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Dear Karen

Final Appraisal Determination: Everolimus for the second line treatment advanced or metastatic renal cell cancer

Thank you for your response to the initial scrutiny of your appeal lodged against this FAD. This letter represents the final decision on initial scrutiny.

1.1 NICE's failure to disclose to Novartis the modified economic model upon which its guidance is based lacks transparency and is unfair

Initial scrutiny allows for more than a pass/fail response. At the initial scrutiny stage, I not infrequently give guidance to appellants with a view to ensuring that the subsequent appeal hearing can be conducted fairly. (I also occasionally make it clear where I have made a particular assumption in agreeing that a given complaint passes the threshold for an appeal, as this may be relevant to the appeal panel. However that is not in issue here.)

Whether an appellant chooses to take my guidance is a matter for it, although it will have been put on notice as to a possible issue with the fairness of the appeal hearing. If it should turn out to be impossible for the appeal panel fully to consider the appellant's case as a result of not following my guidance, the panel would be entitled (but not required) to consider that the appellant should bear the consequences. In this particular case there was also the separate issue that your case as originally described was too general for me to be sure it was a valid point, albeit, as I have already indicated, I did expect that you would be able to satisfy me on that point. (And I can confirm your letter has now done so.)

It was not my intention to dictate precisely how you present your argument. I would have no power to do so, although I think it is fair to alert you to matters the appeal panel is likely to find relevant. I also acknowledge that it is possible that the appraisal committee may itself make comments on the day which you cannot anticipate and to which you are of course free to respond. Equally, I am sure you will accept that understanding whether there is or is not unfairness which was caused by how information about an economic model is presented (or not presented at all, as the case may be) is likely to be a complex question. It is potentially unfair to all parties, including the appellant, if an appeal panel has to approach it ex tempore. Hence my requests, to which you have now responded (and, in line with my approach above, I do not intend to express a view as to the quality of that response, other than that it has passed the threshold for consideration). I do not feel this has amounted to an addition to the published process, although now that you have raised the issue I would agree that my first letter could have been more clearly expressed as recommendations and guidance. I am grateful for you having made the point.

You in turn ask for notice for the appraisal committee's reason for non-disclosure. The appraisal committee will see copies of this correspondence, and I draw their attention to the general points made above. If there is a reason for non-disclosure that might require preparation in advance on your part, and if it is not provided in advance, then it may be that the committee will have to bear any consequences. I will leave it to their judgement whether in light of that comment they wish to provide anything in advance in writing, just as I left it to you to choose how to respond to my first request.

To conclude: I can confirm this is a valid appeal point.

1.2 The lack of transparency in relation to the extrapolation of data on OS associated with everolimus therapy using a Weibull curve is unfair

Thank you for your additional information. I can confirm this is a valid appeal point.

2.1 The reasons given by the Appraisal Committee for refusing to consider the investigation of uncertainty surrounding the hazard ratio for overall survival (OS) based on a more clinically plausible range, carried out by Novartis, are inconsistent with the evidence and therefore perverse

Thank you for your additional information. I can confirm this is a valid appeal point

2.2 The approach of the Appraisal Committee to the possibility of uncertainty in the assessment of cost effectiveness is inconsistent with that followed in other appraisals and is therefore perverse

I have carefully considered your additional points, but I am afraid I am unpersuaded by them. The heart of your contention is essentially that a given ICER in one appraisal must form something approaching a hard edged boundary for subsequent appraisals. As I said in my first letter, appraisals differ too much for a hard edged consistency to be a reasonable expectation. Even superficially similar outputs (two values for an ICER, for example) will have hidden within them substantial differences in reasoning and judgement. Each committee makes its own judgement on the appraisal in front of it, and they do not bind each other. Each appraisal principally stands or falls on its own reasonableness.

In essence, your argument seeks to replace a test of reasonable justification on an appraisal's own merits, which allows for judgements and for judgements that vary, with a rigid, almost mechanistic application of precedent. I do not think that can be a valid ground of appeal. It is too simplistic to argue that if an ICER of £X has been deemed likely to be acceptably cost effective for treatment A and condition B, then it is perverse not to recommend treatment C for condition D simply because it has a similar ICER. Of course, in some cases the similarities between appraisals may be so strong for a consistency argument to be tenable as an aspect of reasonableness (the recommendations for primary prevention and for secondary prevention of osteoporotic fracture, for example, where the subject matters are so similar that it is reasonable to expect a consistent approach). And a wholly capricious or arbitrary approach would be a valid appeal point. But I am satisfied that the points you are raising here are not capable of falling into those categories.

I therefore conclude this is not a valid appeal point.

2.4 The Appraisal Committee has disregarded the available evidence for OS in patients who receive BSC

I am willing to agree that the point should go forward as you have recast it, i.e. "*the overwhelming thrust of all of the available evidence and views of UK treating physicians...and clinical experts...support an OS figure of 2-6 months in patients who receive [BSC]"* [and that the failure to agree this is perverse].

2.5 The estimates of mean OS associated with BSC alone, relied upon by the Appraisal Committee are inconsistent and do not reflect the referenced calculations of the ERG

Thank you for your additional information. I can confirm this is a valid appeal point

2.6 The reliance of the Appraisal Committee on a mean probabilistic ICER to justify the decision not to recommend everolimus is perverse as the mean probabilistic ICER will vary from one run to another

Thank you for your additional explanation. Although I appreciate the deterministic ICER falls below £50,000 and the probabilistic ICER falls above that level, to give this great significance is treating £50,000 as a hard edged boundary which is not correct. (To make the point in a different way, the Committee's reasoning seems to me to have been based on a probability of cost effectiveness at a willingness to pay of £50,000 see FAD 4.17. That does not seem to me to be a simplistic application of an "above or below a threshold" test, and I cannot see that it could be argued to be unreasonable.) I also do not think it is arguable to pick out only this mean probabilistic ICER as the reason for the recommendation: it seems to me the FAD has to be read in the round, and in broader context, the probabilistic ICER cannot be argued to have been an unreasonable tool to have taken into account.

I can appreciate that it is possible to argue for and against either approach in this case, but it remains my view this can only be a matter for expert discussion, rather than a question of possible unreasonableness.

Conclusion

This is the final decision on initial scrutiny. The valid appeal points are 1.1, 1.2, 1.3, 2.1 2.3, 2.4 and 2.5.

Yours sincerely

Maggie Helliwell

Appeals Committee Chair

National Institute for Health and Clinical Excellence