NICE National Institute for Health and Care Excellence

NICE guidance

Iptacopan for treating paroxysmal nocturnal haemoglobinuria

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendation

1.1 Iptacopan is recommended, within its marketing authorisation, as an option for treating paroxysmal nocturnal haemoglobinuria (PNH) in adults with haemolytic anaemia. Iptacopan is only recommended if the company provides it according to the commercial arrangement.

Why the committee made this recommendation

Standard care for PNH with haemolytic anaemia includes eculizumab and ravulizumab, which are C5 inhibitors. Most people with PNH have ravulizumab. People who still have anaemia after having a C5 inhibitor usually have pegcetacoplan or ravulizumab.

Evidence from clinical trials shows that iptacopan increases the level of haemoglobin in the blood and reduces the need for blood transfusions.

For people who have not had a C5 inhibitor, an indirect comparison suggests that iptacopan is more effective than eculizumab and ravulizumab, but these results are uncertain.

For people who still have anaemia after having a C5 inhibitor, clinical trial evidence shows that iptacopan is more effective than eculizumab and ravulizumab. An indirect treatment comparison suggests that iptacopan is more effective than pegcetacoplan, but the results are uncertain.

The cost-effectiveness estimates for iptacopan are within the range that NICE considers an acceptable use of NHS resources. So, it is recommended.

2 Information about iptacopan

Marketing authorisation indication

2.1 Iptacopan (Fabhalta, Novartis) is indicated as 'monotherapy in the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for iptacopan.

Price

2.3 The list price for iptacopan is £26,500 per 56-pack of 200 mg capsules (excluding VAT; company submission).

2.4 The company has a commercial arrangement. This makes iptacopan available to the NHS with a discount. The size of the discount is commercial in confidence.

3 Committee discussion

The evaluation committee considered evidence submitted by Novartis, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

PNH is a rare condition

3.1 Paroxysmal nocturnal haemoglobinuria (PNH) is a rare blood condition caused by an acquired mutation of the PIG-A gene within bone marrow stem cells. In England, around 650 to 900 people have PNH. PNH results in the body's immune system attacking its red blood cells. The breakdown of red blood cells can happen within the blood vessels (intravascular haemolysis) or outside the blood vessels (extravascular haemolysis). This often results in anaemia, which needs blood transfusions, and symptoms of haemolysis and thrombosis. Because PNH is a chronic condition, the symptoms continue for a long time. Symptoms can also include abdominal pain, kidney problems, fatigue, shortness of breath, bleeding, difficulty swallowing, and organ damage.

Treatment pathway

3.2 The current standard care for newly diagnosed PNH is intravenous treatment with a C5 inhibitor, either eculizumab every 2 weeks, or ravulizumab every 8 weeks, in line with NICE's technology appraisal guidance on ravulizumab. The clinical experts explained that ravulizumab is the preferred treatment option, but eculizumab is used during pregnancy because its side effect profile is more established. People usually switch back to ravulizumab after pregnancy. The clinical experts added that around 10 to 20 people in England may currently have eculizumab because of preference, and that this number is likely to reduce over time. If there is residual anaemia after treatment, people with PNH can either stay on treatment with the same or an alternative C5 inhibitor, or switch to

pegcetacoplan in line with NICE's technology appraisal guidance on pegcetacoplan (TA778). Pegcetacoplan is a C3 inhibitor administered by subcutaneous infusion twice a week. The clinical experts noted that there is normally a good response when switching to pegcetacoplan, but some people with residual anaemia may not switch because it is a self-administered treatment. Iptacopan is a proximal complement inhibitor that can control both intra- and extravascular haemolysis, and is an oral treatment taken twice daily. The company positioned iptacopan as a first-line treatment option for PNH in adults with haemolytic anaemia and as a second-line treatment option for PNH in adults who have residual anaemia after treatment with a C5 inhibitor. The committee agreed with the clinical experts that ravulizumab is the preferred C5 inhibitor. So, it concluded that ravulizumab and pegcetacoplan are the most relevant comparators.

