Dr Mark Chakravarty

Lead Non-executive Director NICE Appeals – Technology Appraisals and Highly Specialised Technologies

National Institute for Health and Care Excellence (NICE) 2nd Floor

2 Redman Place London E20 1JQ

9 October 2024

By email: [appeals@nice.org.uk](mailto:appeals@nice.org.uk)

Dear Dr Chakravarty,

**Re: Final Draft Guidance (FDG) - Crovalimab for treating paroxysmal nocturnal haemoglobinuria in people 12 years and over [ID6140]**

PNH Support would like to appeal against the Final Appraisal Determination for the above mentioned technology appraisal on the following grounds:

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

The following statement is included in the final draft guidance (FDG) for this appraisal: “when switching from eculizumab or ravulizumab to crovalimab, some people can experience adverse events called transient immune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”.

PNH Support made submissions to NICE relating to their understanding that three patients globally (of which they were aware) who had switched from ravulizumab to crovalimab in the trial had experienced serious adverse events which are not “transient.”

On 29 May 2024, PNH Support uploaded their patient organisation submission for this appraisal to the NICE platform stating as follows in response to the question “Are there any other issues that you would like the committee to consider?”:

“We are aware that there are three groups of patients who have been treated with crovalimab in trials: 1) treatment naïve patients; 2) those switched from eculizumab; and 3) those switched from ravulizumab. Over the last month we have become aware of three patients globally who had serious adverse reactions when switched from ravulizumab to crovalimab and at least two of whom we understand are still negatively affected by these injuries today. We are hopeful that these serious adverse events were correctly represented in terms of their severity and duration in the data submitted to the regulators, however as the data for the patients who were switched from ravulizumab to crovalimab has not yet been published, we have not been able to satisfy ourselves that this is the case. We are deeply concerned that patients who may switch from ravulizumab to crovalimab may be at risk of experiencing a serious adverse event which could be life changing and that the nature of this risk should be appropriately understood, represented and disseminated. We are

aware of a patient in England who switched from ravulizumab to crovalimab two years ago (April 2022) and then stopped the crovalimab trial after experiencing a serious adverse event. To this day, this patient experiences constant numbness and pain in both hands which are very sensitive to changes in temperature and which numbness makes it difficult to write and otherwise use their hands. The patients also has frequent pain and numbness down one side (arm and leg) and severe cramping in her legs and hands. The patient currently takes Pregabalin and Duloxetine to assist with these symptoms (which have side effects e.g. fatigue and is also under the care of neurologists and a physiotherapist, who are attempting to treat her as she understands she has nerve damage. Her quality of life, her mental health, as well as her family and social life have been significantly negatively impacted by this situation over the last two years. She is also now unable to work as a result of her injuries which has also had financial implications.”

On 17 August 2024, PNH Support sent a further communication by email to NICE to which confirmation of receipt was received by NICE on 19 August 2024, setting out as follows:

“The Board of PNH Support has become aware of a compensation claim against Roche relating to a participant of a crovalimab trial who suffered injury (to which we referred in our patient organisation submission for this appraisal) and we would like to bring this to the Committee’s attention so they are aware:

[https://www.leighday.co.uk/news/news/2024-news/investigations-into-crovalimab-drug-](http://www.leighday.co.uk/news/news/2024-news/investigations-into-crovalimab-drug-) trial-compensation-claim-after-participant-s-nerve-damage-diagnosis/

If you require us to submit this information in another format, please let us know how.” No further communication was received by us from NICE about this.

The results relating to serious adverse events (SAEs) concerning the patients switched from

ravulizumab to crovalimab have been redacted in the FDG Committee Papers at B.3.10.3. under the heading “*Safety in patients switching from ravulizumab treatment.”*

NICE informed PNH Support by email on 23 September 2024, that “The company has marked this information as confidential as it relates to study results which will remain confidential indefinitely.”

Due to our inability to review this aspect of the clinical trial results from patients switching from ravulizumab to crovalimab, we are unable to satisfy ourselves as to: a) what SAEs were reflected in the trial results submitted to NICE for this appraisal for this cohort; b) what the SAEs were; and c) whether the SAEs reported in the results submitted to NICE reflect those of which we are aware. As we are aware of three patients globally (including the UK patient now taking legal action against Roche as communicated to NICE on 17 August 2024) who suffered SAEs following switching from ravulizumab to crovalimab and which SAEs cannot be described as immune complex reactions which “did not last long”, we have reason to believe that the data for these SAEs was not included in the data submitted to NICE for patients switching from ravulizumab to crovalimab. Otherwise, it is inconceivable that a conclusion could be drawn in the FDG which states that “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”.

The safety of patients is paramount and we are gravely concerned that in light of the information of which we are aware, that patients treated with ravulizumab who switch to crovalimab in future may be at risk of experiencing SAEs which are much more serious and long lasting (and potentially life changing) than what has been described in the FDG. Therefore, we consider that the recommendation is unreasonable as it was based on information submitted to NICE which led to the 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”.

We do not have a preference as to whether this appeal proceeds to an oral or written appeal.

Yours sincerely

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Chair

PNh Support