

sent via email: and

Dr Jasmin Barman-Aksözen and Dr Rocco Falchetto
IPPN
The Hague
Holland

3 July 2018

Dear Drs Barman- Aksözen and Falchetto

Final Evaluation Determination: Afamelanotide for treating erythropoietic protoporphyria (EPP)

Thank you for your letter of 28 June. I have considered your further points.

Ground 1 (a)

1a.1 The Committee failed to act fairly by not acknowledging the evidence provided in patient testimonies and by expert physicians on the overwhelming clinical benefit [of treatment]

It still seems to me that it cannot be said that this material was not taken into account. Rather it did not persuade, which is a question of the committee's judgement and therefore must be considered under ground 2.

In passing I note that your letter says "*By accepting all three appeal points on the unreasonable recommendation in the light of the provided evidence, ...The Vice Chair agrees that the provided evidence is not adequately reflected in the FED...*" As my initial scrutiny letter made clear, by accepting an appeal point as valid I have agreed that it arguably falls within a permitted ground of appeal, and contains the necessary information. I have not agreed or disagreed that the recommendations are in fact unreasonable in light of the evidence submitted. The Appeal Panel will take that decision, and not me.

This point will be considered by the appeal panel, but under ground 2.

1a.2 The committee failed to act fairly by omitting to discuss the evidence and the arguments provided by the consultees in a scientific and transparent way.

Thank you for your comments, and your agreement that this point will not be put to the appeal panel.

1a.3 The committee failed to act fairly by choosing an approach for its assessment which knowingly underestimates the benefit of the treatment and therefore actively discriminates against EPP patients

As I do not accept your view in ground 1a.1 I am still of the view that this is not a valid appeal point. I am confident that the sentence objected to was the Committee acknowledging and taking account of an underestimate in the ERG approach, and not the Committee deliberately making a choice to adopt an approach that might understate benefit to prejudice patients.

1a.4 The committee failed to act fairly by denying a managed access agreement based on the same arguments put forward on why it had already rejected a recommendation [to use]

In view of your comments about PASS I agree that the appeal panel should consider the question of rejection of a managed access agreement. However the committee has considered and given reasons for its rejection and I cannot see this is arguably procedurally unfair. Your complaint is rather that the decision that data collection would not resolve uncertainty is wrong, and it is wrong because PASS is an example of data collection which (I assume you argue) will resolve those uncertainties. I am going to assume in your favour that that is arguable, although the appeal panel will no doubt want to investigate whether PASS is collecting data on the issues which troubled the committee. Therefore I will refer this appeal point to an appeal panel, but under ground 2.

1a.5 The committee failed to act fairly by not ensuring full representation of the patients voice at the committee meetings

I think the additional points you make here all fall into your ground 1a.6 (and I should repeat again that in accepting that point as "valid" I have only referred it on to the appeal panel, whose job it is to uphold or not uphold appeal points). I do not consider this to be a valid appeal point.

1a.7 The Committee failed to act fairly by not declaring a conflict of interest of a lead committee member

I note that you are concerned about potential rather than actual conflicts of interest. I set out in my previous letter the test I was applying to this allegation, and to be clear it would not be necessary to prove that [redacted] had in fact acted to favour his employer's interests. If an objective observer would feel that was a real possibility that would be sufficient. I am taking that to be what you mean by a potential conflict of interest, so we are in agreement on what the test is. However for the reasons given in my previous letter I do not think that any objective observer could conclude that there was a real possibility that [redacted] would act improperly in these circumstances, and therefore this is not a valid ground of appeal.

Ground 1b

1b.1 The Committee exceeded its powers by basing its decision on opinion rather than on evidence

In referring to patient and physician "opinion" I did not intend to suggest that such opinions were without merit. Be that as it may I am happy to refer to experience or evidence instead, and apologise if I have inadvertently caused offence.

Both your original and your latest letter focus on an alleged lack of reasoning in the FED as leading to a conclusion that the decision was not evidence based, but was a matter of arbitrary or ill formed opinion. Whether the committee's decisions are arbitrary or mere ill formed opinion will be investigated as part of your ground 2 points. If in the course of that investigation it emerges that in fact the committee's decision is not rooted in evidence at all, but is a matter of arbitrary opinion, then the decision could not be considered reasonable and the appeal would succeed. On those facts the appeal panel might also find a breach of appeal ground 1b but it would really add nothing to the conduct of the appeal. Put simply you will win under ground two if the committee's decision "does not add up" in light of the evidence. It is true that one way in which a decision might not add up is if the evidence has been ignored in favour of opinion, but you do not need to go so far. If the evidence has been taken into account in forming opinions, but the opinions are not sustainable, your appeal would still succeed. That

being so, and as I do not agree that the FED is so lacking in reasoning that this appeal point is arguable, I will not refer it to the appeal panel.

1b.2 The committee exceeded its powers by arbitrarily deciding on the validity of arguments put forward

As another appellant is arguing that the committee's decision does not take proper account of equality issues, I will now put this point to the appeal panel, but on that basis.

1b.3 The committee exceeded its powers by reassessing the regulatory conclusions of the [EMA]

My view remains that the committee has not reassessed the work of the EMA or exceeded its powers and that this is not a valid appeal point.

This is my final decision on initial scrutiny, and the valid appeal points are: 1a.1, 1a.4 (both under ground 2) 1a.6, 1b.2, 2.1, 2.2, and 2.3.

Yours sincerely

Dr Rosie Benneyworth
Vice Chair
National Institute for Health and Care Excellence