptacopan (subject to NICE evaluation) • Danicopan with a C5 inhibitor (subject to NICE evaluation)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • intravascular haemolysis • extravascular haemolysis • breakthrough haemolysis • transfusion avoidance • haemoglobin • thrombotic events • adverse effects of treatment • health-related quality of life.

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
Other considerations	<p>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.</p>
Related NICE recommendations	<p>Related technology appraisals:</p> <p>Pegcetacoplan for treating paroxysmal nocturnal haemoglobinuria (2022) NICE technology appraisal guidance 778.</p> <p>Ravulizumab for treating paroxysmal nocturnal haemoglobinuria (2021) NICE technology appraisal guidance 698.</p> <p>Related technology appraisals in development:</p> <p>Danicopan with a C5 inhibitor for treating paroxysmal nocturnal haemoglobinuria with extravascular haemolysis [ID5088] Publication date to be confirmed.</p> <p>Iptacopan for treating paroxysmal nocturnal haemoglobinuria [ID6176] Publication date to be confirmed.</p>
Related National Policy	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2018) Highly specialised services 2018</p> <p>NHS England (2018) NHS manual for prescribed specialist services (2018/2019) Chapter 86, Paroxysmal nocturnal haemoglobinuria service (adults and adolescents)</p>

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

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

Is pegcetacoplan a relevant comparator for crovalimab in people with PNH currently treated with complement inhibitors?

Would crovalimab be a candidate for managed access?

Do you consider that the use of crovalimab 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 the treatment 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 is considering evaluating this technology through its cost comparison evaluation process.

Please provide comments on the appropriateness of appraising this topic through this 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-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost,

compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's [health technology evaluations: the manual](#) states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?
- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. PNH National Service (2023) [The National PNH Service](#). Accessed August 2023.
2. NORD (2023) [Paroxysmal Nocturnal Hemoglobinuria](#). Accessed August 2023.
3. Orphanet (2023) [Paroxysmal nocturnal hemoglobinuria](#). Accessed August 2023.
4. Office for National Statistics (2022) [Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2021](#). Accessed August 2023.
5. NHS England (2013) [NHS standard contract for paroxysmal nocturnal haemoglobinuria service \(adults and adolescents\)](#) Ref. B05/S(HSS)/a.