National Institute for Health and Care Excellence

Health Technology Evaluation

Iptacopan for treating paroxysmal nocturnal haemoglobinuria [ID6176]
Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Novartis	Novartis agrees that an evaluation of iptacopan for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) as a single technology appraisal is appropriate. While the topic does not meet the criteria for an evaluation under the highly specialised technology (HST) route, it should be noted that PNH is an ultra-rare disease and the associated challenges in evidence generation should be considered accordingly.	Thank you for your comments. No action is needed.
	National paroxysmal nocturnal haemoglobinuria (NPNH) service & the Royal College of	The evaluation is appropriate. Iptacopan is the first oral monotherapy for patients with PNH being assessed through NICE.	Thank you for your comments. No action is needed.

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	Pathologists (RCP)		
	NHS England (NHSE)	This is an appropriate topic for evaluation as is the evaluation route	Thank you for your comment. No action is needed.
	Genetic Alliance UK	PNH is a rare condition that can have a significant impact on quality of life. As this technology has been routed through an STA rather than HST pathway, its evaluation may be disadvantaged by the evidence constraints of smaller population numbers therefore this would be a good case for the committee to exercise flexibility in their decision making.	Thank you for your comments. No action is needed.
	PNH support	PNH is a rare condition that can have a significant impact on quality of life. As this technology has been routed through an STA rather than HST pathway, its evaluation may be disadvantaged by the evidence constraints of smaller population numbers therefore this would be a good case for the committee to exercise flexibility in their decision making. This is the first oral monotherapy for PNH to be reviewed by NICE.	Thank you for your comments. No action is needed.
Wording	Novartis	Novartis agrees that the wording of the remit is appropriate.	Thank you for your comment. No action is needed.
	NPNH service & RCP	There is no information included in the draft scope in relation to current clinical trial data, where the technology will be utilised within the treatment pathway or the cost effectiveness of iptacopan.	This will be discussed in detail during the appraisal. Please include all relevant

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			information in your submission. No action is needed.
	NHSE	The wording of the remit reflects the clinical and cost effectiveness about this technology.	Thank you for your comments. No action is needed.
	PNH support	No clinical trial or proposed label data has been included in the scope, nor does it include any information about cost effectiveness or quality of life data.	This will be discussed in detail during the appraisal. Please include all relevant information in your submission. No action is needed.
Timing	Novartis	Iptacopan is expected to be the first oral monotherapy licensed for the treatment of PNH. Novartis believes that a timely appraisal that allows the publication of guidance shortly after a marketing authorisation is obtained would be of value to patients and the NHS.	Thank you for your comments. No action is needed.
	NPNH service & RCP	Standard timing is appropriate.	Thank you for your comment. No action is needed.
	NHSE	This is not an urgent evaluation.	Thank you for your comment. No action is needed.

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	PNH support	Patients being treated with a C5 inhibitor who experience clincially significant extravascular haemolysis and have anaemia after at least 3 months of treatment with a C5 inhibitor have the option of treatment with pegcetacoplan which is licenced and available so there is no urgency. However depending on the label and whether this treatment will be available to C5 inhibitor naïve paitents as well as those treated with a C5 inhibitor treatment, it may be that both of these groups of patients would prefer taking oral medication instead of medication with an intravenous or sub-cutaneous delivery method. It is also important to note that having multiple treatment options for the same condition improves patient care and outcomes. Also our current understanding as to why some PNH patients respond better to some medications rather than others is still developing therefore having more treatment options means that patients are able to access the best treatment option for them.	Thank you for your comments. No action is needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Novartis	Novartis would like to propose the following amendments to the background information for clarity and consistency with previous appraisals. The background section should be amended to describe both intravascular and extravascular haemolysis, in line with previous appraisals. We suggest that the second sentence be amended to say, "*The body's immune system attacks and ruptures red blood cells (complement-mediated intravascular haemolysis)* …" and that the following text is added, as per the ravulizumab [TA698] and pegcetacoplan [TA778] final scopes, *"PNH can also lead to*	Thank you for your comments. The background and technology sections were updated as suggested. We have not added information on how many people are treated with