Treatment options and effects on quality of life

3.3 The clinical and patient experts explained that there is an unmet need for treatment options for PNH that have different modes of administration and that effectively manage the condition, including anaemia, symptoms, and need for blood transfusions. The patient experts added that living with a chronic condition such as PNH has a large impact on daily life. For example, being unable to attend events and travel, feeling isolated from friends and family, and considerations around family planning. Another patient expert highlighted that having an effective treatment can have a positive impact on family members who may be caregivers because they may be able to return to work. The patient experts highlighted the benefits of having an oral treatment option compared with the current standard care of intravenous infusions or subcutaneous infusions. These included a greater independence in managing the condition, being able to work or travel more easily, not having to handle sharp needles or sharps bins at home, and fewer hospital visits. The clinical experts added that having an oral treatment option benefits people with poor venous access, needle aversion or limited dexterity. The committee concluded that there is an unmet need for treatment options for PNH that effectively manage symptoms and improve quality of life.

Clinical effectiveness

Clinical trials

3.4 The pivotal clinical-effectiveness evidence for iptacopan came from the APPOINT-PNH and APPLY-PNH trials:

- APPOINT-PNH was an international, phase 3, multicentre, single-arm trial. It included adults with PNH who had not had a C5 inhibitor and who had a mean haemoglobin level below 10 g/dl. The trial included 24 weeks of core treatment with iptacopan, then 24 weeks of treatment extension, with a rollover extension programme after the end of the study at 48 weeks. The primary outcome was haematological response at 24 weeks, defined as an increase in haemoglobin from baseline of 2 g/dl or more, with no blood transfusions. The haematological response at 48 weeks was independent of blood transfusions. At 24 weeks, 92.2% of people had a haematological response, and 97.4% at 48 weeks.
- APPLY-PNH was an international, phase 3, multicentre, randomised controlled trial. It included adults with PNH who had stable treatment with a C5 inhibitor for 6 months or more before randomisation and who had a mean haemoglobin level below 10 g/dl. The trial compared iptacopan with C5 inhibitors for 24 weeks. At week 24, people continued iptacopan for a further 24-week treatment-extension period and people having C5 inhibitors switched to iptacopan. There was a rollover extension period at the end of 48 weeks. The primary outcome was haematological response at 24 weeks, with co-primary endpoints of an increase in haemoglobin from baseline of 2 g/dl or more, and a haemoglobin level of 12 g/dl or more, with no blood transfusions. The haematological response at 48 weeks was independent of blood transfusions. At 24 weeks, 82.3% of people having iptacopan had an increase in haemoglobin of 2 g/dl or more, compared with 2.0% of people having C5 inhibitors. Also at 24 weeks, 68.8% of people having iptacopan had a haemoglobin level of 12 g/dl or more, compared with 1.8% of people having C5 inhibitors. In the 48-week analysis, 86.4% of people having iptacopan had an increase in haemoglobin of 2 g/dl or more, compared with 72.4% of people who switched from C5 inhibitors to iptacopan at 24 weeks. At 48 weeks, 67.8% of people having iptacopan had a haemoglobin level of 12 g/dl or more,

compared with 58.6% of people who switched from C5 inhibitors to iptacopan at 24 weeks.

The committee concluded that iptacopan was clinically effective at achieving a haematological response for people who have not had C5 inhibitors. It was also clinically effective compared with C5 inhibitors for people with residual anaemia after treatment with a C5 inhibitor.

Indirect treatment comparison for population with no previous C5 inhibitor

3.5 Because APPOINT-PNH was a single-arm trial, the company did an indirect treatment comparison of iptacopan with C5 inhibitors for people who have not had a C5 inhibitor. The company did an unanchored matching-adjusted indirect comparison (MAIC). This used individual patient data from APPOINT-PNH and published data from Study 301, a randomised controlled trial comparing eculizumab and ravulizumab in people with PNH who had not had a C5 inhibitor. The outcomes of the indirect treatment comparison included transfusion avoidance, and changes from baseline in lactate dehydrogenase (LDH) level and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score. The EAG noted that an unanchored comparison adds uncertainty, and no data was reported on the relative effect of iptacopan on haematological response. The company also did an augmented inverse probability weighting analysis that used individual patient data from the real-world evidence study APPEX, which was weighted to match APPOINT-PNH. The outcomes of this indirect treatment comparison included haematological response, transfusion avoidance, and changes from baseline in LDH level and reticulocyte count. The EAG noted the uncertain treatment effects associated with an unanchored comparison, and a lack of control for potential selection bias and confounding variables. The committee concluded that, overall, the indirect treatment comparisons favoured iptacopan compared with C5 inhibitors, but noted that the results were uncertain.

