Sent by e-mail only: XXXXXXXXXXXXX

FAO XXXXXXXXXXX

Chair
PNH Support

Monday 11 November 2024

Dear XXXXXXXXXX

**Re: Final Draft Guidance ("FDG") – Crovalimab for treating paroxysmal nocturnal haemoglobinuria in people 12 years and over [ID6140]**

Thank you for your letter of 31 October 2024 responding to my initial scrutiny views. This is my final decision on initial scrutiny.

***Ground 2:******the recommendation is unreasonable in the light of the evidence submitted to NICE***

**Appeal point 2.1:** "That the committee's conclusion that "*when switching from eculizumab or ravulizumab to crovalimab some people can experience adverse events called transient immune complex reactions. But these usually do not last long and so are not included in the economic model"* is unreasonable on the basis of the evidence put to the committee regarding "*three patients globally who had serious adverse reactions when switched from ravulizumab to crovalimab*"."

In my letter dated 16 October 2024, I explained why I was not minded to refer this point to the Appeal Panel. I described that it seemed to me possible for both the statement in the FDG which you sought to challenge to be true, and for three patients (among a larger patient population) to experience long lasting SAEs.

I now understand from your response to my initial scrutiny letter, that the three patients who experienced SAEs formed part of the 21 patients in the COMMODORE 1 study who switched from ravulizumab to crovalimab.

In order to refer an appeal point for consideration by an appeal panel, it must be at least arguable that the guidance is **obviously and unarguably wrong, illogical, or** **so absurd that a reasonable advisory committee could not have reached such conclusion.**

I have considered the evidence available to the committee in reaching its decision.

* The external assessment group's ("EAG") Report to the Committee refers to PNH Support UK's concern regarding *"three patients who had serious adverse reactions when switched from ravulizumab to crovalimab (*at page 271 of the Committee Papers)".
* The Company responded to PNH's clarification question (at page 191 of the Committee Papers), explaining that "*the majority of TH3 reactions experienced across the COMMODORE trials were self-limiting, with or without treatment, with no life-threatening or fatal events reported, and resolved without change in crovalimab treatment*".
* Notwithstanding the fact that it is redacted, the Committee had the benefit of the section headed "*Safety in patients switching from ravulizumab treatment"* at Page 89.
* The Committee was also presented with your own submission, where you explain the concern of the three patients that had experienced SAEs.

The Committee were presented with evidence relating to the SAEs experienced by three ravulizumab to crovalimab switch patients by multiple sources on different occasions throughout the appraisal process. The Committee papers also include the total number of patients in the non-randomised Arm C of the COMMODORE 1 who switched from ravulizumab to crovalimab.

I am satisfied that the Committee had enough evidence before to adequately consider whether it was appropriate to include the SAEs experienced by this patient population in the economic model, and that the conclusion it reached could not arguably be said to be so absurd that a reasonable advisory committee could not have reached it.

You explain in your letter your view that NICE ought to "*include the information about these risks in the "Recommendations" section of the FDG"*. You will be aware that NICE's role is to appraise the cost-effectiveness of new technologies within their Market Authorisation. It is for the Medicines & Healthcare Products Regulatory Agency ("MHRA") to authorise the technology for use. Where there are special warnings and precautions for use of a technology within its market authorisation, it is for MHRA to note this in its Summary of Product Characteristics.

Taking all of the above together, I consider that the statement in the FDG that adverse events "usually do not last long and so are not included in the economic model" is reasonable, and am therefore not persuaded that your appeal point is arguable.

I note that you indicate at the end of your letter that updates to clinical efficacy and safety results are planned to be shared at an upcoming meeting (American Society of Haematology Annual Meeting) later in 2024. It may assist you to note that NICE regularly monitors its published technology guidance to check for any new evidence or information that could affect the recommendations. This is explained in further detail at Section 8 of NICE's Health Technology Evaluations Manual.

Conclusion

For the reasons set out above, I will not refer your appeal point for consideration at an appeal hearing. This letter therefore brings NICE's internal appeal process to a close.

Thank you for your comments and engagement in the appeals process.

Yours sincerely

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Sharmila Nebhrajani OBE

Chairman and Non-executive director

National Institute for Health and Care Excellence