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		extravascular haemolysis (haemolysis taking place in the liver, spleen, bone marrow, and lymph nodes)". The current phrasing suggests that the thrombosis risk may only be elevated in PNH patients that are pregnant, which would be incorrect. Therefore, we suggest that the text be amended to "*The risk of thrombosis is increased in people with PNH and increased further for those with PNH and who are pregnant.",* in line with the scope of previous appraisals [TA698, TA778]. The second paragraph details that there are currently about 905 people living with PNH in England. However, not all PNH patients require treatment with a complement inhibitor. The most recent annual report from the PNH National Service indicates that close to 300 patients in England are currently treated with complement inhibitors (1). Novartis suggests that this information be added. Additionally, this paragraph refers to 10-year survival rates of 65% to 78%, however these figures represent outcomes from before the introduction of eculizumab. Following the availability of complement inhibitors, PNH patients' survival is now comparable to the general population (2) and Novartis requests that this wording be removed. The current wording states that "*Clinical management for PNH includes treatment with complement inhibitor eculizumab*". Novartis believes that this wording may be misleading by omission, and suggests that this be amended to state "… *treatment with complement inhibitors, including the C5 inhibitors eculizumab and ravulizumab and the C3 inhibitor pegcetacoplan".*	complement inhibitors as the scope only includes a brief introduction to the disease area. Please include all relevant information in your submission.

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		The "The Technology" section of the draft scope states that iptacopan "*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".* This phrasing omits that patients must have continued to have anaemia while on treatment with their previous regimen, which was a key inclusion criterion in the APPLY-PNH trial and will be important to define the target population for treatment with iptacopan in clinical practice. Additionally, for consistency with language used in previous appraisals, Novartis suggests that the scope refers to C5 inhibitors, as opposed to anti-C5 antibody treatment. As such, we ask for the following amendment: "*Iptacopan has also been compared with eculizumab and ravulizumab in a randomised controlled trial of adults with residual anaemia despite treatment with a C5 inhibitor."*	
	NPNH service & RCP	The background information given is correct but additional information is presented below relating to clinical trial data. Extravascular haemolysis only occurs in patients with PNH being treated with a C5 inhibitor (Eculizumab/Ravulizumab/Crovalimab - three of the comparator treatments). Iptacopan is a proximal complement inhibitor so does not cause extravascular haemolysis. The APPLY study was presented at the American Society of Hematology Annual meeting in December 2022 and evaluated iptacopan in 97 patients with PNH who had residual anaemia despite treatment with eculizumab or ravulizumab. The primary efficacy and safety data from the 24 week	Thank you for your comments. The background section was updated to include information on extravascular haemolysis and types of complement inhibitors. Information about the trials was not added as the scope only includes a brief introduction to the disease area. Please include all

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		randomised treatment period was presented. Iptacopan was superior to the standard of care with C5 inhibitors for both primary endpoints: An increase from baseline in haemoglobin of ≥2 g/dL in the absence of transfusions (51/60 patients treated with iptacopan and 0/35 patients treated with C5 inhibition). Haemoglobin level of ≥12 g/dL in the absence of transfusions (42/60 patients treated with iptacopan and 0/35 patients treated with C5 inhibition). The APPOINT study evaluated patients with PNH patients who were naive to complement inhibitor therapy. 92.2% of patients achieved a 2 g/dL or more haemoglobin level increase from baseline without the need for transfusions after the 24-week treatment period. This study also demonstrated clinically meaningful benefits for secondary endpoints with an estimated 62.8% of patients achieving haemoglobin levels of 12 g/dL or more without the need for transfusions. Iptacopan demonstrated a tolerability and safety profile consistent with previously reported data	relevant information in your submission.
	NHSE	The background is accurate and reflects the natural history of the disease, the epidemiology and the commissioned treatment pathways.	Thank you for your comment. No action is needed.
	Alexion	Alexion believes that the background information currently presented on the clinical management for PNH does not fully reflect the current clinical practice, we believe the wording should be changed to:	Thank you for your comments. We have made changes based on your suggestion.