Indirect treatment comparison for population with previous C5 inhibitor

3.6 The company did an indirect treatment comparison of iptacopan with pegcetacoplan for people who have had a C5 inhibitor. The company did an anchored indirect treatment comparison and unanchored MAIC using individual patient data from APPLY-PNH and published data from PEGASUS. PEGASUS was a randomised controlled trial comparing pegcetacoplan with eculizumab. PEGASUS had a 4-week run-in period in which people had combined treatment. Whereas, people in APPLY-PNH had C5 inhibitor monotherapy, which may impact the similarity between the control arms. The company preferred the unanchored approach. This was because there were unexplainable differences in the data between the control arms even after adjusting for differences in the trial populations and endpoint definitions. The outcomes of the indirect treatment comparison, which included the change in haemoglobin level from baseline and transfusion avoidance, favoured iptacopan. But the EAG noted that the relative treatment effects were not well established because of inconsistencies in the relative effect estimates on haemoglobin levels and transfusion avoidance outcomes. Also, there was a small effective sample size for iptacopan, and differences in the C5 inhibitor comparator arms, because of the run-in period in PEGASUS. The EAG preferred to base conclusions on the anchored comparison in line with NICE Decision Support Unit's technical support document 18. The committee concluded that, overall, the results from the indirect treatment comparisons suggest that iptacopan has more favourable outcomes compared with pegcetacoplan. But, it noted the uncertainty in the relative treatment effects.

Economic model

Company's modelling approach

3.7 The company presented a cohort semi-Markov model to estimate the cost effectiveness of iptacopan compared with C5 inhibitors and pegcetacoplan. Overall, the company's model was consistent with the model structure used in TA778. Iptacopan was modelled to improve health-related quality of life by increasing the proportion of people having no blood transfusions and no anaemia,

and reducing the proportion of people needing blood transfusions. It was also modelled to have no administration costs as an oral tablet, have lower resource use through improved health states, and reduce the incidence rate of breakthrough haemolysis events. The model cycle was 4 weeks with a half-cycle correction and included a lifetime time horizon. The committee concluded that the company's model structure was appropriate for decision making.

Assumptions informing the model

3.8 The economic model used clinical efficacy data from APPOINT-PNH and APPLY-PNH, real-world evidence from APPEX, and published results from PEGASUS. The results from the indirect treatment comparisons did not inform the model. The company explained that this was because the health-state definition in the model needs both haemoglobin and blood transfusion outcomes, so the transition probabilities were derived independently. The clinical experts agreed that no anaemia and no blood transfusions is the aim when managing PNH. The company added that the transfusion outcomes in the trials focus on the proportion of people who are transfusion-avoidant or transfusion-dependent, but do not consider transfusion frequency. But, the model considers that more than 1 transfusion is possible because data was incorporated on transfusions in 4-week time periods. Also, in the trials, haematological response was defined as an increase in haemoglobin of 2 g/dl or more, and a haemoglobin level of 12 g/dl or more, and no transfusions (for the 24-week analyses; see section 3.4). But the model defines health states based on a haemoglobin threshold below 10.5 g/dl, whereas the inclusion criteria in the trials specified a haemoglobin level below 10 g/dl. A threshold below 10.5 g/dl was used to enable a comparison with pegcetacoplan, because published transition probabilities for pegcetacoplan used this threshold. The EAG highlighted the uncertainty in the treatment-effectiveness evidence that informed the model without a direct comparison of trial endpoints and modelled health-state transitions. The EAG did a scenario analysis that incorporated a threshold of below 10 g/dl to define anaemia for iptacopan and C5 inhibitors. The clinical and patient experts added that, in clinical practice, the difference between 10 g/dl and 10.5 g/dl is small. The committee noted the small impact of the different thresholds and concluded that the 10.5 g/dl threshold is appropriate to include in the model.

Modelled treatment sequence

3.9 In the company's model, 1 line of subsequent treatment could be modelled. For the population with no previous C5 inhibitor, discontinuation to a subsequent treatment was:

- a continuous discontinuation of iptacopan to ravulizumab in each model cycle
- a one-time discontinuation of C5 inhibitors to pegcetacoplan at 24 weeks.

For the population with residual anaemia after a C5 inhibitor, discontinuation to a subsequent treatment was:

- a continuous discontinuation of iptacopan to ravulizumab in each model cycle
- a continuous discontinuation of pegcetacoplan to ravulizumab in each model cycle
- no discontinuation of C5 inhibitors.

