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Dear Mr Nicolls

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

Thank you for your letter of 17 February. This is my final decision on initial scrutiny.

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.

In my initial letter I drew attention to the appeal panel decision in the guidance on *Ranibizumab for the treatment of diabetic macular oedema*. In that appeal the panel noted that the role of an expert might be to "clarify" evidence but that "*the committee are correct to argue that the role of the clinical specialists is essentially evidential. It is not to assist in the formation of judgments on evidence*"

Your appeal point appears to me to be about the judgments formed on evidence. You say that the Committee has reached views "*unsupported by evidence*", that it disputed the relevance of a review, that the conclusions do not "*appropriately reflect the situation of patients*" and that "*the issue raised by Sanofi in this appeal is....our view that the utility data from the EAP are reliable*." This is all a challenge to the judgment of the Committee and so a matter to be considered under ground 2 (as to which see my comments below).

You are also concerned that the committee did not base its comments on "*the informed advice of the experts*". The difficulty with that concern is that it is the committee which has to issue guidance, and the role of the expert is only to provide evidence, which was done at the first committee meeting. Again you seem be arguing that the expert should have played a role in the evaluation of evidence (specifically your ACD response) and the formulation of guidance, which is not correct.

I do not agree this is a valid ground 1 point, but see below for my comments on ground 2.

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.

I have the same concern on this appeal point. You comment that "*We are particularly concerned that the conclusions drawn in relation to the EAP utility data are flawed in the light of the evidence presented"* which is an almost exact paraphrase of the second appeal ground, rather than unfairness. I note your request that the committee representatives explain their reasoning. I do not accept on the points that you raise that that was required in the appraisal, at least in the level of detail you suggest, but I do note that this will be possible if these issues are ventilated at an appeal under ground 2 (as to which see below). That will meet any obligation there may be to explain these points.
I do not agree this is a valid ground 1 point

1.4 The basis for the committee's conclusion that utility values for second line metastatic prostate cancer patients must be lower than demonstrated by EAP is unexplained

I apologise that this point was omitted in error from my earlier letter. In respect of this point only, this letter contains my initial view, and I invite you to comment on it.

This point seems to me to repeat your complaint at point 1.2. The appeal panel have considered similar issues in recent appeals, and have agreed with the committee that it is for a manufacturer to make a case for cost effectiveness. Although guidance must be reasoned to be called guidance at all, where the manufacturer's case fails to convince, it does not follow that a Committee must present evidence for an alternative case. FAD 4.14 seems to give three reasons for the Committee to have doubted your preferred values (1) wide CI, (2) inherent implausibility that metastatic cancer is not impacting on quality of life and (3) that patients in trials may be healthier than the wider patient population. I express no view on the validity of those reasons, but I do not understand how it is you can say the Committee's position is unexplained?

I am not presently minded to refer this point to an appeal panel under ground one.

Ground 2

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

In light of your further comments, and my conclusions under ground one above, I now agree that this is a valid appeal point.

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

In light of your further comments, and my conclusions under ground one above, I now agree that this is a valid appeal point.

Conclusion

Save for point 1.4 this is the final decision on initial scrutiny. The valid appeal points are 1.3, 2.1, 2.2 and 2.3. I will consider any further comment you wish to make under 1.4 within

seven days of the date of this letter, alternatively, you may wish to deal with the points you are seeking to raise as an aspect of your appeal under point 2.1 and 2.2 .

Yours sincerely

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