Sent by e-mail only: XXXXXXXXXXXXXXXXXXXXXX

FAO XXXXXXXXXXXXXXXX

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Pfizer

11 September 2023

Dear XXXXXXXXXXXXXXXXX

**Re: Final Appraisal Document — Voxelotor for treating haemolytic anaemia caused by sickle cell disorder (SCD) (ID1403)**

Thank you for your letter of 1 September 2023 responding to my initial scrutiny views. This is my final decision on initial scrutiny.

I consider the ground 1(a) points and then the ground 2 point.

***Ground 1(a): In making the assessment that preceded the recommendation, NICE has failed to act fairly***

**Appeal point 1(a).3; In a situation where the Committee considered there still to be multiple sources of uncertainty by the time of the second Appraisal Committee meeting (‘ACM2’), it was unfair nevertheless to proceed directly to the publication of the FDG with no opportunity for a further ACM or to explore suggestions such as managed access.**

Having considered the additional arguments made in your letter of 1 September 2023, I agree that this is a valid appeal point.

**Appeal point 1(a).5; The Committee should have explained more clearly, during the appraisal process, how it intended to take (or not take) the health inequalities in relation to SCD into account in its decision-making and why.**

Having considered the additional arguments made in your letter of 1 September 2023, I remain of the view that the appraisal papers demonstrate that the Committee were aware of the issues raised regarding health inequalities and explained the adjustments that were taken into account, specifically by allowing for a higher ICER threshold. I therefore remain of the view that your argument at para 41 of your response letter as to the adequacy of the explanation in the ACD and/or FDG does not support a valid arguable appeal point.

However, taking into consideration your additional arguments I accept that there is an arguable point that the Committee did not provide stakeholders with "*a fair opportunity to influence the outcome of the Committee’s consideration of this issue … and that the failure to allow such an opportunity was procedurally unfair"* as, for example, you say "*Pfizer may, with adequate notice, have been able to bring evidence to bear on the issue, which in the event was not made available to NICE because of this procedural shortcoming*" and "*Pfizer and other stakeholders should at the very least have been told well in advance of ACM2 and with sufficient time to prepare responses, what the Committee’s approach was to the detailed submissions made on this point following ACD*". Therefore I will refer your point 2.1 limited to your argument that the Committee did not provide adequate opportunity for stakeholders to participate in the process regarding health inequalities.

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

**Appeal point 2.1; The Committee’s conclusion that there was too much uncertainty, such that it could not assess the cost-effectiveness of voxelotor, was irrational.**

Having considered the additional arguments made in your letter of 1 September 2023, particularly the question of whether "*the degree of uncertainty here permitted the Committee to take the unusual steps of not formulating an ICER, nor taking other steps to mitigate or deal with the types of uncertainties that frequently arise in other cases* ", I agree that this is a matter a valid appeal point that can be explored by the Appeal Panel. I anticipate that in preparing for the hearing you will wish to focus on why it was unreasonable on the evidence submitted to NICE for the Committee to conclude that the degree of uncertainty prevented calculation of a sufficiently reliable most plausible ICER (or ICER range).

Conclusion

Therefore the valid appeal points are:

• 1(a).1 It was procedurally unfair for the Committee not to give, at any point during the appraisal process, any indication of what it considered to be the plausible cost-effectiveness of voxelotor.

• 1(a).2 It was procedurally unfair for the Committee not to inform Pfizer, in sufficient time in advance of ACM2, of the estimates generated by the exploratory scenario analyses of the external assessment group (‘EAG’).

• 1(a).3 In a situation where the Committee considered there still to be multiple sources of uncertainty by the time of ACM2, it was unfair nevertheless to proceed directly to the publication of the FDG with no opportunity for a further ACM or to explore suggestions such as managed access.

• 1(a).4 Given the nature of the outstanding issues, the Committee should have ensured that a clinical and/or patient expert was invited to ACM2, to speak directly on issues where their input would have been valuable.

• 1(a).5 The Committee unfairly failed to provide adequate opportunity for stakeholders, during the appraisal process, to comment on how it intended to take (or not take) health inequalities in relation to SCD into account in its decision-making and why.

• 1(b).1 The adjustment made by the Committee to reflect the health inequalities associated with SCD, while welcome, was inadequate and should not have been so limited in scope.

• 2.1 The Committee’s conclusion that there was too much uncertainty, such that it could not assess the cost-effectiveness of voxelotor, was irrational.

• 2.2 The Committee misunderstood the relationship between the proposed positioning/NHS population and the trial population. It drew incorrect conclusions.

• 2.3 To the extent that the Committee considered that the rates of RTT modelled in the voxelotor and SoC arms of the model could be the same, and relied in the FDG on that being a possibility, it was unreasonable to do so.

NICE shares the valid appeal grounds of each appellant with the other appellants in the appeal papers to assist with preparation for the hearing.

NICE will be in contact with you regarding the administration of the appeal, which will be held orally.

Yours sincerely

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Dr Mark Chakravarty

Lead Non-Executive Director for Appeals & Vice Chairman

National Institute for Health and Care Excellence