The EAG explained that the company's approach to modelling the treatment sequence did not take into account the full range of possible sequences. For example, discontinuing iptacopan to ravulizumab, then to pegcetacoplan. The EAG also noted the inconsistency created by the choice of transition probabilities in the population with no previous C5 inhibitor. This was because transition probabilities for second-line pegcetacoplan were used from the population with previous C5 inhibitor treatment. Also, people who stop a first-line C5 inhibitor and have pegcetacoplan are considered as having a previous complement inhibitor at this point. The EAG considered that the cost effectiveness of iptacopan compared with C5 inhibitors may be masked because pegcetacoplan is not a relevant comparator for the population with no previous complement inhibitor. So, the EAG's base case did not model discontinuation of C5 inhibitors, and used transition probabilities from the population with no previous C5 inhibitor to enable consistency. The company explained that APPEX was used as the source for transition probabilities for C5 inhibitors. This was because it included people whose PNH responded well to treatment and people whose PNH did not respond well enough, whereas in APPLY-PNH there was an insufficient response to C5 inhibitors. So, the company considered that APPEX was more

generalisable to a population with no previous C5 inhibitor. The company added that transition probabilities from PEGASUS (the population with previous C5 inhibitor treatment) were used to model discontinuation from C5 inhibitors to pegcetacoplan in the population with no previous complement inhibitor treatment. This was because people who stop complement inhibitors would be those with residual anaemia, as reflected in PEGASUS. A clinical expert highlighted that switching from a proximal complement inhibitor (iptacopan) to a terminal complement inhibitor (C5 inhibitors) is possible but this is a new area in clinical practice. The clinical experts agreed that people who stop treatment would then be considered as having had a previous complement inhibitor. They noted that the reasons for stopping would be insufficient response or tolerability issues. They added that the aim is to use only 1 or 2 treatments rather than have multiple treatment switches. A patient expert agreed that switching treatments can be burdensome and finding a stable treatment is important. The committee concluded that the company's approach to modelling the treatment sequence is appropriate.

Transition probabilities

3.10 For the population with previous C5 inhibitor treatment, the transition probabilities for C5 inhibitors in the economic model were derived from the APPLY-PNH population. The EAG noted that C5 inhibitor transition probabilities derived from PEGASUS, which included data on pegcetacoplan, had large differences compared with data from APPLY-PNH. The EAG added that the transition probabilities from PEGASUS did not include the 4-week run-in period with combination treatment (see section 3.6), so this was unlikely to be the reason for the differences. So, the EAG had concerns that APPLY-PNH and PEGASUS may have distinctly different populations, and it included a scenario that used transition probabilities from PEGASUS rather than APPLY-PNH. One of the differences was that the Markov trace (showing the expected proportion of individuals in each health state over the modelled time horizon) showed very few people in the no-anaemia and no-blood transfusion health state in PEGASUS compared with APPLY-PNH. The clinical experts agreed that in clinical practice, around 30% to 40% of people having a C5 inhibitor would be in a health state with no anaemia and no blood transfusions at any given timepoint. But, this is

variable because the condition will improve in some people and get worse in others. The committee agreed that the results from using APPLY-PNH in the model were more clinically plausible than from using PEGASUS. It concluded that transition probabilities from APPLY-PNH should be used to inform the transition probabilities in the population with previous C5 inhibitor treatment.

Assessment time period

3.11 The assessment time period used in the economic model varied for iptacopan and its comparators. For iptacopan, data from the 48-week analyses of APPOINT-PNH and APPLY-PNH were used to inform the transition probabilities, annual discontinuation and breakthrough haemolysis rates. For C5 inhibitors and pegcetacoplan, 24-week data was used to inform the transition probabilities, as well as the utility values for iptacopan and its comparators. The EAG agreed that a longer follow up is best practice. But it highlighted the inconsistencies in data cuts across modelled parameters and its concerns that the 48-week analysis was not making a fair comparison of iptacopan with its comparators. So, the EAG presented its cost-effectiveness estimates for both the 24-week and 48-week analyses, with a larger effect in the population with previous complement inhibitor treatment. The company clarified that the 48-week data was used to inform the discontinuation rate for pegcetacoplan, which was the most important driver in the model in terms of cost effectiveness (see section 3.12). The committee agreed that in general, longer-term data is preferred and would be more representative. It concluded that the 48-week data should be used in the model.