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		"Clinical management for PNH includes treatment with complement inhibitor eculizumab and ravulizumab. Eculizumab and ravulizumab are both commissioned for this indication by NHS England through the national PNH highly specialised service."	
	PNH support	The description of iptacopan does not include that it is an oral capsule taken twice per day (kept in cold chain during trials) which we consider to be relevant. The description of PNH does not refer to the fact that some people treated with C5 inhibitors often continue to experience clinically significant extravascular haemolysis.	Thank you for your comments. The background section was updated to include information on extravascular haemolysis. Information about delivery was not added as the scope only includes a brief introduction to the disease area.
Population	Novartis	The expected licensed indication for iptacopan in PNH will only cover adults and this should be reflected in the population wording (*"Adults with…"*).	Thank you for your comment. We have made changes based on your suggestion.
	NPNH service & RCP	Yes	No action is needed.

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	NHSE	Yes	No action is needed.
Subgroups	Novartis	Novartis believes that subgroups based on previous treatment are appropriate, given the design of the two iptacopan Phase 3 trials and the fact that one of the comparators (pegcetacoplan) is only licensed and recommended for one of the subgroups. However, in line with the population included in the APPLY-PNH study, clinical evidence for treatment experienced patients will only allow for an evaluation in patients that continue to experience anaemia while treated with a complement inhibitor. Therefore, we ask for the subgroup description to be amended to *"previous treatment: treatment naïve vs treatment experienced with residual anaemia"*. Regarding the other suggested subgroup analysis, Novartis does not believe that it is possible or appropriate to partition patients into subgroups based on type of haemolysis. Intravascular haemolysis (IVH) is a key characteristic of untreated PNH (3). C5 inhibitors control IVH, however due to their mode of action, extravascular haemolysis (EVH) may arise as a consequence in some patients (4). Therefore, the same patients may experience both IVH and EVH at different points in the course of the disease. Furthermore, intravascular breakthrough haemolysis (BTH) may occur in all patients treated with a complement inhibitor, including those treated with a C5 inhibitor who have EVH (5).	Thank you for your comments. We have made changes based on your suggestion.
	NPNH service & RCP	No	No action is needed
	NHSE	No	No action is needed

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	PNH support	Patients treated with C5 inhibitors who continue to experience clinically significant extravascular haemolysis resulting in suboptimal disease control are the subgroup which would benefit most from this treatment which addresses both intravascular haemolysis and extravascular haemolysis.	Thank you for your comments. A subgroup of people with PNH who have anaemia despite previous treatment was added.
Comparators	Novartis	Novartis agrees with the inclusion of eculizumab, ravulizumab, and pegcetacoplan as comparators in the appraisal. However, it is important to note that pegcetacoplan is only an option for patients who continue to have anaemia after at least 3 months of treatment with a C5 inhibitor, as per TA778. We would also like to highlight that the use of eculizumab is declining, as it is increasingly being replaced by ravulizumab as a similar drug with equal efficacy and less frequent administration, which is associated with improved quality of life in comparison to eculizumab [TA698]. At the time of writing, neither crovalimab nor danicopan with a C5 inhibitor have a license or are available to PNH patients in the UK (outside clinical trials or any potential pre-license access programmes). Based on information available in the public domain, this is not expected to change prior to the submission of iptacopan to NICE. For this reason, we do not consider that either treatment option is an appropriate comparator in the appraisal of iptacopan, as they cannot be considered standard treatments used in the NHS.	Thank you for your comments. Based on anticipated appraisal timelines, crovalimab has been removed from the scope. In the event that danicopan becomes established clinical practice prior to the appraisal of iptacopan by committee, it has been included as a comparator.

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		We would also like to highlight that there appear to be inconsistencies across PNH appraisals in terms of inclusion of treatments which are not currently licensed/available as comparators.	
	NPNH service & RCP	The comparators listed are appropriate. Eculizumab, ravulizumab and crovalimab are C5 inhibitors. Crovalimab is not currently available on the NHS. These therapies prevent intravascular haemolysis but can cause an increase in extravascular haemolysis. Pegcetacoplan is the only proximal complement inhibitor currently licenced that treats intravascular haemolysis without causing an increase in extravascular haemolysis. Not all patients with extravascular haemolysis are suitable for or wish to utilise Pegcetacoplan in view of choice and also modality of administration (subcutaneous infusion twice weekly). Danicopan is an oral factor D inhibitor, to treat patients with PNH on a C5 inhibitor experiencing extravascular haemolysis. It is planned in combination with a C5 inhibitor as a combination treatment.	Thank you for your comments. Based on anticipated appraisal timelines, crovalimab has been removed from the scope. In the event that danicopan becomes established clinical practice prior to the appraisal of iptacopan by committee, it has been included as a comparator.
	NHSE	Yes, these are the appropriate comparators	No action needed.
	Genetic Alliance UK	Two of the comparators stated in the draft scope are described as ‘subject to a NICE ongoing appraisal’, therefore they are not widely available. As far as we understand, the definition of a comparator is a technology that is routinely used in the NHS, therefore we have concerns that these comparators appear to be outside of the usual definition of a comparator. We understand that there may be circumstances that are appropriate to use technologies that are currently being assessed by NICE as a comparator but	Thank you for your comments. Based on anticipated appraisal timelines, crovalimab has been removed from the scope.

