Sharmila Nebhrajani OBE

Non-Executive Director and Chairman

National Institute for Health and Care Excellence 2nd Floor

2 Redman Place London E20 1JQ

31 October 2024

**By email:** appeals@nice.org.uk

Dear Ms Nebhrajani,

Re: Final Draft Guidance (FDG) - Crovalimab for treating paroxysmal nocturnal haemoglobinuria in people 12 years and over [ID6140]

Please note that this reply has been submitted after the 5pm deadline as your letter dated 16 October 2024 did not state a time this response was due.

We refer to your letter dated 16 October 2024 in reply to our letter dated 9 October 2024.

In your letter you state that “On its face, the evidence of three patients (globally) experiencing long lasting SAEs does not seem capable of rendering unreasonable the conclusion that such events **“usually”** do not last long.” We consider that 3 patients out of a cohort of 21 who were switched from ravulizumab to crovalimab (i.e. 14%) is not “usual”.

How many long lasting or serious SAEs would need to be evidenced before this was considered to be “unusual” and/or for NICE to include the information about these risks in the “Recommendations” section of the final guidance (which is the section which is public facing which most clinicians/patients would read)? The numbers concerned i.e. 3/21 are even more relevant in light of the fact that PNH is an ultra- rare disease so the population is much smaller and the number of patients involved in clinical trials is also smaller.

We are aware that at least 2 of the 3 patients, to whom we referred in our submission, stopped taking the trial medication. Therefore, in order to confirm whether these 2 patients’ SAE data was included in the trial data and the data submitted to NICE we would need to check the safety data for the ravulizumab to crovalimab switch patients which has not yet been published (and which is redacted in the NICE papers). The company stated in the NICE papers (p192) that “Updates to clinical efficacy and safety results are planned to be shared at an upcoming meeting (American Society of Hematology Annual Meeting) later in 2024.

The company has also committed to support a publication around T3H reaction events, led by clinical experts in the field of PNH, to inform and further educate the clinical community on these adverse events, again to be published later in 2024. In summary, while the evidence shows that T3H reaction events occur relatively rarely and resolve in a timely manner in the majority of cases, the company remains committed to exploring these

reactions further and optimising their management in collaboration with the PNH clinical

community.”

If the ravulizumab to crovalimab switch patient safety data is made public at this ASH meeting, it will only then be possible for us to cross reference the SAEs of which we are aware with those contained in the clinical trial data to understand if they were included in the data submitted to NICE (which is currently redacted in the papers) and represented appropriately as to their severity and duration. This would then aid understanding as to whether they should have been included in the economic model or at least referenced by way of warning in the wording of the “Recommendations” section of NICE’s final guidance.

Yours sincerely

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XXXXXXXXX Chair

PNH Support