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27 January 2010

Dear [redacted]

Final Appraisal Determination: Sorafenib for treatment of advanced hepatocellular carcinoma

Thank you for your letter of 13 January 2010, setting out Bayer's response to my initial scrutiny letter of 11 December 2009. I have considered the points you have raised and set out my final decision below.

Appeal Point 1.4 – in reaching its recommendation, the Institute has failed to place adequate weight on innovation and has therefore acted unfairly and not fulfilled its obligations to the Secretary of State in considering the long term benefits to the NHS of innovation.

I am not sure that we differ substantially on this point.

In my letter of 11 December 2009 I explained my view that an allegation of failure to give adequate weight does not amount to an allegation of unfairness contrary to ground one of the Institute's appeal grounds. However, I was content for the appeal panel to consider whether any pronouncement of the Institute has created any specific expectation as to the treatment of innovation which has not been satisfied here.

In your letter of 13 January 2010 you sought to clarify your point and to challenge the conclusions I had drawn from the case of *Douglas Fraser and Kevin Short v the National Institute for Health and Clinical Excellence*.

On that latter point I do not think any distinctions can usefully be drawn in this context between the role of the GDG in the development of a Guideline and the role of the Appraisal Committee in producing the FAD. In both instances, the decision-maker is an expert body that must examine the scientific evidence and develop recommendations through a highly structured process.

Similarly, I do not agree with your argument that simply because NICE's procedures require that innovation be taken into account, the Appeal Panel should look into the weight given to the factor in under the ground of fairness. This is really simply repeating the same, in my view incorrect, point.

However the nub of the permitted argument is at the very end of your comments on this point, where you assert that " *the approach of the Appraisal Committee is not consistent with the Institute's own explanation of how it is expects that* [innovation is to be taken into account]." In my initial letter I stated that the Appeal Panel will consider whether any pronouncement of the Institute has created any specific expectation as to the treatment of innovation which has not been satisfied in the FAD. I am equally happy that the appeal panel should consider your formulation, (which seems to me in substance to be the same as mine) that the appraisal committee has not acted consistently with the Institute's explanation of how this factor should be treated.

My final decision is therefore that the point should be considered, but on the basis above.

Appeal point 1.6 – The Institute acted unfairly by not accounting for the degree of clinical need of patients under consideration as directed by the Secretary of State

Originally your complaint was that inadequate weight was placed on the circumstances of patients with advanced HCC. My initial view was that this was not a valid ground one appeal point because it was clear from the FAD that the circumstances of this patient group had been taken into account.

In your letter of 13 January 2010 you raise a new point that *"In circumstances where patients with hepatocellular carcinoma clearly have an extremely high clinical need and where sorafenib is the only treatment with proven efficacy for the condition, a fair procedure requires that the Appraisal Committee explains how it has considered the clinical need of patients with the condition."* Strictly you should not be raising new points at this stage, but I will consider the argument.

It is clear that clinical need must be taken into account in an appraisal. Reasons should be given to the extent necessary to enable consultees to engage with the main issues in an appraisal. My view is that one must look at all of an appraisal's documents, as well as NICE's published processes, and not

just the FAD, to see the appraisal committee's approach to clinical need.

I note the description and critique of the health problem and current provision at sections 2.1 and 2.2 of the ERG report, and the expert statements the Committee received from health practitioners and a patient. I am satisfied that the Committee would have been aware of clinical need, and that you could examine and comment on the evidence before them on that issue. I am also satisfied that the discussion of clinical need and clinical effectiveness in the FAD sets out the committee's consideration of the ability of sorafenib to meet that need sufficiently clearly. The FAD also provides figures for possible ICERs and concludes that the reason treatment is not recommended is that " *the magnitude of additional weight that would need to be assigned to the original QALY benefits in this patient group for the cost effectiveness of the drug to fall within the current threshold range would be too great* "

I note that the Guide to Technology Appraisals explains that technologies with a most plausible ICER below £20,000 will normally be recommended. Above a most plausible ICER of £30,000 per QALY gained, the Committee will need to identify an increasingly stronger case for supporting the technology as an effective use of NHS resources. Treatments with a most plausible ICER of £30,000 are rarely recommended (subject to the supplementary end of life guidance).