Treatment discontinuation

3.12 For iptacopan and pegcetacoplan, the economic model included an annual discontinuation rate that was independent of health state. The EAG had concerns about the large difference in the annual discontinuation rates of iptacopan to ravulizumab (3.43% using 24-week data or 2.72% using 48-week data) and pegcetacoplan to ravulizumab (16.13%) in the population with previous C5 inhibitor treatment. It was concerned about whether these reflect NHS clinical practice. The discontinuation rates were informed by treatment-specific all-cause

discontinuation in APPLY-PNH for iptacopan, and in PEGASUS for pegcetacoplan. The EAG highlighted that this is an important driver in the cost-effectiveness results because second-line ravulizumab in the model is associated with more uncontrolled anaemia and more transfusion-dependence. The EAG added that PEGASUS included reasons for discontinuing that were not treatment-specific, for example, diffuse large B-cell lymphoma and acute leukaemia. So, the EAG preferred a lower discontinuation rate of pegcetacoplan to ravulizumab of 10.00%, with scenarios of 3.43% (or 2.72% using the 48-week data) and 5.00%. A clinical expert explained that the trial methodology may be associated with the high discontinuation rate for pegcetacoplan. This was because in PEGASUS a small number of people discontinued in the first 16 weeks and there was no option for managing events such as breakthrough haemolysis. Another reason for the high discontinuation rate for pegcetacoplan compared with iptacopan may be associated with its administration twice a week. This is because some people may need a greater frequency of treatment, and iptacopan is administered twice daily. One clinical expert estimated that around 10% to 15% of people would stop pegcetacoplan in clinical practice. They also noted that people may be more likely to switch to other treatments if they have access to alternative options, compared with restricted options in a clinical trial. They explained that real-world evidence from people having pegcetacoplan in the UK (Griffin et al. 2024) shows that pegcetacoplan does not adequately control PNH in 11 out of 48 people. But, some people in this population were not eligible for inclusion in PEGASUS. The company added that it did an additional analysis that only included discontinuations of pegcetacoplan that were related or possibly related to pegcetacoplan treatment in 'the eyes of the PEGASUS investigators', as done in PEGASUS. This resulted in an annual discontinuation rate of 12.40%. The committee considered that a 16.13% discontinuation rate for pegcetacoplan was too high in comparison with iptacopan. It agreed that a value would be closer to 10.00% to 12.00%. So, it concluded that the EAG's scenario of 10.00% is appropriate.

Health-related quality of life

Utility values

3.13 The economic model used treatment-dependent utility values that were based on 24-week data from the iptacopan trials (see section 3.11). These results suggested an improved health-related quality of life with iptacopan compared with C5 inhibitors. The company explained that this could be because of the oral administration, and better haematological response and less fatigue as shown in APPLY-PNH. The company added that although the model defined anaemia as a haemoglobin level below 10.5 g/dl, there may still be differences in quality of life at various haemoglobin levels below 10.5 g/dl. Also, in some analyses, people having iptacopan had a higher mean haemoglobin or better FACIT-Fatigue score than people having C5 inhibitors within the same health state. The EAG suggested that the only reason for a difference in utility values based on treatment would be the mode of administration. But, the size of the difference between the utility values of iptacopan and C5 inhibitors does not correspond. The EAG added that the data informing the treatment-dependent utility values is uncertain because the number of observations varies substantially between iptacopan and C5 inhibitors. For example, 568 observations informed the mean haemoglobin value in the no-anaemia and no-blood transfusion health state from APPLY-PNH for iptacopan, but 8 observations informed the mean haemoglobin value for C5 inhibitors. This suggested that people having iptacopan had less anaemia and fatigue. Also, the economic model used in TA778, which the company's model was based on, also used treatment-independent utility values. A patient expert added that the fortnightly (eculizumab) or 8-weekly (ravulizumab) intravenous infusion results in a feeling of treatment waning before the next dose is due. Iptacopan is taken twice daily, so there would be fewer peaks and troughs of treatment effect that impact quality of life. The committee concluded that, overall, it preferred to use treatment-independent utility values.

