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3 February 2012

Dear Mr Nicolls

Final Appraisal Determination Cabazitaxel for the treatment of metastatic hormone-refractory prostate cancer

Thank you for lodging your appeal against the above Final Appraisal Determination.

Introduction

The Institute's appeal procedures provide for an initial scrutiny of points that an appellant wishes to raise, to confirm that they are at least arguably within the permitted grounds of appeal ("valid"). The permitted grounds of appeal are:

- Ground 1: The Institute has failed to act fairly
- Ground 2: The Institute has formulated guidance which cannot reasonably be justified in the light of the evidence submitted.
- Ground 3: The Institute has exceeded its powers.

This letter sets out my initial view of the points of appeal you have raised: principally whether they fall within any of the grounds of appeal, or whether further clarification is required of any point. Only if I am satisfied that your points contain the necessary information and arguably fall within any one of the grounds will your appeal be referred to the Appeal Panel.

You have the opportunity to comment on this letter in order to elaborate on or clarify any of the points raised before I make my final decision as to whether each appeal point should be referred on to the Appeal Panel.

I can confirm that there will be an oral hearing of the appeal.

Initial View

Ground 1

1.1: The failure to invite clinical or patient experts to the second Appraisal Committee meeting is contrary to NICE's processes and was unfair.

An appeal panel has recently considered the requirements of fairness as they relate to inviting clinical or patient experts to a second committee meeting. (Paragraphs 49-55 of the decision letter for Ranibizumab for the treatment of diabetic macular oedema: http://www.nice.org.uk/nicemedia/live/13125/57323/57323.pdf) I would expect a subsequent appeal panel to be guided by this approach. There do not seem to have been obvious gaps in the evidence base which might have required experts to attend the second meeting, and I do not see what the basis is for your assertion that the committee could not "interpret, refute or confirm" the comments on the ACD. May I ask you to review the FAD and the table of comments received and response to them (http://www.nice.org.uk/nicemedia/live/13237/57804/57804.pdf) with a view to giving examples of comments which were not understood?

I am afraid your example of the utility data did not help me, first because FAD 4.6 seems uncontroversial, and second because any appraisal committee will be well familiar with EQ-5D, which as you point out later in your letter is used in the NICE reference case. I could accept that a clinical expert might have a perspective on the use of EQ-5D in a particular condition, but given the committee's experience, and the presence of experts at the first meeting, I cannot at present see how it would be argued that it was unfair not to have experts present at the second meeting.

I look forward to your comments but I am not presently minded to refer this point to an appeal panel.

1.2: The Committee has failed to properly take account of various sources of evidence provided by the manufacturer through the consultation process; or has failed to explain why these have been disregarded.

Your appeal letter does not explain how this allegation relates to unfairness. An appeal panel has no role in judging whether an appraisal committee has "properly" taken account of evidence. It is the appraisal committee and not an appeal panel which has broad based technical expertise and close familiarity with the evidence base. An appeal panel may intervene only if evidence has not been looked at at all (which would be unfair) or if evidence has been so misunderstood that the guidance cannot be justified.

I do not think it is reasonable to infer that because something is not referred to in an FAD, or was not discussed in the open part of a committee meeting, it was disregarded. FAD's are guidance to the NHS rather than a completely comprehensive review. It is right to look at all of the documentation produced during an appraisal to see what was considered. Considering the ERG report, the table of comments on the consultation exercise, and the documentation generally, I have not found evidence that any information provided was not taken into account. I can see differences of opinion, but not why that could lead to a finding of unfairness. Nor does the guidance appear inadequately reasoned, as it seems that you knew what the issues in the appraisal were and were able to address them fully.

I look forward to your comments but I am not presently minded to refer this point to an appeal panel.

1.3: The Committee failed to submit questions to Sanofi in relation to the evidence and prohibited Sanofi from commenting on matters of factual accuracy during the Appraisal Committee meeting; this is contrary to NICE's processes.

I agree this is a valid appeal point, with the caveat that the appeal ground is unfairness, rather than acting contrary to NICE's processes.

Ground 2

2.1: The description of the EAP trial was misinterpreted, resulting in perverse conclusions in the FAD.

I doubt your complaint is arguable when the relevant sections of the FAD are read as a whole. The statement that the utility value for the stable disease state is based on a small selected sample is, I take it, factually accurate, and you omit the FAD's further reservation about wide CI intervals. As a general proposition the fact that patients who participate in trials may be healthier than the general patient population is widely accepted, for reasons that are not limited to an ability and willingness to travel to hospital. It is right that the participants in the EAP trial must be included in the patient population, but that is not necessarily informative of whether that population also includes those whose baseline utility is lower than the EAP participants. And finally the committee's reservation appears to have been to EQ-5D in an open label setting, and whilst open label self assessment may well be the best that can be achieved in this case, the observation that the data generated shows a bias towards a beneficial effect seems to be a mainstream expert opinion.

In each case, I am willing to accept that your opinions are also reasonably held. But the appeal panel would have to ask if the guidance is capable of justification. At present the issues you have raised do not seem to me to be able to support a conclusion that the guidance cannot be justified, and subject to your further clarification I would not be minded to allow this point to proceed.

2.2: Data from the EAP trial, and additional contextual data from the literature, were incorrectly interpreted resulting in perverse conclusions in the FAD.

I have a similar reservation to this point, which is clearly connected in as much as if the committee is entitled to be sceptical of your utility values, then the complaint falls away. These issues are discussed at FAD 4.14-16. The discussion appears on its face to be one reasonable approach to the issue (again, I accept that contrary approaches might also be reasonable). It seems to me that it was for you to advocate your preferred utility values, and that if the committee found your arguments unconvincing in its reasonable judgment, that would be a matter for it. The panel cannot balance the arguments and choose which it prefers, it can only act if the committee's position seems to be unjustifiable.

At present the issues you have raised do not seem to me to be able to support a conclusion that the guidance cannot be justified, and subject to your further clarification I would not be minded to allow this point to proceed.

2.3: The Committee failed to understand the nature of interim data, resulting in perverse conclusions in the FAD.

This point relates to your appeal point 1.3, and so I will refer it to an appeal panel.

Conclusion

As I agree some of your appeal points are valid I will pass them to an appeal panel for consideration. I would be grateful for your response to the points I consider potentially not valid by Friday 17 February 2012, so that I may take a final decision.

Yours sincerely

Dr Maggie Helliwell
Appeals Committee Chair
National Institute for Health and Clinical Excellence