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sent by email:

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Dear Lachlan Hay

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

Thank you for your letter of 28 June. As a preliminary point, I should explain there will not be an opportunity to revisit points that I have rejected at initial scrutiny on 30 July. There will of course be an opportunity to make submissions on the points that I have referred on to the appeal panel. It is the appeal panel that will decide whether the appeal points before it are made out, and they are not bound by or even required to take account of anything I have said at the initial scrutiny stage. They will form their own view. Therefore you may or may not want to address them on the subject of initial scrutiny.

I note your comments concerning the scheduling of the hearing. You have had my view on that and I do not think I can usefully add to what I have said already in correspondence.

Ground one: NICE acted unfairly in that (i) one influential panel member of the HST committee was not impartial and (ii) NICE failed to take action in respect of his partiality upon notification by the company

I accept that you need not provide further information beyond that set out in your appeal letter, although it makes it more difficult to judge the relevance and risk of the information to which

was privy. I will also assume for present purposes that there is indeed a real risk that had he so chosen would have been able to recall some of that information, even in general terms, during the appraisal.

I cannot quite accept the analogy with a judge. Context is important, and a judge hearing a case alone may have to be more careful to avoid demonstrating apparent bias than one committee member amongst a number of others. Nor am I sure whether the analogy of information relating to strategy in legal proceedings is valid. I am told was privy to pricing and commercial strategy, but NICE is not a price regulator or a commissioner. The relevance of his information to a decision as to whether a product is cost effective at whatever price point you chose to offer is not immediately apparent.

As to the point about duty of confidentiality, my point was not that I was confident he would not have shared the information with others (although I am confident of that). It was rather that as a professional person active in the field he would understand the need and have the necessary mental discipline to ensure that he did not use information received for one purpose for another purpose. The fact that the information would not be fresh in his mind provides further reassurance here.

I remain of the view that this is not a valid appeal point.

Ground four: NICE acted unfairly by failing to give the Company an opportunity to discuss and negotiate its proposed MAA to NHS England before presenting it

In light of your further information I agree that this point should be considered by the appeal panel.

Ground 2

Ground two: NICE acted unreasonably and/or irrationally in light of the evidence in treating the ICER expressed as a cost per QALY as effectively determinative of its decision not to recommend the product

I agree that the test is whether the reasoning in the FED does not "add up" in this case. I had not intended to suggest otherwise. I also note that at initial scrutiny it is enough that this is arguable.

The allegation is that the ICER effectively drove the decision, and that this was unreasonable (did not add up). I can see that the cost effectiveness of the treatment, expressed as ICERS, plays a, if not the, major part in the FED reasoning. However I cannot see that this is to the exclusion of other considerations (see for example FED 4.21), and as I remarked in my earlier letter, given the ICERs generated it is perhaps unsurprising that they carry major weight. The committee refers to uncertainty in the ICERs and so seems to have taken this into account.

No doubt a range of different approaches to the use of ICERs are possible, but I cannot see that it is arguable that the approach actually taken in this case does not add up.

Ground three: NICE acted unreasonably and/or irrationally in departing from the conclusions of the EMA in its assessment of the Product without proper justification and without transparency

Thank you for your further elaboration, but I do not think that I did misunderstand your ground of appeal. The argument as now put is that as the EMA departed from its normal, strict guidelines, NICE should have done the same. I am still of the view that this is too far from the facts of the Servier case (EMA accepts an analysis as evidence of clinical effect, NICE rejects the very same analysis on the same issue) for that case to assist. First, I think the argument would fail on the facts (the HST process is indeed a departure from the usual HTA process). Second a general willingness to be flexible on the part of the EMA in evaluating clinical efficacy and safety for the purpose of a marketing authorisation cannot impose an obligation of flexibility[1] on NICE, tasked with evaluating cost efficacy with a view to recommending use within a national health system. The two bodies have different roles, and the national body occupies a space (allocation of national financial resources in healthcare) typically outside EU competence.

Therefore the appeal points that I will refer to the appeal panel are points four and five.

Yours sincerely

[1] or to explain a lack of flexibility

Dr Rosie Benneyworth

Vice Chair

National Institute for Health and Care Excellence