Costs

Concomitant acquisition costs for eculizumab

3.14 The economic model included a 4-week concomitant acquisition cost for eculizumab for 12% of people starting pegcetacoplan in the population with previous C5 inhibitor treatment. The summary of product characteristics for pegcetacoplan recommends an overlap transition period for people switching from C5 inhibitors. A clinical expert explained that in clinical practice, the summary of product characteristics would be followed and there would be some overlap of treatments to reach a steady state. This includes ravulizumab, which most people have. The EAG preferred to exclude the concomitant acquisition costs because the transition probabilities in the model are based on weeks 4 to 16 of PEGASUS, which excludes the concomitant period of eculizumab as well as any effects of this period. But, the EAG highlighted that the impact on the cost-effectiveness results is small because it affects 12% of people for a 4-week period. The committee noted the small impact on the cost-effectiveness results. It agreed that the concomitant acquisition costs for eculizumab should be excluded from the model.

Cost-effectiveness estimates

Acceptable ICER

3.15 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty, specifically the:

- relative effect of iptacopan compared with C5 inhibitors in the population with no previous C5 inhibitor treatment

- relative effect of iptacopan compared with pegcetacoplan in the population with previous C5 inhibitor treatment
- transition probabilities in the model, which did not directly reflect trial endpoints.

So, the committee concluded that an acceptable ICER would be around £20,000 per QALY gained.

Company and EAG cost-effectiveness estimates

3.16 The committee considered the ICERs for iptacopan compared with ravulizumab in the population with no previous C5 inhibitor treatment, and ravulizumab and pegcetacoplan in the population with previous C5 inhibitor treatment. Because of confidential commercial arrangements for iptacopan and comparators, the ICERs are confidential and cannot be reported here. The committee's preferred cost-effectiveness estimates included the following assumptions:

- ravulizumab as the most relevant comparator for people with no previous C5 inhibitor treatment (see section 3.2)
- ravulizumab and pegcetacoplan as the most relevant comparator for people with previous C5 inhibitor treatment (see section 3.2)
- using a 10.5 g/dl threshold to define anaemia (see section 3.8)
- modelling a treatment sequence that includes discontinuation to a subsequent treatment (see section 3.9)
- using transition probabilities from APPLY-PNH in the population with previous C5 inhibitor treatment (see section 3.10)
- including 48-week data from APPOINT-PNH and APPLY-PNH (see section 3.11)
- using a 10% annual discontinuation rate for pegcetacoplan in the population with previous C5 inhibitor treatment (see section 3.12)
- using treatment-independent utility values (see section 3.13)

- excluding concomitant acquisition costs for eculizumab (see section 3.14).

The committee assumptions resulted in ICERs for both populations that were within the range that NICE considers an acceptable use of NHS resources.

Other factors

Equality

3.17 The company highlighted that all current treatments for PNH are administered either through intravenous infusion or subcutaneous infusion, which could disadvantage people with a needle phobia. Also, subcutaneous infusions may be unsuitable for people who are obese because of absorption issues, and may be difficult to self-administer for people with dexterity, visual or cognitive disabilities. The committee considered the points in its decision making but noted that iptacopan is an oral treatment, so these are not equality issues. A clinical expert noted that iptacopan is not advised during pregnancy. The committee agreed that healthcare professionals should follow the guidance about pregnancy in the summary of product characteristics.

Conclusion

Recommendation

3.18 The committee considered that iptacopan is an effective treatment for PNH. Patient and clinical experts explained that further treatment options that target unresolved symptoms and have an oral administration are valuable. When considering the most appropriate comparators for PNH, in both the populations with and without previous C5 inhibitor treatment, the most plausible cost-effectiveness estimates were within the range that NICE considers an effective use of NHS resources. So, iptacopan is recommended.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.

4.2 Section f of The Innovative Medicines Fund Principles states that a discretionary source of early funding (from the overall Innovative Medicines Fund budget) is available for certain medicines recommended by NICE. In this instance, interim funding has been agreed for iptacopan. Interim funding will end 90 days after positive final guidance is published, at which point funding will switch to routine commissioning budgets.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has PNH and the healthcare professional responsible for their care thinks that iptacopan is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees and the highly specialised technologies evaluation committee are standing advisory committees of NICE. This topic was considered as a single technology evaluation by the highly specialised technologies evaluation committee.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Paul Arundel
Chair, highly specialised technologies evaluation committee

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Summaya Mohammad
Technical lead

Caron Jones
Technical adviser

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Jasdeep Hayre
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