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		we would appreciate an overview of how decisions about expanding the definition of a comparator are made, and a discussion with the patient community as to the potential risks and benefits of using comparators outside of the definition and when it may be appropriate to do so. Otherwise, we fear this may lead to an inconsistency and inequality between appraisals. Additionally, we have been made aware by the PNH support group that there is a proportion of patients that are not well served by C5 inhibitors, whereas Iptacopan is likely to effectively treat the whole PNH population. As most of the comparators listed are C5 inhibitors, they are therefore not directly comparable. It is our understanding that Pegcetacoplan is the only listed comparator that is a monotherapy that serves the whole PNH population, similarly to Iptacopan. It is also important to note that having multiple treatment options for the same condition improves patient care and outcomes. Our current understanding as to why some people respond better to some medications than others is still developing therefore having multiple options means that patients can find the best treatment option for them.	In the event that danicopan becomes established clinical practice prior to the appraisal of iptacopan by committee, it has been included as a comparator.
	PNH support	Two of the comparators stated in the draft scope are described as 'subject to a NICE ongoing appraisal', therefore they are not widely available. As far as we understand, the definition of a comparator is a technology that is routinely used in the NHS, therefore we have concerns that these comparators appear to be outside of the usual definition of a comparator. We understand that there may be circumstances that are appropriate to use technologies that are currently being assessed by NICE as a comparator but we would appreciate an overview of how decisions about expanding the definition of a comparator are made, and a discussion with the patient	Thank you for your comments. Based on anticipated appraisal timelines, crovalimab has been removed from the scope.

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		community as to the potential risks and benefits of using comparators outside of the definition and when it may be appropriate to do so. Otherwise, we fear this may lead to an inconsistency and inequality between appraisals. The following comparators which are listed only address intravascular haemolysis so would not be suitable comparators to iptacopan which, as we understand it, addresses both intravascular haemolysis and extravascular haemolysis: • eculizumab • ravulizumab • crovalimab (subject to NICE ongoing appraisal –see comments above) The following named comparator does address both intravascular haemolysis and extravascular haemolysis • pegcetacoplan The following named comparator only addresses extravascular haemolysis if used in conjunction with either eculizumab or ravulizumab (which address intravascular haemolysis) so on its own would not be a relevant comparator. • danicopan with a C5 inhibitor (subject to NICE ongoing appraisal – see comments above)	In the event that danicopan becomes established clinical practice prior to the appraisal of iptacopan by committee, it has been included as a comparator.
Outcomes	Novartis	Novartis agrees with the outcomes listed in the draft scope, however we would ask that *"stabilised haemoglobin"* be amended to state *"haemoglobin"* more generally, as increased haemoglobin or haemoglobin normalisation would also be relevant outcomes. This is aligned with the wording in the final scope for TA778 (pegcetacoplan).	Thank you for your comments. We have made the suggested changes.
	NPNH service & RCP	Yes, these are both appropriate and will capture the most important health related benefits.	No action needed.