In this appraisal, the FAD records that the base-case ICER presented by Bayer, taking into account the patient access scheme, was £51,900 (see para 4.8). This was already substantially above the £30,000 threshold outlined above. After identifying various adjustments it considers appropriate the Appraisal Committee notes a figure of £76,000 per QALY at para 4.13 and concludes that a recommendation for sorafenib would not be a cost-effective use of NHS resources. This does not appear to have been a borderline case. The conclusion is that the treatment is not sufficiently cost effective, and there is considerable further reasoning explaining how cost effective it was thought to be, and what the usual thresholds are. The stated conclusion is that the committee did not find anything sufficiently exceptional to justify a recommendation at the levels of cost effectiveness considered. I do not see that it can have been unfair not to have said so at any greater length.

My view is that the main issues leading to this conclusion are undoubtedly sufficiently clear for you to have been able to engage with them and that the appeal point cannot be valid.

Appeal point 1.7 – The Appraisal Committee's approach to the difference between independent and investigator assessments of time to disease progression in the SHARP trial is inappropriate and unfair.

Initially you argued that the Appraisal Committee had acted unfairly because:
(a) it failed to record an ICER that took account of the patient access scheme equivalent to the ICER of £76,000 quoted in paragraph 4.13 of the FAD
(b) it appears not to have recognised that the approach of the trial investigators more was likely to

reflect that of treating physicians in clinical practice than that of the independent assessors.

Your letter suggests that there may have been some misunderstanding of this appeal ground, so I will elaborate on my reasoning. Beginning with point (a), failing to record a fact in the FAD cannot be a valid ground one appeal point, unless somehow its omission means that the reader is unable to understand the approach taken on one of the principal issues (bearing in mind that for these purposes the reader is expected to read all of an appraisal's documents, and may not restrict him or herself to the FAD). It is clear that you have followed the approach that the Committee has taken. Therefore this is not a valid ground.

Insofar as point (b) is concerned, Bayer's argument is recorded at paragraph 3.14 of the FAD: *"In the patient access scheme, all patients stop treatment at the point of progression (determined by investigator assessment), as in the SHARP trial. The manufacturer stated that this was consistent with clinical practice."* As this point has clearly been considered by the Appraisal Committee, it is cannot form the basis of a valid ground one appeal. As explained previously, once a factor has been taken into account, it is for the decision-maker to decide how much weight to give it.

Furthermore, I note that simply because the FAD records a figure for the revised ICER where the independent assessment of time to progression is used does not mean that this was the approach preferred by the Committee. This FAD gives a range of ICERs depending on the various factors discussed in the FAD itself.

It therefore remains my view this is not a valid appeal point

Appeal point 1.8 – the Appraisal Committee has not explained its conclusion that the magnitude of additional weight that would need to be assigned to the original QALY benefits would be too great for the product to be cost effective.

I note and accept your correction of my wording as regards the guidance on sunitinib. I read the guidance as a finding that the ICER was less that £50,000 but I accept that it can be read as merely saying this was possible.

As regards the comparison with sunitinib only, I now agree that it is not appropriate to dispose of this point at initial scrutiny, and that this appeal point should be considered by an appeal panel.

For guidance in preparing for the appeal, read in isolation I would have felt that this guidance was sufficiently reasoned. The issues which have persuaded me to allow the point to go forward are whether the sunitinib guidance has any relevance at all to the degree of reasoning needed in this guidance, and, if it does, whether the reasoning in this guidance is inadequate as a result. I do not express any views on those issues, other than to suggest the appeal panel may wish to consider

them.

Therefore the valid grounds of appeal (subject in some cases to the comments I have made in this correspondence) are: 1.1/1.2, 1.3, 1.4, 1.8.

Yours sincerely

[redacted]

Appeals Committee chair
National Institute for Health and Clinical Excellence