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	NHSE	Yes, these are the appropriate outcomes	No action needed.
	Genetic Alliance UK	It is important to recognise that quality of life goes beyond understanding if an individual is able to continue their usual activities as some individuals may be able to do more as a result of their new treatment. For example, some may be able to start working when they weren't able to before. This type of information is not usually captured well in standard quality of life surveys therefore patient testimonies are important to truly understand the impact on overall quality of life.	Thank you for your comments. No action needed.
	Alexion	We would suggest that outcome measures should be aligned with other recent appraisal outcomes for PNH. • Overall survival • Intravascular haemolysis • Extravascular haemolysis • Breakthrough haemolysis • Transfusion avoidance • Haemoglobin • Thrombotic events • Adverse effects of treatment • Health-related quality of life.	Thank you for your comments. The outcomes are now aligned.
	PNH support	Additional outcome measures would be: • LDH level • Specifically in relation to HRQOL, the ability of a patient on the treatment to start to work/study or return to work /study as a result of improvement in their quality of life since treatment with the drug or as a result of the convenience of taking an oral tablet (so time off work is not required in order to receive an infusion). EQ 5D is not specific enough to collect relevant information about those who have been able to start working or work more, study or study more	Thank you for your comments. We have aligned the outcomes with outcomes in other PNH scopes.

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		since starting treatment as it asks about “USUAL ACTIVITIES (e.g. work, study, housework, family or lesisure)”. If work or study hadn’t been a “usual activity” for someone prior to treatment then this question doesn’t capture the fact of someone who can now work, work more, study, study more etc since starting treatment.	During the appraisal it will be discussed if all benefits of iptacopan were captured in the cost-effectiveness analyses. Please include all relevant information in your submission.
Equality	Novartis	Novartis does not envisage any equality issues related to the proposed remit or scope. However, we would like to highlight that pegcetacoplan is currently the only treatment specifically licensed for PNH patients who continue to have anaemia on C5 inhibitors. However, some patients may find self-administering pegcetacoplan, as a subcutaneous (SC) infusion, difficult, or some patients might not be able to self-administer pegcetacoplan at all. This may include people with dexterity, visual or cognitive disabilities. Iptacopan, as an oral drug, would allow these patients access to a treatment which is easy to administer and, in addition to controlling IVH, is also able to control EVH. When appraising treatments for PNH, the committee should consider how these patient groups may be impacted by their recommendations	Thank you for your comments. We have noted your comments on the equality impact assessment (EIA) form.
	NPNH service & RCP	Access for all patients will be via the nationally commissioned PNH service.	Thank you for your comment. No action needed.

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	NHSE	We do not think that the scope needs to be changed in relation to any equalities considerations.	Thank you for your comment. No action needed.
	PNH support	Age and pregnancy are protected characteristics and if different recommendations are made for children, adults and pregnant women, this could lead to inequality. However, it is acknowledged that there is unlikely to be trial data for children and pregnant women at this stage.	Thank you for your comments. We have noted your comments on the equality impact assessment (EIA) form.
Other considerations	Novartis	N/A	-
	Genetic Alliance UK	Burden of treatment should also be considered as part of this technology appraisal. Current treatment options include the requirement for hospital visits for transfusions which may be difficult to get to and impact a person's ability to work full time. Other options include subcutaneous injections that can be difficult to self administer and may lead to an individual being less able to travel with these injections or stay away from home for longer periods of time. Iptacopan is considered to be a significant step-change in treatment options as it can be self administered orally, therefore it more easily fits around a person's day to day life, lessening the burden of treatment and improving overall quality of life.	Thank you for your comments. The methods of administration will be discussed during the appraisal. No action is needed.
	PNH support	Burden of treatment should also be considered as part of this technology appraisal. Current treatment options include infusions which may impact a person's veins and ability to work or study full time. Other options include subcutaneous injections that can be difficult to self administer and may lead to an individual being less able to travel with these injections or stay away	Thank you for your comments. The methods of administration will be

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		from home for longer periods of time. Iptacopan is considered to be a significant step-change in treatment options as it can be self administered orally, therefore it more easily fits around a person's day-to- day life, allieviating vein problems caused by infusions, or injection site issues including bruising and pain, lessening the burden of treatment and improving overall quality of life.	discussed during the appraisal. No action is needed.
Questions for consultation	Novartis	*Where do you consider iptacopan will fit into the existing care pathway for paroxysmal nocturnal haemoglobinuria?* Based on the available evidence, Novartis expects that iptacopan may be a treatment option for adult patients with PNH who are complement inhibitor naïve and have haemolysis with clinical symptoms, as well as adult PNH patients who are already being treated with a complement inhibitor and continue to have anaemia. If recommended, we expect that iptacopan can be integrated into the existing national PNH Service. *Would iptacopan be a candidate for managed access?* Novartis believes that the evidence available at time of the NICE appraisal will be sufficient for the committee to make a decision on the use of iptacopan in routine clinical practice. *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.*	Thank you for the comments. During the appraisal it will be discussed if all benefits of iptacopan were captured in the cost-effectiveness analyses. No action is needed.

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		Anaemia-related fatigue is one of the main patient-reported symptoms of PNH and evidence of improvements in fatigue are available from the iptacopan clinical trials. However, standard generic health-related quality of life (HRQoL) instruments utilised for generating health state utility values for economic modelling may not be able to capture the full impact of fatigue on patients' HRQoL. In particular, the EQ-5D has been shown to have low sensitivity to the impact of fatigue on HRQoL (6, 7). Consequently, benefits of iptacopan in terms of reducing fatigue may not be fully captured in QALYs based on health state utility values generated from a generic HRQoL instrument. Iptacopan is expected to be the first oral monotherapy for the treatment of PNH. Benefits in terms of convenience of oral administration vs current IV/SC infusions may not be fully captured in QALYs. Patients may perceive oral administration as less burdensome and disruptive to their lives, as they would not need to schedule regular IV infusions as with eculizumab or ravulizumab. While pegcetacoplan can be self-administered, some patients may find twice weekly SC infusions with a duration of 30 to 60 minutes each time-consuming and cumbersome, and the requirement to store pegcetacoplan in the fridge can, for example, impact patients' travel plans. Some patients may also perceive an oral treatment as less invasive compared with IV/SC infusion treatments. These potential benefits may not be captured in QALYs. An effective oral treatment may also have benefits on workplace productivity that are not captured due to the healthcare system perspective of the analysis. Time off work could be required for infusion of IV and SC treatments. Anaemia-related fatigue and the requirement for blood transfusions can also impact patients' productivity.	

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		The impact of reduced need for blood transfusions on NHS direct costs will be captured in the submission, however there is also a wider benefit for the NHS as it frees up HCP time and blood for other purposes.	
	NPNH service & RCP	*Where do you consider iptacopan will fit into the existing care pathway for paroxysmal nocturnal haemoglobinuria?* As either 1st line treatment or in patients who are anaemic on a C5 inhibitor. *Would iptacopan be a candidate for managed access?* Yes. *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?* Improvements in quality of life, ability to work and do normal activities. *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* Clinical trial data. *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:*	Thank you for your comments. No action is needed.

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		• *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.* The remit and scope does not need to be changed. *Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.* Clinical trial data as above.	
	PNH support	**Where do you consider iptacopan will fit into the existing care pathway for paroxysmal nocturnal haemoglobinuria?** As a treatment for those who meet the criteria for C5 treatment but have not commenced treatment with it as well as those being treated with a C5 inhibitor who still have clinically signification extra vascular haemolysis. **Would iptacopan be a candidate for managed access?** Yes **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?**	Thank you for your comments. During the appraisal it will be discussed if all benefits of iptacopan were captured in the cost-effectiveness analyses. Please include all relevant information in your submission.

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		A patient (and also potentially their carer) could start to work/study or return to work/study/caregiving duties following receipt of this treatment which addresses both intravascular and extravascular haemolysis. This could reduce and/or remove support previously required from the State when they had remaining unmet need from being treated with a C5 inhibitor and had clinically significant extravascular haemoloysis. In addition the convenience of taking an oral tablet removes any requirement to miss work/study through the need to stay home/attend hospital to receive infusions or administer sub-cutaneous injections. It is assumed that transfusions and hospital visits/in-patient stays as a result of uncontrolled symptoms and anaemia from clinically significant extravascular haemolysis is included in the QALY otherwise these costs could be quantified as savings if a patient using iptacopan no longer needed these. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** The PNH National Service (and PNH Support) could obtain data from patients currently on the trials for iptacopan (and their carers) about their quality of life (including burden of treatment) since receiving the medication, in particular any change in their ability to work/study/undertake caregiving duties. The PNH National Service could also quantify the cost of blood transfusions, in-patient stays, additional outpatient visits to address uncontrolled symptoms and anaemia resulting from clinically significant extravascular haemolysis of those treated with C5 inhibitors who experience this. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.	

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		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 licenced; • 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.	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

None.